

APPENDIX A

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APPENDIX B

All Journals Hand Searched
December 2005-February 2006

American Journal of Medicine
Clinical Therapeutics
Diabetic Medicine
Diabetes and Metabolism
Diabetes
Diabetes Care
Diabetes, Obesity & Metabolism
Diabetes Research and Clinical Practice
Diabetologia
Hormone and Metabolic Research
Journal of Clinical Endocrinology and Metabolism
Lancet
Metabolism: Clinical and Experimental
Practical Diabetes International

APPENDIX C

Detailed Electronic Database Search Strategies for Systematic Reviews

MEDLINE Strategy

Terms	Returns
For systematic reviews: ("diabetes mellitus, type 2"[mh] or "type 2 diabetes"[tiab] or (diabetes[tiab] and ("non-insulin dependent"[tiab] or type-2[tiab] or "type II"[tiab]))) AND ("hypoglycemic agents"[mh] or "thiazolidinediones"[mh] or "sulfonylurea compounds"[mh] or "chlorpropamide"[mh] or "glipizide"[mh] or "glyburide"[mh] or "biguanides"[mh] or "metformin"[mh] or "benzamides" or "carbamates"[mh] or "piperidines"[mh] or "cyclohexanes"[mh] or "phenylalanine"[mh] or "acarbose"[mh] or "alpha-glucosidases"[mh] or "thiazoles"[mh] or "drug combinations"[mh] or "antidiabetic drugs"[tiab] or hypoglycemic[tiab] or anti-hyperglycemic[tiab] or thiazolidinedione*[tiab] or pioglitazone[tiab] or rosiglitazone[tiab] or muraglitazar[tiab] or sulfonylurea[tiab] or chlorpropamide [tiab] or glipizide[tiab] or glyburide[tiab] or glimepiride[tiab] or biguanide*[tiab] or metformin[tiab] or "insulin secretagogues"[tiab] or meglitinide*[tiab] or repaglinide[tiab] or nateglinide[tiab] or "alpha-glucosidase inhibitors"[tiab] or "alpha-glucosidase inhibitor"[tiab] or acarbose[tiab] or avandamet[tiab] or glucovance[tiab] or metaglip[tiab]) AND (("review"[tiab] or review[pt] or "meta-analysis"[tiab] or meta-analysis[pt]) NOT (letter[pt] or comment[pt] or editorial[pt])) NOT (animal[mh] NOT human [mh])	2186
For primary studies: ("diabetes mellitus, type 2"[mh] or "type 2 diabetes"[tiab] or (diabetes[tiab] and ("non-insulin dependent"[tiab] or type-2[tiab] or "type II"[tiab]))) AND ("hypoglycemic agents"[mh] or "thiazolidinediones"[mh] or "sulfonylurea compounds"[mh] or "chlorpropamide"[mh] or "glipizide"[mh] or "glyburide"[mh] or "biguanides"[mh] or "metformin"[mh] or "benzamides" or "carbamates"[mh] or "piperidines"[mh] or "cyclohexanes"[mh] or "phenylalanine"[mh] or "acarbose"[mh] or "alpha-glucosidases"[mh] or "thiazoles"[mh] or "drug combinations"[mh] or "antidiabetic drugs"[tiab] or hypoglycemic[tiab] or anti-hyperglycemic[tiab] or thiazolidinedione*[tiab] or pioglitazone[tiab] or rosiglitazone[tiab] or muraglitazar[tiab] or sulfonylurea[tiab] or chlorpropamide [tiab] or glipizide[tiab] or glyburide[tiab] or glimepiride[tiab] or biguanide*[tiab] or metformin[tiab] or "insulin secretagogues"[tiab] or meglitinide*[tiab] or repaglinide[tiab] or nateglinide[tiab] or "alpha-glucosidase inhibitors"[tiab] or "alpha-glucosidase inhibitor"[tiab] or acarbose[tiab] or avandamet[tiab] or glucovance[tiab] or metaglip[tiab]) AND English[lang] NOT (animal[mh] NOT human [mh])	

EMBASE Strategy

Terms	Returns
For systematic reviews: 'non insulin dependent diabetes mellitus'/exp OR 'non insulin dependent diabetes mellitus' OR 'type 2' AND ('diabetes'/exp OR 'diabetes')) AND ('muraglitazar'/exp OR 'muraglitazar' OR 'thiazolidinedione'/exp OR 'thiazolidinedione' OR 'rosiglitazone'/exp OR 'rosiglitazone' OR 'pioglitazone'/exp OR 'pioglitazone' OR 'meglitinide'/exp OR 'meglitinide' OR 'nateglinide'/exp OR 'nateglinide' OR 'repaglinide'/exp OR 'repaglinide' OR 'biguanide'/exp OR 'biguanide' OR 'metformin'/exp OR 'metformin' OR 'alpha glucosidase inhibitor'/exp OR 'alpha glucosidase inhibitor' OR 'acarbose'/exp OR 'acarbose' OR 'chlorpropamide'/exp OR 'chlorpropamide' OR 'sulfonylurea derivative'/exp OR 'sulfonylurea derivative' OR 'sulfonylurea'/exp OR 'sulfonylurea' OR 'glimepiride'/exp OR 'glimepiride' OR 'glipizide'/exp OR 'glipizide' OR 'glyburide'/exp OR 'glyburide' OR 'avandamet'/exp OR 'avandamet' OR 'metformin plus rosiglitazone'/exp OR 'metformin plus rosiglitazone' OR 'glucovance'/exp OR 'glucovance' OR 'glibenclamide plus metformin'/exp OR 'glibenclamide plus metformin' or metaglip) AND (review:ti,ab,it OR 'meta analysis':ti,ab,it OR metaanalysis:ti,ab,it) NOT (letter:it OR comment:it OR editorial:it)	2616
For primary studies: ('non insulin dependent diabetes mellitus'/exp OR 'non insulin dependent diabetes mellitus' OR 'type 2' AND ('diabetes'/exp OR 'diabetes')) AND ('muraglitazar'/exp OR 'muraglitazar' OR 'thiazolidinedione'/exp OR 'thiazolidinedione' OR 'rosiglitazone'/exp OR 'rosiglitazone' OR 'pioglitazone'/exp OR 'pioglitazone' OR 'meglitinide'/exp OR 'meglitinide' OR 'nateglinide'/exp OR 'nateglinide' OR 'repaglinide'/exp OR 'repaglinide' OR 'biguanide'/exp OR 'biguanide' OR 'metformin'/exp OR 'metformin' OR 'alpha glucosidase inhibitor'/exp OR 'alpha glucosidase inhibitor' OR 'acarbose'/exp OR 'acarbose' OR 'chlorpropamide'/exp OR 'chlorpropamide' OR 'sulfonylurea derivative'/exp OR 'sulfonylurea derivative' OR 'sulfonylurea'/exp OR 'sulfonylurea' OR 'glimepiride'/exp OR 'glimepiride' OR 'glipizide'/exp OR 'glipizide' OR 'glyburide'/exp OR 'glyburide' OR 'avandamet'/exp OR 'avandamet' OR 'metformin plus rosiglitazone'/exp OR 'metformin plus rosiglitazone' OR 'glucovance'/exp OR 'glucovance' OR 'glibenclamide plus metformin'/exp OR 'glibenclamide plus metformin' or metaglip) AND [english]/lim	773

Cochrane Database of Systematic Reviews Strategy

For systematic reviews: (diabetes near type-2) and (muraglitazar or thiazolidinediones or rosiglitazone or pioglitazone or meglitinide or nateglinide or repaglinide or biguanide or metformin or (alpha and glucosidase and inhibitor) or acarbose or chlorpropamide or sulfonylurea or glimepiride or glipizide or glyburide or avandamet or glucovance or metaglip) Restricted to reviews	17
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Cochrane Central Register of Controlled Trials

For primary studies: diabetes near type-2) and (muraglitazar or thiazolidinediones or rosiglitazone or pioglitazone or meglitinide or nateglinide or repaglinide or biguanide or metformin or (alpha and glucosidase and inhibitor) or acarbose or chlorpropamide or sulfonylurea or glimepiride or glipizide or glyburide or avandamet or glucovance or metaglip)	877
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APPENDIX D

List of Excluded Articles

Systematic Reviews

Aronow W S. Oral sulfonylureas and CV mortality. *Geriatrics* 2004;59(9):45-6, 49. **Does not include a systematic review/meta-analysis**

Baba S. Pioglitazone: a review of Japanese clinical studies. *Curr Med Res Opin* 2001;17(3):166-89. **Does not include a systematic review/meta-analysis**

Bailey C J, Turner R C. Metformin. *N Engl J Med* 1996;334(9):574-9. **Does not include a systematic review/meta-analysis**

Bailey C J. Antidiabetic drugs. *Br. J. Cardiol.* 2000;7(6):350+352, 353+356-360. **Does not include a systematic review/meta-analysis**

Bailey C J. Metformin revisited: its actions and indications for use. *Diabet Med* 88;5(4):315-20. **Does not include a systematic review/meta-analysis**

Baynes C, Feher M D, Elkeles R S. The effect of treatment of non-insulin-dependent diabetes mellitus (NIDDM) on serum lipids and lipoproteins. *Q. J. MED.* 89;72(267):579-587. **Does not include a systematic review/meta-analysis**

Belcher G, Lambert C, Goh K L et al. Cardiovascular effects of treatment of type 2 diabetes with pioglitazone, metformin and gliclazide. *Int J Clin Pract* 2004;58(9):833-7. **Primary data only. Does not include a systematic review/meta-analysis**

Bell D S H. Current status of diabetes treatment. *South. Med. J.* 2002;95(1):24-29. **Does not include a systematic review/meta-analysis**

Bell D S H. Diabetes mellitus and coronary artery disease. *J. CARDIOVASC. RISK* 1997;4(2):83-90. **Does not evaluate medications specified in this review. Does not include a systematic review/meta-analysis**

Bell D S H. Secretagogues and Cardiac Risk. *Endocrinologist* 2004;14(1):33-37. **Does not include a systematic review/meta-analysis**

Bell D S. Practical considerations and guidelines for dosing sulfonylureas as monotherapy or combination therapy. *Clin Ther* 2004;26(11):1714-27. Other (no exclusion criteria). **Does not include a systematic review/meta-analysis**

Binder C, Bendtson I. Hypoglycaemia. *BAILLIERE'S CLIN. ENDOCRINOL. METAB.* 1992;6(1):23-39. **Does not evaluate medications specified in this review. Does not include a systematic review/meta-analysis**

Bloomgarden Z T. Glycemic treatment: Control of glycemia. *Diabetes Care* 2004;27(5):1227-34. **Does not include a systematic review/meta-analysis**

Bloomgarden Z T. New and traditional treatment of glycemia in NIDDM. *DIABETES CARE* 1996;19(3):295-299. **Does not include a systematic review/meta-analysis**

Bloomgarden Z T. Pharmacologic treatment of type 2 diabetes. *Diabetes Care* 2003;26(2):526-533. Meeting abstract. **Does not include a systematic review/meta-analysis**

Bloomgarden Z T. Thiazolidinediones. *Diabetes Care* 2005;28(2):488-93. **Does not include a systematic review/meta-analysis**

Braunstein S. New developments in type 2 diabetes mellitus: combination therapy with a thiazolidinedione. *Clin Ther* 2003;25(7):1895-917. **Does not include a systematic review/meta-analysis**

Bressler R, Johnson D G. Pharmacological regulation of blood glucose levels in non-insulin-dependent diabetes mellitus. *Arch Intern Med* 1997;157(8):836-48. **Does not include a systematic review/meta-analysis**

Brown D L, Brillon D. New directions in type 2 diabetes mellitus: an update of current oral antidiabetic therapy. *J Natl Med Assoc* 1999;91(7):389-95. **Does not include a systematic review/meta-analysis**

Burge M R, Sood V, Sobhy T A et al. Sulphonylurea-induced hypoglycaemia in type 2 diabetes mellitus: a review. *Diabetes Obes Metab* 1999;1(4):199-206. **Does not include a systematic review/meta-analysis**

Campbell I W. Long-term glycaemic control with pioglitazone in patients with type 2 diabetes. *Int J Clin Pract* 2004;58(2):192-200. **Does not include a systematic review/meta-analysis**

Carlsen S M, Folling I. Metformin reevaluated - Time for rehabilitation?: METFORMIN REVURDERT - TID FOR REHABILITERING?. *TIDSSKR. NOR. LAEGEFOREN.* 1994;114(9):1074-1076. **Not in English**

Cervený J D, Leder R D, Weart C W. Issues surrounding tight glycemic control in people with type 2 diabetes mellitus. *Ann. Pharmacother.* 1998;32(9):896-905. **Does not apply to a key question. Does not include a systematic review/meta-analysis**

Chang C T, Chen Y C, Fang J T et al. Metformin-associated lactic acidosis: case reports and literature

Appendix D: Excluded Articles

review. *J Nephrol* 2002;15(4):398-402. **Does not include a systematic review/meta-analysis**

Cheng-Lai A, Levine A. Rosiglitazone: an agent from the thiazolidinedione class for the treatment of type 2 diabetes.

Chilton R, Chiquette E. Thiazolidinediones and cardiovascular disease. *Curr. Atheroscler. Rep.* 2005;7(2):115-120. **Does not include a systematic review/meta-analysis**

Clark CM, Helmy A W. Clinical trials with glimepiride. *Drugs Today* 1998;34(5):401-408. **Does not include a systematic review/meta-analysis**

Coniff R, Krol A. Acarbose: a review of US clinical experience. *Clin Ther* 1997;19(1):16-26; discussion 2-3. **Does not include a systematic review/meta-analysis**

Conn J, Betteridge D J. Insulin resistance in cardiovascular disease. *Br. J. Cardiol.* 1998;5(6):329-336. **Does not apply to a key question. Does not include a systematic review/meta-analysis**

Cox S L. Rosiglitazone maleate/metformin hydrochloride: a new formulation therapy for type 2 diabetes. *Drugs Today (Barc)* 2004;40(7):633-43. **Does not include a systematic review/meta-analysis**

Dandona P, Aljada A. A rational approach to pathogenesis and treatment of type 2 diabetes mellitus, insulin resistance, inflammation, and atherosclerosis. *Am J Cardiol* 2002;90(5A):27G-33G. **Does not include a systematic review/meta-analysis**

Davidson J A, Scheen A J, Hewlett H C S. Tolerability profile of metformin/glibenclamide combination tablets (Glucovance(registered trademark)): A new treatment for the management of type 2 diabetes mellitus. *Drug Saf.* 2004;27(15):1205-1216. Other (may have primary data) . **Does not include a systematic review/meta-analysis**

Del Prato S, Aragona M, Coppelli A. Sulfonylureas and hypoglycaemia. *Diabetes Nutr Metab* 2002;15(6):444-50; discussion 450-1. **Does not include a systematic review/meta-analysis**

Del Prato S, Heine R J, Keilson L et al. Treatment of patients over 64 years of age with type 2 diabetes: experience from nateglinide pooled database retrospective analysis. *Diabetes Care* 2003;26(7):2075-80. Other (search strategy not described) . **Does not include a systematic review/meta-analysis**

Delorme S, Chiasson J L. Acarbose in the prevention of cardiovascular disease in subjects with impaired glucose tolerance and type 2 diabetes mellitus. *Curr Opin Pharmacol* 2005;5(2):184-9. **Does not include a systematic review/meta-analysis**

Heart Dis 2000;2(4):326-33. **Does not include a systematic review/meta-analysis**

Ebell M H. Insulin monotherapy vs. combination therapy. *Am Fam Physician* 2005;71(5):899. **Does not include a systematic review/meta-analysis**

Edelman S V. Importance of glucose control. *Med Clin North Am* 1998;82(4):665-87. **Does not include a systematic review/meta-analysis. Does not evaluate medications specified in this review**

Feldman J M. Glyburide: a second-generation sulfonylurea hypoglycemic agent. History, chemistry, metabolism, pharmacokinetics, clinical use and adverse effects. *Pharmacotherapy* 85;5(2):43-62. **Does not include a systematic review/meta-analysis**

Fisman E Z, Tenenbaum A, Motro M et al. Oral antidiabetic therapy in patients with heart disease. A cardiologic standpoint. *Herz* 2004;29(3):290-8. **Does not include a systematic review/meta-analysis**

Freemantle N. How well does the evidence on pioglitazone back up researchers' claims for a reduction in macrovascular events?. *BMJ* 2005;331(7520):836-8. **Does not include a systematic review/meta-analysis**

Fuchtenbusch M, Standl E, Schatz H. Clinical efficacy of new thiazolidinediones and glinides in the treatment of type 2 diabetes mellitus. *Exp Clin Endocrinol Diabetes* 2000;108(3):151-63. **Does not include a systematic review/meta-analysis**

Gale E. Glimepiride: Review of the first available 3rd generation sulphonylurea. *Pract. Diabetes Int.* 1999;16(1 SUPPL.):S1-S3. **Does not include a systematic review/meta-analysis**

Gan S C, Barr J, Arieff A I et al. Biguanide-associated lactic acidosis. Case report and review of the literature. *Arch Intern Med* 1992;152(11):2333-6. **Primary data only. Other (case report). Does not include a systematic review/meta-analysis**

Garber A, Marre M, Blonde L et al. Influence of initial hyperglycaemia, weight and age on the blood glucose lowering efficacy and incidence of hypoglycaemic symptoms with a single-tablet metformin-glibenclamide therapy (Glucovance) in type 2 diabetes. *Diabetes Obes Metab* 2003;5(3):171-9. **Does not include a systematic review/meta-analysis**

Gerich J E. Oral hypoglycemic agents. *NEW ENGL. J. MED.* 89;321(18):1231-1245. **Does not include a systematic review/meta-analysis**

Ghosh J, Weiss M B, Kay R H et al. Diabetes mellitus and coronary artery disease: Therapeutic considerations. *Heart Dis.* 2003;5(2):119-128. **Does not include a systematic review/meta-analysis**

Appendix D: Excluded Articles (continued)

Gillies P S, Dunn C J. Pioglitazone. *Drugs* 2000;60(2):333-43; discussion 344-5. **Does not include a systematic review/meta-analysis**

Goldenberg M M. Rosiglitazone for the treatment of type 2 diabetes mellitus. *P T* 2000;25(6):284-294. **Does not include a systematic review/meta-analysis**

Goldstein B J. Differentiating members of the thiazolidinedione class: a focus on efficacy. *Diabetes Metab Res Rev* 2002;18 Suppl 2S16-22. **Other (search strategy not described). Does not include a systematic review/meta-analysis**

Goldstein B J. Rosiglitazone. *Int. J. Clin. Pract.* 2000;54(5):333-337. **Does not include a systematic review/meta-analysis**

Goodarzi M O, Bryer-Ash M. Metformin revisited: re-evaluation of its properties and role in the pharmacopoeia of modern antidiabetic agents. *Diabetes Obes Metab* 2005;7(6):654-65. **Does not include a systematic review/meta-analysis**

Grant P J. The effects of metformin on cardiovascular risk factors. *Diabetes Metab Rev* 1995;11 Suppl 1S43-50. **Does not include a systematic review/meta-analysis**

Grossman L D. New solutions for type 2 diabetes mellitus: the role of pioglitazone. *Pharmacoeconomics* 2002;20 Suppl 11-9. **Other (economic review). Does not include a systematic review/meta-analysis**

Guthrie R. Treatment of non-insulin-dependent diabetes mellitus with metformin. *J Am Board Fam Pract* 1997;10(3):213-21. **Other (no inclusion/exclusion criteria). Does not include a systematic review/meta-analysis**

Hanefeld M, Belcher G. Safety profile of pioglitazone. *Int. J. Clin. Pract. Suppl.* 2001;-(121):27-31. **Does not include a systematic review/meta-analysis**

Hanefeld M, Cagatay M, Petrowitsch T et al. Acarbose reduces the risk for myocardial infarction in type 2 diabetic patients: meta-analysis of seven long-term studies. *Eur Heart J* 2004;25(1):10-6. **Does not include a systematic review/meta-analysis**

Hanefeld M, Temelkova-Kurktschiev T, Kohler C. Effect of oral antidiabetics and insulin on lipids and coronary heart disease in non-insulin-dependent diabetes mellitus. *Ann N Y Acad Sci* 1997;827246-68. **Does not include a systematic review/meta-analysis**

Hanefeld M. Outcome studies in type 2 diabetes. *Curr Med Res Opin* 2005;21 Suppl 1S41-8. **Other (no exclusion criteria). Does not include a systematic review/meta-analysis**

Hanefeld M. The role of acarbose in the treatment of non-insulin-dependent diabetes mellitus. *J Diabetes*

Complications 1998;12(4):228-37. **Does not include a systematic review/meta-analysis**

Hermann L S, Lindberg G, Lindblad U et al. Efficacy, effectiveness and safety of sulphonylurea-metformin combination therapy in patients with type 2 diabetes. *Diabetes Obes Metab* 2002;4(5):296-304. **Other (search strategy not described). Does not include a systematic review/meta-analysis**

Isley W L, Oki J C. Hepatotoxicity of thiazolidinediones. *Diab. Obesity Metabol.* 2001;3(6):389-392. **Does not include a systematic review/meta-analysis**

Jones T A, Sautter M, Van Gaal L F et al. Addition of rosiglitazone to metformin is most effective in obese, insulin-resistant patients with type 2 diabetes. *Diabetes Obes Metab* 2003;5(3):163-70. **Does not include a systematic review/meta-analysis**

Kanzer-Lewis G. Early combination therapy with a thiazolidinedione for the treatment of type 2 diabetes. *Diabetes Educ* 2003;29(6):954-8, 961. **Does not include a systematic review/meta-analysis**

Killilea T. Long-term consequences of type 2 diabetes mellitus: economic impact on society and managed care. *Am J Manag Care* 2002;8(16 Suppl):S441-9. **Other (economic review). Does not include a systematic review/meta-analysis**

Kilo C. Metformin: a safe and effective treatment in the management of NIDDM. *Mo Med* 1997;94(3):114-23. **Does not include a systematic review/meta-analysis**

Kirpichnikov D, McFarlane S I, Sowers J R. Metformin: an update. *Ann Intern Med* 2002;137(1):25-33. **Does not include a systematic review/meta-analysis**

Kirwin J, Van Amburgh J. Muraglitazar: A dual peroxisome proliferator-activated receptor agonist. *Formulary* 2005;40(9):285-293. **Does not include a systematic review/meta-analysis**

Klepser T B, Kelly M W. Metformin hydrochloride: an antihyperglycemic agent. *Am J Health Syst Pharm* 1997;54(8):893-903. **Does not include a systematic review/meta-analysis**

Klonoff D C, Barrett B J, Nolte M S et al. Hypoglycemia following inadvertent and factitious sulfonylurea overdoses. *DIABETES CARE* 1995;18(4):563-567. **Does not include a systematic review/meta-analysis**

Klonoff D C. Association of hyperinsulinemia with chlorpropamide toxicity. *Am J Med* 88;84(1):33-8. **Other (case report). Does not include a systematic review/meta-analysis**

Krentz A J, Ferner R E, Bailey C J. Comparative tolerability profiles of oral antidiabetic agents. *Drug Saf* 1994;11(4):223-41. **Does not include a systematic review/meta-analysis**

Appendix D: Excluded Articles (continued)

Lalau J D, Race J M. Metformin and lactic acidosis in diabetic humans. *Diabetes Obes Metab* 2000;2(3):131-7. **Does not include a systematic review/meta-analysis**

Laube H. Acarbose: An update of its therapeutic use in diabetes treatment. *Clin. Drug Invest.* 2002;22(3):141-156. **Does not include a systematic review/meta-analysis**

Lawrence J M, Reckless J P. Pioglitazone. *Int J Clin Pract* 2000;54(9):614-8. **Does not include a systematic review/meta-analysis**

Lebovitz H E. Differentiating members of the thiazolidinedione class: a focus on safety. *Diabetes Metab Res Rev* 2002;18 Suppl 2S23-9. **Does not include a systematic review/meta-analysis**

Leonhardt W, Hanefeld M, Fischer S et al. Efficacy of alpha-glucosidase inhibitors on lipids in NIDDM subjects with moderate hyperlipidaemia. *Eur J Clin Invest* 1994;24 Suppl 345-9. **Other (may have primary data). Does not include a systematic review/meta-analysis**

Lester J W, Fernandes A W. Pioglitazone in a subgroup of patients with type 2 diabetes meeting the criteria for metabolic syndrome. *Int J Clin Pract* 2005;59(2):134-42. **Does not apply to a key question**

Lester J W, Fernandes A W. Pioglitazone in a subgroup of patients with type 2 diabetes meeting the criteria for metabolic syndrome. *Int J Clin Pract* 2005;59(2):134-42. **Does not include a systematic review/meta-analysis**

Lynch J C. Drug therapy for type 2 diabetes. *J. Pharm. Pract.* 1999;12(2):84-97. **Does not include a systematic review/meta-analysis. Does not include a systematic review/meta-analysis**

Malinowski J M, Bolesta S. Rosiglitazone in the treatment of type 2 diabetes mellitus: a critical review. *Clin Ther* 2000;22(10):1151-68; discussion 1149-50. **Other (no inclusion/exclusion criteria). Does not include a systematic review/meta-analysis**

Massi-Benedetti M. Glimepiride in type 2 diabetes mellitus: a review of the worldwide therapeutic experience. *Clin Ther* 2003;25(3):799-816. **Other (no exclusion criteria). Does not include a systematic review/meta-analysis**

Meta-analysis shows: insulin sensitizer is safe for the liver: METAANALYSE ZEIGT: INSULINSENSITIZER SICHER FUR DIE LEBER.. *MMW Fortschr Med* 2002;144(40):47. **Not in English**

Metelko Z, Pavlic-Renar I, Novak B et al. Prandial regulation of glycemia. *Diabetol. Croat.* 2000;29(4):181-192. **Does not include a systematic review/meta-analysis**

Metformin. PHASE III DRUG PROFILES 1994;4(2):1-15. **Does not include a systematic review/meta-analysis**

Moses R. Repaglinide in combination therapy. *Diabetes Nutr Metab* 2002;15(6 Suppl):33-8. **Primary data only. Does not include a systematic review/meta-analysis**

Mudaliar S, Chang A R, Henry R R. Thiazolidinediones, peripheral edema, and type 2 diabetes: incidence, pathophysiology, and clinical implications. *Endocr Pract* 2003;9(5):406-16. **Does not include a systematic review/meta-analysis**

Mudaliar S, Henry R R. Combination therapy for type 2 diabetes. *Endocr Pract* 1999;5(4):208-19. **Other (no exclusion criteria). Does not include a systematic review/meta-analysis**

Nathan D M. Initial management of glycemia in type 2 diabetes mellitus. *New Engl. J. Med.* 2002;347(17):1342-1349. **Does not include a systematic review/meta-analysis**

Neeser K, Lubben G, Siebert U et al. Cost effectiveness of combination therapy with pioglitazone for type 2 diabetes mellitus from a german statutory healthcare perspective. *Pharmacoeconomics* 2004;22(5):321-41. **Other (economic review). Does not include a systematic review/meta-analysis**

Noble J, Baerlocher M O, Silverberg J. Management of type 2 diabetes mellitus. Role of thiazolidinediones. *Can Fam Physician* 2005;51:683-7. **Other (no inclusion/exclusion criteria). Does not include a systematic review/meta-analysis**

O'Connor P J, Spann S J, Woolf S H. Care of adults with type 2 diabetes mellitus. A review of the evidence. *J Fam Pract* 1998;47(5 Suppl):S13-22. **Does not evaluate medications specified in this review. Does not apply to a key question**

Oliver A, Pritchard C. Economic evaluations relating to diabetes: A descriptive review and their compliance with guidance. *Value Health* 2000;3(SUPPL. 1):S7-S14. **Other (economic review)**

Oliver A, Pritchard C. Economic evaluations relating to diabetes: A descriptive review and their compliance with guidance. *Value Health* 2000;3(SUPPL. 1):S7-S14. **Does not include a systematic review/meta-analysis**

Omari A, Yue D K, Twigg S M. Exercise, metformin and hypoglycaemia: A neglected entity. *Br. J. Diabetes Vasc. Dis.* 2005;5(2):106-108. **Does not include a systematic review/meta-analysis**

O'Meara N M, Shapiro E T, Van Cauter E et al. Effect of glyburide on beta cell responsiveness to glucose in non-insulin-dependent diabetes mellitus. *Am J Med* 1990;89(2A):11S-16S; discussion 51S-53S. **Primary data only. Other (may have primary data). Does not include a systematic review/meta-analysis**

Owens D R, McDougall A. Repaglinide: prandial glucose regulation in clinical practice. *Diabetes Obes Metab* 2000;2

Appendix D: Excluded Articles (continued)

Suppl 1S43-8. **Does not include a systematic review/meta-analysis**

Owens D R. Repaglinide--prandial glucose regulator: a new class of oral antidiabetic drugs. *Diabet Med* 1998;15 Suppl 4S28-36. **Does not include a systematic review/meta-analysis**

Page R L, 2nd Gozansky W S, Ruscini J M. Possible heart failure exacerbation associated with rosiglitazone: case report and literature review. *Pharmacotherapy* 2003;23(7):945-54. **Other (search strategy not described). Does not include a systematic review/meta-analysis**

Palmer A J, Valentine W J, Ray J A. Thiazolidinediones for diabetes mellitus: Considerations for reimbursements by third-party payers. *Dis. Manage. Health Outcomes* 2004;12(6):363-375. **Other (economic review)**

Parulkar A A, Pendergrass M L, Granda-Ayala R et al. Nonhypoglycemic effects of thiazolidinediones. *Ann Intern Med* 2001;134(1):61-71. **Does not include a systematic review/meta-analysis**

Patel C, Wyne K L, McGuire D K. Thiazolidinediones, peripheral oedema and congestive heart failure: What is the evidence?. *Diabetes Vasc. Dis. Res.* 2005;2(2):61-66. **Does not include a systematic review/meta-analysis**

Pendergrass M, Johnson J. Pathophysiology and management of type 2 diabetes. *Cardiovasc. Rev. Rep.* 2001;22(11):665-673. **Does not include a systematic review/meta-analysis**

Plosker G L, Figgitt D P. Repaglinide : a pharmaco-economic review of its use in type 2 diabetes mellitus. *Pharmacoeconomics* 2004;22(6):389-411. **Other (economic review)**

Pontiroli A E, Calderara A, Pozza G. Secondary failure of oral hypoglycaemic agents: frequency, possible causes, and management. *Diabetes Metab Rev* 1994;10(1):31-43. **Does not include a systematic review/meta-analysis**

Prendergast B D. Glyburide and glipizide, second-generation oral sulfonylurea hypoglycemic agents. *Clin Pharm* 84;3(5):473-85. **Does not include a systematic review/meta-analysis**

Raikou M, McGuire A. The economics of screening and treatment in type 2 diabetes mellitus. *Pharmacoeconomics* 2003;21(8):543-564. **Other (economic review)**

Rendell M S, Kirchain W R. Pharmacotherapy of type 2 diabetes mellitus. *Ann Pharmacother* 2000;34(7-8):878-95. **Other (no inclusion/exclusion criteria). Does not include a systematic review/meta-analysis**

Reusch J E, Gadsby R. Thiazolidinedione therapy: the benefits of aggressive and early use in type 2 diabetes. *Diabetes Technol Ther* 2003;5(4):685-93. **Does not include a systematic review/meta-analysis**

Roskamps R. Safety aspects of oral hypoglycaemic agents. *Diabetologia* 1996;39(12):1668-72. **Does not include a systematic review/meta-analysis**

Saenz Calvo A, Fernandez Esteban I, Mataix Sanjuan A et al. [Metformin for type-2 diabetes mellitus. Systematic review and meta-analysis]. *Aten Primaria* 2005;36(4):183-91. **Not in English**

Salpeter S R, Greyber E, Pasternak G A et al. Review: Metformin does not increase risk of lactic acidosis or increase lactate levels in type 2 diabetes. *Evid.-Based Med.* 2004;9(4):111. **Other (duplicate)**

Schafers R F. Do effects on blood pressure contribute to improved clinical outcomes with metformin?. *Diabetes Metab* 2003;29(4 Pt 2):6S62-70. **Does not include a systematic review/meta-analysis**

Schatz H. Glitazone outcome studies on progression of type 2 diabetes and cardiovascular endpoints: STUDIEN ZUR WIRKUNG VON GLITAZONEN AUF DIE PROGRESSION DES TYP-2-DIABETES UND AUF KARDIOVASKULARE ENDPUNKTE. *Dtsch. Med. Wochenschr.* 2005;130(31-32):1825-1830. **Not in English**

Schatz H. Preclinical and clinical studies on safety and tolerability of repaglinide. *Exp Clin Endocrinol Diabetes* 1999;107 Suppl 4S144-8. **Does not include a systematic review/meta-analysis**

Scheen A J. Clinical efficacy of acarbose in diabetes mellitus: a critical review of controlled trials. *Diabetes Metab* 1998;24(4):311-20. **Other (search strategy not described). Does not include a systematic review/meta-analysis**

Scheen A J. Hepatotoxicity with thiazolidinediones: is it a class effect?. *Drug Saf* 2001;24(12):873-88. **Does not include a systematic review/meta-analysis**

Scheen A J. Thiazolidinediones and liver toxicity. *Diabetes Metab* 2001;27(3):305-13. **Does not include a systematic review/meta-analysis**

Scherthaner G. Clinical importance of metformin in the treatment of type-2 diabetes mellitus: Effect on insulin resistance, diabetes control, and cardiovascular risk factors: DIE BEDEUTUNG VON METFORMIN IN DER THERAPIE DES TYP-2-DIABETES: EFFEKT AUF INSULINRESISTENZ, DIABETESEINSTELLUNG UND KARDIOVASKULARE RISIKOFAKTOREN. WIEN. KLIN. WOCHENSCHR. 1994;106(24):793-802. **Not in English**

Schneider H L, Hornbach K D, Kniaz J L et al. Chlorpropamide hepatotoxicity: report of a case and review of the literature. *Am J Gastroenterol* 84;79(9):721-4. **Other (search strategy not described). Does not include a systematic review/meta-analysis**

Appendix D: Excluded Articles (continued)

Schneider J. An overview of the safety and tolerance of glimepiride. *Horm Metab Res* 1996;28(9):413-8. **Does not include a systematic review/meta-analysis**

Setter S M, Iltz J L, Thams J et al. Metformin hydrochloride in the treatment of type 2 diabetes mellitus: a clinical review with a focus on dual therapy. *Clin Ther* 2003;25(12):2991-3026. **Other (no inclusion/exclusion criteria). Does not include a systematic review/meta-analysis**

Seufert J, Lubben G, Dietrich K et al. A comparison of the effects of thiazolidinediones and metformin on metabolic control in patients with type 2 diabetes mellitus. *Clin Ther* 2004;26(6):805-18. **Other (no exclusion criteria). Does not include a systematic review/meta-analysis**

Shaughnessy A F, Slawson D C. What happened to the valid POEMs? A survey of review articles on the treatment of type 2 diabetes. *BMJ* 2003;327(7409):266. **Does not apply to a key question**

Sirtori C R, Pasik C. Re-evaluation of a biguanide, metformin: mechanism of action and tolerability. *Pharmacol Res* 1994;30(3):187-228. **Other (search strategy not described). Does not include a systematic review/meta-analysis**

Smith S I. PPAR-gamma receptor agonists--a review of their role in diabetic management in Trinidad and Tobago. *Mol Cell Biochem* 2004;263(1-2):189-210. **Does not include a systematic review/meta-analysis**

Sood V, Collieran K, Burge M R. Thiazolidinediones: a comparative review of approved uses. *Diabetes Technol Ther* 2000;2(3):429-40. **Does not include a systematic review/meta-analysis**

Stamm P L, Kelley K W, Donaldson A R. Minimizing cardiovascular morbidity and mortality in patients with type 2 diabetes mellitus: A literature review. *Adv. Pharm.* 2005;3(1):23-50. **Other (no inclusion/exclusion criteria). Does not include a systematic review/meta-analysis**

Stolar M W, Chilton R J. Type 2 diabetes, cardiovascular risk, and the link to insulin resistance. *Clin Ther* 2003;25 Suppl BB4-31. **Other (no inclusion/exclusion criteria). Does not include a systematic review/meta-analysis**

Tan M H. Thiazolidinediones: Effect of the pioglitazone on hyperglycemia, dyslipidemia and cardiovascular risk: TIAZOLIDINADIONAS: EFECTO DE LA PIOGLITAZONA SOBRE LA HIPERGLUCEMIA, LA DISLIPIDEMIA Y EL RIESGO CARDIOVASCULAR. *Rev. Clin. Esp.* 2003;203(1):33-40. **Not in English**

Tessier D. Stepwise Approach to the treatment of diabetes in the older adult. *Geriatr. Aging* 2005;8(2):11-15. **Other (no inclusion/exclusion criteria). Does not include a systematic review/meta-analysis**

The pharmacological treatment of hyperglycemia in NIDDM. American Diabetes Association. *Diabetes Care*

1995;18(11):1510-8. **Does not include a systematic review/meta-analysis**

Tolman K G, Chandramouli J. Hepatotoxicity of the thiazolidinediones. *Clin. Liver Dis.* 2003;7(2):369-379. **Does not include a systematic review/meta-analysis**

Van Basten J P, Van Hoek B, Zeijen R et al. Glyburide-induced cholestatic hepatitis and liver failure. Case-report and review of the literature. *NETH. J. MED.* 1992;40(6):305-307. **Does not include a systematic review/meta-analysis**

Verges B. Diabetic dyslipidaemia: insights for optimizing patient management. *Curr Med Res Opin* 2005;21 Suppl 1S29-40. **Other (no exclusion criteria). Does not include a systematic review/meta-analysis**

Vijan S, Stevens D L, Herman W H et al. Screening, prevention, counseling, and treatment for the complications of type II diabetes mellitus: Putting evidence into practice. *J. GEN. INTERN. MED.* 1997;12(9):567-580. **Does not apply to a key question. Does not include a systematic review/meta-analysis**

Wagstaff A J, Goa K L. Rosiglitazone: a review of its use in the management of type 2 diabetes mellitus. *Drugs* 2002;62(12):1805-37. **Other (search strategy not described). Does not include a systematic review/meta-analysis**

Wallace T M, Matthews D R. Assessment of the effects of insulin secretagogues in humans. *Diabetes Obes Metab* 2000;2(5):271-83. **Does not evaluate medications specified in this review. Does not apply to a key question. Does not include a systematic review/meta-analysis**

Wang C-H, Weisel R D, Liu P P et al. Glitazones and heart failure: Critical appraisal for the clinician. *Circulation* 2003;107(10):1350-1354. **Does not include a systematic review/meta-analysis**

Wang F, Aleksunes L M, Reagan L A et al. Management of rosiglitazone-induced edema: two case reports and a review of the literature. *Diabetes Technol Ther* 2002;4(4):505-14. **Does not include a systematic review/meta-analysis**

Wang F. Focus on repaglinide: An oral hypoglycemic agent with a more rapid onset and shorter duration of action than the sulfonylureas. *Formulary* 1998;33(5):409-423. **Does not include a systematic review/meta-analysis**

Ward A, O'Brien J, Salas M. Cost-effectiveness of oral hypoglycaemic agents for the treatment of type 2 diabetes mellitus. *Expert Opin. Pharmacother.* 2005;6(4):601-608. **Other (economic review). Does not include a systematic review/meta-analysis**

Werner A L, Travaglini M T. A review of rosiglitazone in type 2 diabetes mellitus. *Pharmacotherapy* 2001;21(9):1082-99. **Does not include a systematic review/meta-analysis**

Appendix D: Excluded Articles (continued)

Wiles P G, Pyke D A. The chlorpropamide alcohol flush. Clin Sci (Lond) 84;67(4):375-81. **Does not include a systematic review/meta-analysis**

Williams G. Management of non-insulin-dependent diabetes mellitus. Lancet 1994;343(8889):95-100. **Does not include a systematic review/meta-analysis**

Wolffenbutter B H, Sels J P, Huijberts M S. Rosiglitazone. Expert Opin Pharmacother 2001;2(3):467-78. **Does not include a systematic review/meta-analysis**

Yates S W. Comparative effects of available thiazolidinediones: A review of the literature. P T 2004;29(9):584-588+590. **Does not include a systematic review/meta-analysis**

Yki-Jarvinen H. Thiazolidinediones. N Engl J Med 2004;351(11):1106-18. **Does not include a systematic review/meta-analysis**

Zhao H-L, Thomas G N, Leung W et al. An update on the management of nephropathy in type 2 diabetes. J. Chin. Med. Assoc. 2003;66(11):627-636. Other (no inclusion/exclusion criteria) . **Does not apply to a key question. Does not include a systematic review/meta-analysis**

Zinman B. PPAR gamma agonists in type 2 diabetes: how far have we come in "preventing the inevitable"? A review of the metabolic effects of rosiglitazone. Diabetes Obes Metab 2001;3 Suppl 1S34-43. **Does not include a systematic review/meta-analysis**

Primary Data

Abbasi F, Kamath V, Rizvi A A et al. Results of a placebo-controlled study of the metabolic effects of the addition of metformin to sulfonylurea-treated patients. Evidence for a central role of adipose tissue. Diabetes Care 97;20(12):1863-9. **N<40.**

Actos(registered trademark) may reduce heart attack and stroke in patients with type 2 diabetes. Exp. Rev. Cardiovasc. Ther. 2005;3(6):981-982 **Not an original article**

Agardh E, Agardh C D, Koul S et al. A four-year follow-up study on the incidence of diabetic retinopathy in older onset diabetes mellitus. Diabet Med 94;11(3):273-8. **Does not evaluate medications in this study. .Does not apply to the key questions.**

Aguilar C, Reza A, Garcia J E et al. Biguanide related lactic acidosis: incidence and risk factors. Arch Med Res 92;23(1):19-24. **Does not evaluate medications in this study.**

Allen B T, Feinglos M N, Lebovitz H E. Treatment of poorly regulated non-insulin-dependent diabetes mellitus with combination insulin-sulfonylurea. Arch Intern Med 85;145(10):1900-3. **N<40. Oral medication is compared or added to insulin.**

Bastyr E J, Stuart C A, Brodows R G. Targeting postprandial blood glucose concentrations reduced haemoglobin A1c concentrations in type 2 diabetes mellitus. Evid.-Based Med. 2001;6(3):80. **Oral medication is compared or added to insulin.**

Belcher G, Lambert C, Goh K L et al. Cardiovascular effects of treatment of type 2 diabetes with pioglitazone, metformin and gliclazide. Int J Clin Pract 2004;58(9):833-7. **Evaluates combinations of greater than 2 oral medications in one arm.**

Ben-Ami H, Nagachandran P, Mendelson A et al. Glibenclamide-induced hypoglycemic coma in 51 older patients with type 2 diabetes mellitus. J Am Geriatr Soc 99;47(5):631-3 **Not an original article. Other (no denominator).**

Berger M, Muhlhauser I, Sawicki P T. Possible risk of sulphonylureas in the treatment of non-insulin- dependent diabetes mellitus and coronary artery disease [5]. Diabetologia 98;41(6):744 **Not an original article**

Berger W. Incidence of severe sideeffects during therapy with sulfonylureas and biguanides. Horm Metab Res Suppl 85;15111-5 **Not an original article**

Blickle J F, Brogard J M. (alpha)-Glucosidase inhibitors - A new approach to the treatment of diabetes. EUR. J. INTERN. MED. 91;2(1):37-42 **Not an original article**

Blonde L, Joyal S, Henry D et al. Durable efficacy of metformin/glibenclamide combination tablets (Glucovance) during 52 weeks of open-label treatment in type 2 diabetic patients with hyperglycaemia despite previous sulphonylurea monotherapy. Int J Clin Pract 2004;58(9):820-6 **Not an original article**

Brady P A, Al-Suwaidi J, Kopecky S L et al. Sulfonylureas and mortality in diabetic patients after myocardial infarction. Circulation 98;97(7):709-10. **Oral medication is compared or added to insulin.**

Brown J B, Pedula K, Barzilay J et al. Lactic acidosis rates in type 2 diabetes. Diabetes Care 98;21(10):1659-63. **Does not evaluate medications in this study.**

Brown R R. Cost-effectiveness and clinical outcomes of metformin or insulin add-on therapy in adults with type 2 diabetes. Am J Health Syst Pharm 98;55(24 Suppl 4):S24-7. **Oral medication is compared or added to insulin.**

Burge M R, Schmitz-Fiorentino K, Sood V et al. Effect of immediate-release glipizide on hypoglycemic vulnerability in fasted, elderly patients with type 2 diabetes. JAMA 99;281(12):1084-5. **N<40.**

Buse J B, Rubin C J, Frederich R et al. Muraglitazar, a dual (alpha/gamma) PPAR activator: A randomized, double-blind, placebo-controlled, 24-week monotherapy trial in adult patients with type 2 diabetes. Clin Ther 2005;27(8):1181-95. **Does not evaluate medications in this study.**

Buse J, Hart K, Minasi L. The PROTECT Study: final results of a large multicenter postmarketing study in patients with type 2 diabetes. Precose Resolution of Optimal Titration to Enhance Current Therapies. Clin Ther 98;20(2):257-69. **Evaluates acarbose or miglitol added to any other oral medication in one arm. Study is a pharmacokinetic or dosing study.**

Appendix D: Excluded Articles (continued)

- Campbell I W, Chalmers J, Herlihy O M. Sulphonylurea-induced hypoglycaemia in elderly people with diabetes. PRACT. DIABETES 94;11(3):102-103 **Not an original article**
- Cardiovascular risk reduction with pioglitazone. Cardiovasc J S Afr 2002;13(4):218 **Not an original article**
- Chan N N, Feher M D. Metformin and perioperative risk [9]. Br. J. Anaesth. 99;83(3):540-541 **Not an original article**
- Choe H M, Cornish L, Townsend K et al. Monitoring safety and effectiveness in patients receiving metformin. Am J Health Syst Pharm 2004;61(15):1550-1. **Does not apply to the key questions.**
- Clarke B F, Campbell I W. Long-term comparative trial of glibenclamide and chlorpropamide in diet-failed, maturity-onset diabetics. Lancet 75;1(7901):246-8. **Evaluates only first generation sulfonylurea.**
- Clarke P M, Gray A M, Briggs A et al. Cost-utility analyses of intensive blood glucose and tight blood pressure control in type 2 diabetes (UKPDS 72). Diabetologia 2005;48(5):868-77. **Does not apply to the key questions.**
- Corsonello A, Pedone C, Corica F et al. Antihypertensive drug therapy and hypoglycemia in elderly diabetic patients treated with insulin and/or sulfonylureas. Gruppo Italiano di Farmacovigilanza nell'Anziano (GIFA). Eur J Epidemiol 99;15(10):893-901. **Does not apply to the key questions. Oral medication is compared or added to insulin.**
- Crandall J, Barzilai N. Treatment of diabetes mellitus in older people: oral therapy options. J Am Geriatr Soc 2003;51(2):272-4 **Not an original article**
- Dailey G E, 3rd Noor M A, Park J S et al. Glycemic control with glyburide/metformin tablets in combination with rosiglitazone in patients with type 2 diabetes: a randomized, double-blind trial. Am J Med 2004;116(4):223-9. **Evaluates combinations of greater than 2 oral medications in one arm.**
- Dasgupta K, Grover S A, Lowensteyn I et al. Sulfonylurea use associated with reduction in blood glucose levels during exercise stress testing. J. Cardiopulm. Rehabil. 2005;25(4):222-225. **Does not apply to the key questions.**
- Davidson J, Howlett H. New prolonged-release metformin improves gastrointestinal tolerability. Br. J. Diabetes Vasc. Dis. 2004;4(4):273-277 **Not an original article**
- Davis T M, Cull C A, Holman R R. Relationship between ethnicity and glycemic control, lipid profiles, and blood pressure during the first 9 years of type 2 diabetes: U.K. Prospective Diabetes Study (UKPDS 55). Diabetes Care 2001;24(7):1167-74. **Does not apply to the key questions.**
- Davis T M, Jackson D, Davis W A et al. The relationship between metformin therapy and the fasting plasma lactate in type 2 diabetes: The Fremantle Diabetes Study. Br J Clin Pharmacol 2001;52(2):137-44. **Does not apply to the key questions.**
- Deerochanawong C, Serirat S, Kornthong P. Efficacy of acarbose as monotherapy in NIDDM patients. J Med Assoc Thai 96;79(2):69-75. **N<40.**
- DeFronzo R A, Reasner C A. Treatment of type 2 diabetes mellitus: A rational approach based on its pathophysiology. Am. Fam. Phys. 2001;63(9):1687-1694 **Not an original article**
- Drouin P, Standl E. Gliclazide modified release: results of a 2-year study in patients with type 2 diabetes. Diabetes Obes Metab 2004;6(6):414-21. **Oral medication is compared or added to insulin. Other (not a head to head comparison).**
- Erratum: Long-term glycaemic control with pioglitazone in patients with type 2 diabetes (International Journal of Clinical Practice (2004) vol. 58 (192-200)). Int. J. Clin. Pract. 2004;58(10):993 **Not an original article. Other (follow-up on error).**
- Escobar-Jimenez F, Barajas C, De Leiva A et al. Efficacy and tolerability of miglitol in the treatment of patients with non-insulin-dependent diabetes mellitus. CURR. THER. RES. CLIN. EXP. 95;56(3):258-268. **Does not evaluate medications in this study. Evaluates acarbose or miglitol added to any other oral medication in one arm.**
- Fanghanel G, Sanchez-Reyes L, Trujillo C et al. Metformin's effects on glucose and lipid metabolism in patients with secondary failure to sulfonylureas. Diabetes Care 96;19(11):1185-9. **Oral medication is compared or added to insulin.**
- Faure E, Pallardo L F, Mesa J et al. HbA(1c) and glycemic profile, basal- and post-treatment with Miglitol, in an area with a Mediterranean diet. Diabetes Care 2002;25(10):1896-8. **Does not apply to the key questions.**
- Feinglos M N, Bethel M A. Therapy of type 2 diabetes, cardiovascular death, and the UGDP. Am Heart J 99;138(5 Pt 1):S346-52 **Not an original article**
- Feinglos M N, Lebovitz H E. Long-term safety and efficacy of glipizide. Am J Med 83;75(5B):60-6. **N<40.**
- Filioussi K, Bonovas S, Katsaros T. Should we screen diabetic patients using biguanides for megaloblastic anaemia?. Aust Fam Physician 2003;32(5):383-4. **Does not apply to the key questions.**
- Freed M I, Ratner R, Marcovina S M et al. Effects of rosiglitazone alone and in combination with atorvastatin on the metabolic abnormalities in type 2 diabetes mellitus. Am J Cardiol 2002;90(9):947-52. **Other (no variability in rosiglitazone between arms).**
- Gerber P, Lubben G, Heusler S et al. Effects of pioglitazone on metabolic control and blood pressure: a randomised study in patients with type 2 diabetes mellitus. Curr Med Res Opin 2003;19(6):532-9. **Study is a pharmacokinetic or dosing study.**
- Gerich J, Raskin P, Jean-Louis L et al. PRESERVE-beta: two-year efficacy and safety of initial combination therapy with nateglinide or glyburide plus metformin. Diabetes Care 2005;28(9):2093-9. **Evaluates nateglinide or repaglinide added to any other oral medication in one arm.**
- Gill G V, Huddle K R. Hypoglycaemic admissions among diabetic patients in Soweto, South Africa. DIABETIC MED. 93;10(2):181-183. **Does not evaluate medications in this study. Other (no denominator).**
- Giugliano D, Quatraro A, Consoli G et al. Metformin for obese, insulin-treated diabetic patients: improvement in glycaemic control and reduction of metabolic risk factors. Eur J Clin Pharmacol 93;44(2):107-12. **Oral medication is compared or added to insulin.**
- Glazer N B, Wishner W. Thiazolidinedione side effects comparison elicits clarification. Formulary 2000;35(11):914 **Not an original article**

Appendix D: Excluded Articles (continued)

- Glimepiride--well tolerated in daily practice. *Cardiovasc J S Afr* 2002;13(4):214-5 **Not an original article**
- Goddijn P P, Bilo H J, Feskens E J et al. Longitudinal study on glycaemic control and quality of life in patients with Type 2 diabetes mellitus referred for intensified control. *Diabet Med* 99;16(1):23-30. **Does not evaluate medications in this study.**
- Golay A, Guillet-Dauphine N, Fendel A et al. The insulin-sparing effect of metformin in insulin-treated diabetic patients. *DIABETES METAB. REV.* 95;11(SUPPL. 1):S63-S67. **Evaluates acarbose or miglitol added to any other oral medication in one arm. Oral medication is compared or added to insulin.**
- González-Ortiz M, Martínez-Abundis E, Grupo para et al. Efficacy and safety of glimepiride plus metformin in a single presentation, as combined therapy, in patients with type 2 diabetes mellitus and secondary failure to glibenclamide, as monotherapy. *Revista de investigacion clinica; organo del Hospital de Enfermedades de la Nutricion* 2004;56(3):327-33. **Not written in English**
- Groop L, Widen E, Franssila-Kallunki A et al. Sulfonylureas and/or insulin in Type 2 diabetes. **Not an original article**
- Groop P H, Groop L, Totterman K J et al. Metabolic effects of glibenclamide and glipizide in patients with type 2 diabetes. *ACTA ENDOCRINOL. SUPPL.* 82;100(Suppl. 247):25. **N<40.**
- Grossman E. Rosiglitazone reduces blood pressure and urinary albumin excretion in type 2 diabetes: G Bakris et al. *J Hum Hypertens* 2003;17(1):5-6 **Not an original article**
- Grunberger G. Continuous versus intermittent sulphonylurea therapy in non-insulin-dependent diabetes mellitus. *Drug Saf* 93;9(4):249-53. **N<40.**
- Hae M C, Cornish L, Townsend K et al. Monitoring safety and effectiveness in patients receiving metformin [1]. *Am. J. Health-Syst. Pharm.* 2004;61(15):1550-1551. **Does not apply to the key questions.**
- Harrower A D. Efficacy of gliclazide in comparison with other sulphonylureas in the treatment of NIDDM. *Diabetes Res Clin Pract* 91;14 Suppl 2S65-7. **Does not apply to the key questions.**
- Hayakawa T, Noda A, Kondo T et al. Effects of acarbose, an alpha-glucosidase inhibitor (Bay G 5421), on orally loaded glucose, maltose and sucrose and on blood glucose control in non-insulin-dependent diabetics. *Nagoya J Med Sci* 85;47(1-2):35-41. **N<40.**
- Hayakawa T, Yoneshima M, Abe T et al. Pneumatosis cystoides intestinalis after treatment with an (alpha)- glucosidase inhibitor [6]. *Diabetes Care* 99;22(2):366-367 **Not an original article**
- Herman W H, Dirani R G, Horblyuk R et al. Reduction in use of healthcare services with combination sulfonylurea and rosiglitazone: findings from the Rosiglitazone Early vs SULfonylurea Titration (RESULT) study. *Am J Manag Care* 2005;11(4):273-8. **Does not apply to the key questions.**
- Honisett S Y, Stojanovska L, Sudhir K et al. Rosiglitazone lowers blood pressure and increases arterial compliance in postmenopausal women with type 2 diabetes. *Diabetes Care* 2003;26(11):3194-5. **N<40.**
- Hristov V, Sheinkova G, Simeonov S et al. Clinical assessment of glimepiride (Amaril(registered trademark)) in the treatment of type 2 diabetes mellitus patients (results of a multicenter study). *Endocrinologia (Bulgaria)* 2002;7(1):30-35. **Not written in English**
- Hussein Z, Wentworth J M, Nankervis A J et al. Effectiveness and side effects of thiazolidinediones for type 2 diabetes: real-life experience from a tertiary hospital. *Med J Aust* 2004;181(10):536-9. **Evaluates combinations of greater than 2 oral medications in one arm.**
- Ikedo T, Murakami I, Tokumori Y. Comparison of the clinical effects of acarbose and voglibose on glycemic control in subjects with type 2 diabetes mellitus.. *Therapeutic Research* 2003;24(9):1867-1872. **Not written in English. Other (abstract only).**
- Ina K. How about the effect of thiazolidinediones in diabetic nephropathy?. *Med. Sci. Monit.* 2004;10(6):LE7 **Not an original article**
- Inzucchi S E. Metformin and heart failure: innocent until proven guilty. *Diabetes Care* 2005;28(10):2585-7 **Not an original article**
- Jackson J E, Bressler R. Use oral hypoglycemics with caution... *Geriatrics* 88;43(8):77-83 **Not an original article**
- Jackson M, Nussey S, Mudan S. Metformin induced lactic acidosis. *Clin. Intensive Care* 2000;11(4):209-213 **Not an original article. Other (case-report).**
- Jerums G, Murray R M L, Seeman E. Lack of effect of gliclazide on early diabetic nephropathy and retinopathy: A two-year controlled study. *DIABETES RES. CLIN. PRACT.* 87;3(2):71-80. **N<40.**
- Jick S S, Stender M, Myers M W. Frequency of liver disease in type 2 diabetic patients treated with oral antidiabetic agents. *Diabetes Care* 99;22(12):2067-71. **Other (unspecified medications).**
- Kane J P. Does hypertriglyceridemia present an indication for pioglitazone therapy in diabetes?. *Diabetes Technol Ther* 2002;4(2):153-5 **Not an original article**
- Katakami N, Yamasaki Y, Gorogawa S et al. Additive metformin attenuates progression of carotid Intima-Media Thickness in subjects with Type 2 diabetes treated with sulfonylureas. *Diabetologia* 2002;45(Suppl 2):A274-A275 **Not an original article**
- Kemp T M, Barr E L, Zimmet P Z et al. Glucose, lipid, and blood pressure control in Australian adults with type 2 diabetes: the 1999-2000 AusDiab. *Diabetes Care* 2005;28(6):1490-2. **Does not apply to the key questions. Other (outcomes not separated by medication type).**
- Kennedy F P. Do thiazolidinediones cause congestive heart failure?. *Mayo Clin Proc* 2003;78(9):1076-7 **Not an original article**
- Kennedy L, Herman W H. Renal status among patients using metformin in a primary care setting. *Diabetes Care* 2005;28(4):922-4. **Does not apply to the key questions.**
- King J E. Why hold the metformin?. *Nursing* 2004;34(7):20 **Not an original article**
- King K A, Levi V E. Prevalence of edema in patients receiving combination therapy with insulin and thiazolidinedione. *Am. J. Health-Syst. Pharm.* 2004;61(4):390-393. **Oral medication is compared or added to insulin.**
- Kirby M. Diabetes in the new General Medical Services contract: targets and adherence to metformin therapy. *Int J Clin Pract* 2005;59(3):263-6 **Not an original article**
- Ko G T C, Tsang C-C, Ng C-W et al. Use of acarbose or bedtime insulin after failure of treatment with conventional oral

Appendix D: Excluded Articles (continued)

- antidiabetics: A one-year randomised clinical trial. Clin. Drug Invest. 2001;21(6):401-408. **Evaluates acarbose or miglitol added to any other oral medication in one arm. Oral medication is compared or added to insulin.**
- Ko G T, Chan W B, Chan J C et al. Gastrointestinal symptoms in Chinese patients with Type 2 diabetes mellitus. Diabet Med 99;16(8):670-4. **Does not apply to the key questions.**
- Koppel H, Horn S, Pieber T et al. Observations on the effect of glibenclamide on noninvasive clinical parameters of myocardial ischemia. Cardiovasc Drugs Ther 98;12(4):383-5. **Does not apply to the key questions. N<40.**
- Kordella T. Research profile. Is there a link? TZDs and congestive heart failure. Andrew Karter, PhD. Diabetes Forecast 2004;57(6):98-100 **Not an original article**
- Koro C E, Bowlin S J, Weiss S R. Antidiabetic therapy and the risk of heart failure in type 2 diabetic patients: an independent effect or confounding by indication. Pharmacoepidemiol Drug Saf 2005;14(10):697-703. **Evaluates combinations of greater than 2 oral medications in one arm.**
- Kure J. Glipizide and glyburide. N C Med J 86;47(3):149-53 **Not an original article**
- Laube H, Federlin K, Hillebrand I. Effect of alpha-inhibitors on blood glucose and insulin levels. Adv Exp Med Biol 88;246287-93. **N<40.**
- Levin F, Kazim M, Smith T J et al. Rosiglitazone-induced proptosis. Arch Ophthalmol 2005;123(1):119-21. **N<40.**
- Lipid effects of pioglitazone studied. Br. J. Diabetes Vasc. Dis. 2004;4(3):209 **Not an original article. Evaluates nateglinide or repaglinide added to any other oral medication in one arm. Evaluates combinations of greater than 2 oral medications in one arm. Oral medication is compared or added to insulin.**
- Lopez-Garcia F, Borrás J, Verdu C et al. Cholestatic hepatitis associated with repaglinide. Diabetes Care 2005;28(3):752-3. **N<40.**
- Maaravi Y, Stessman J. Mild, reversible pancytopenia induced by rosiglitazone. Diabetes Care 2005;28(6):1536. **N<40.**
- Manalo G G, Villareal D T, Anel-Quimpo J et al. Body weight as a predictor of response to sulfonylurea therapy. PHILIPP. J. INTERN. MED. 93;31(3):135-143. **Does not apply to the key questions.**
- Masud F, Hasan M, Abaidullah S et al. Assessment of metabolic profile and body mass index (BMI) in type II diabetics treated with metformin and insulin. SPECIALIST 92;9(1):29-34. **N<40. Oral medication is compared or added to insulin.**
- Mayou R, Bryant B, Turner R. Quality of life in non-insulin-dependent diabetes and a comparison with insulin-dependent diabetes. J. PSYCHOSOM. RES. 90;34(1):1-11. **Does not evaluate medications in this study. Other (no break down of medication type).**
- Mazze R S, Simonson G, Strock E et al. Staged Diabetes Management: A systematic evidence-based approach to the prevention and treatment of diabetes and its co-morbidities: Proceedings of Staged Diabetes Management: Worldwide Outcomes 2000 November 2000. Puebla, Mexico. Pract. Diabetes Int. 2001;18(7):S1-S16 **Not an original article. Does not apply to the key questions**
- McBain A M, Brown I R, Menzies D G et al. Effects of improved glycaemic control on calcium and magnesium homeostasis in type II diabetes. J Clin Pathol 88;41(9):933-5. **Does not apply to the key questions. N<40.**
- Meier J J, Deifuss S, Klamann A et al. Plasma glucose at hospital admission and previous metabolic control determine myocardial infarct size and survival in patients with and without type 2 diabetes: The Langendreer Myocardial Infarction and Blood Glucose in Diabetic Patients Assessment (LAMBDA). Diabetes Care 2005;28(10):2551-2553. **Does not evaluate medications in this study.**
- Mertes G. Efficacy and safety of acarbose in the treatment of type 2 diabetes: data from a 2-year surveillance study. Diabetes Res Clin Pract 98;40(1):63-70. **Evaluates acarbose or miglitol added to any other oral medication in one arm. Other (lacks details).**
- Metaglip and Avandamet for type 2 diabetes. Med Lett Drugs Ther 2002;44(1146):107-9. **Not an original article**
- Mitra P K, Dutta S K. Microvascular changes in diabetes mellitus--relation to control of diabetes and oral hypoglycaemic agents. Indian J Pathol Microbiol 87;30(1):105-11. **Does not apply to the key questions.**
- Mitra P K, Dutta S K. Microvascular changes in diabetes mellitus--relation to control of diabetes and oral hypoglycaemic agents. Indian J Pathol Microbiol 87;30(1):105-11. **N<40.**
- Monsaert R P. An ounce of prevention. Diabetes Forecast 2004;57(8):11 **Not an original article**
- Morton A P, McIntyre H D. Effectiveness and side effects of thiazolidinediones for type 2 diabetes. Med J Aust 2005;182(9):492-3. **Evaluates combinations of greater than 2 oral medications in one arm.**
- Mullen K D, Howard R. Is acarbose an effective drug for treating patients with cirrhosis and hepatic encephalopathy?. Nat. Clin. Pract. Gastroenterol. Hepatol. 2005;2(6):264-265 **Not an original article. Other (insufficient data).**
- Nakamura T, Ushiyama C, Osada S et al. Effect of pioglitazone on dyslipidemia in hemodialysis patients with type 2 diabetes. Ren Fail 2001;23(6):863-4. **N<40.**
- Nakamura T, Ushiyama C, Osada S et al. Pioglitazone reduces urinary podocyte excretion in type 2 diabetes patients with microalbuminuria. Metabolism 2001;50(10):1193-6. **N<40. . Other (case-controlled study).**
- Nan D N, Hernandez J L, Fernandez-Ayala M et al. Acute hepatotoxicity caused by repaglinide. Ann Intern Med 2004;141(10):823 **Not an original article**
- Nateglinide improves postprandial glucose as monotherapy or in combination with metformin. Geriatrics 2002;57(8):35 **Not an original article**
- Nielsen N V. Diabetic retinopathy II. The course of retinopathy in diabetics treated with oral hypoglycaemic agents and diet regime alone. A one year epidemiological cohort study of diabetes mellitus. The Island of Falster, Denmark. Acta Ophthalmol (Copenh) 84;62(2):266-73. **Does not apply to the key questions. . Other (does not specify study drugs).**
- Nissen S E, Wolski K, Topol E J. Effect of muraglitazar on death and major adverse cardiovascular events in patients with type 2

Appendix D: Excluded Articles (continued)

- diabetes mellitus. JAMA 2005;294(20):2581-6. **Does not evaluate medications in this study.**
- Noyon R, Pagano Mirani-Oostdijk C, van Gent C M et al. Long-term effect of acarbose on diurnal serum triglyceride, glucose, insulin and adipose tissue lipoprotein lipase levels in patients with primary endogenous hypertriglyceridaemia, with or without type II diabetes. Neth J Med 86;29(5):157-64. **N<40.**
- Ose H, Fukui M, Kitagawa Y et al. Efficacy of glimepiride in patients with poorly controlled insulin-treated type 2 diabetes mellitus. Endocr J 2005;52(5):563-9. **Oral medication is compared or added to insulin.**
- Palmer A J, Roze S, Lammert M et al. Comparing the long-term cost-effectiveness of repaglinide plus metformin versus nateglinide plus metformin in type 2 diabetes patients with inadequate glycaemic control: an application of the CORE Diabetes Model in type 2 diabetes. Curr Med Res Opin 2004;20 Suppl 1S41-51. **Evaluates nateglinide or repaglinide added to any other oral medication in one arm.**
- Parra D, Legreid A M, Beckey N P et al. Metformin monitoring and change in serum creatinine levels in patients undergoing radiologic procedures involving administration of intravenous contrast media. Pharmacotherapy 2004;24(8):987-93. **Does not apply to the key questions.**
- Peacock I, Hawkins M, Heptinstall S. Platelet behaviour in non-insulin-dependent diabetes--influence of vascular complications, treatment and metabolic control. Thromb Haemost 86;55(3):361-5. **Does not apply to the key questions. Oral medication is compared or added to insulin.**
- Perez A, Khan M, Johnson T et al. Pioglitazone plus a sulphonylurea or metformin is associated with increased lipoprotein particle size in patients with type 2 diabetes. Diab Vasc Dis Res 2004;1(1):44-50. **Does not apply to the key questions.**
- Pitale S, Kernan-Schroeder D, Emanuele N et al. Health-related quality of life in the VA Feasibility Study on glycemic control and complications in type 2 diabetes mellitus. J Diabetes Complications 2005;19(4):207-11. **Oral medication is compared or added to insulin.**
- Quesada-Gomez J M, Serrano-Alferez I. Nonhypoglycemic effects of thiazolidinediones [3]. Ann. Intern. Med. 2001;135(11):1007-1008 **Not an original article**
- Quevedo S F, Westrick E. Glycemic control in type 2 diabetes mellitus. Med Health R I 98;81(11):345-8 **Not an original article**
- Rakovac I, Jeitler K, Gfrerer R J et al. Patients with Type 2 diabetes treated with metformin: prevalence of contraindications and their correlation with discontinuation. Diabet Med 2005;22(5):662-4. **Does not apply to the key questions.**
- Ramachandran A. Monotherapy of type 2 diabetes with once-daily glimepiride modified release in primary care. Diabetes Res Clin Pract 2003;62(1):63-4. **Does not evaluate medications in this study.. Other (no comparison of study drugs).**
- Raz I, Gilhar D, Hoffman A. Prolonged response to glibenclamide in NIDDM patients in a normoglycemic state. Isr J Med Sci 94;30(10):775-8. **N<40.**
- Reaven G M. Effect of metformin on various aspects of glucose, insulin and lipid metabolism in patients with non-insulin-dependent diabetes mellitus with varying degrees of hyperglycemia. Diabetes Metab Rev 95;11 Suppl 1S97-108 **Not an original article**
- Rendell M S, Glazer N B, Ye Z. Combination therapy with pioglitazone plus metformin or sulfonylurea in patients with Type 2 diabetes: influence of prior antidiabetic drug regimen. J Diabetes Complications 2003;17(4):211-7. **Does not apply to the key questions.**
- Rosak C, Haupt E, Walter T et al. The effect of combination treatment with acarbose and glibenclamide on postprandial glucose and insulin profiles: additive blood glucose lowering effect and decreased hypoglycaemia. Diabetes Nutr Metab 2002;15(3):143-51. **Other (one-day study).**
- Roy R, Navar M, Palomeno G et al. Real world effectiveness of rosiglitazone added to maximal (tolerated) doses of metformin and a sulfonylurea agent: a systematic evaluation of triple oral therapy in a minority population. Diabetes Care 2004;27(7):1741-2. **Evaluates combinations of greater than 2 oral medications in one arm.**
- Schneider J, Erren T, Zofel P et al. Metformin-induced changes in serum lipids, lipoproteins, and apoproteins in non-insulin-dependent diabetes mellitus. Atherosclerosis 90;82(1-2):97-103. **Other (duplicate of another study).**
- Schofi C, Luebben G. Pioglitazone improves diabetic dyslipidaemia in patients with type 2 diabetes mellitus with or without lipid-lowering therapy. Clin. Drug Invest. 2005;25(5):341-345. **Does not evaluate medications in this study.**
- Schwarzbeck A, Hastka J, Kuhnle F et al. Metformin-associated lactic acidosis in diabetic patients with acute renal failure. Nephrol Dial Transplant 95;10(3):425-6 **Not an original article**
- Sclar D A, Robison L M, Skaer T L et al. Sulfonylurea pharmacotherapy regimen adherence in a Medicaid population: influence of age, gender, and race. Diabetes Educ 99;25(4):531-2, 535, 537-8. **Does not apply to the key questions.**
- Shimizu H, Monden T, Nagai T et al. Insulin resistance determines efficacy of glimepiride in Type 2 diabetic patients not well controlled by diet alone. Diabet Med 2005;22(2):225-6. **N<40.**
- Soegondo S, Subekti I, Luthariana L. The efficacy of repaglinide monotherapy and in combination with metformin in Indonesian type 2 diabetes mellitus patients. Acta Med Indones 2004;36(3):142-7. **Evaluates nateglinide or repaglinide added to any other oral medication in one arm.**
- Spengler M, Cagatay M. The use of acarbose in the primary-care setting: evaluation of efficacy and tolerability of acarbose by postmarketing surveillance study. Clin Invest Med 95;18(4):325-31. **Evaluates acarbose or miglitol added to any other oral medication in one arm.**
- Sugarman J R. Hypoglycemia associated hospitalizations in a population with a high prevalence of non-insulin-dependent diabetes mellitus. Diabetes Res Clin Pract 91;14(2):139-47. **N<40.**
- Takagi T, Yamamuro A, Tamita K et al. Thiazolidinedione treatment attenuates diffuse neointimal hyperplasia in restenotic lesions after coronary stent implantation in type 2 diabetic patients: an intravascular ultrasound study. J Cardiol 2005;45(4):139-47. **Does not apply to the key questions.**

Appendix D: Excluded Articles (continued)

- Tan G D, Fielding B A, Currie J M et al. The effects of rosiglitazone on fatty acid and triglyceride metabolism in type 2 diabetes. *Diabetologia* 2005;48(1):83-95. **N<40.**
- Tang W H, Francis G S, Hoogwerf B J et al. Fluid retention after initiation of thiazolidinedione therapy in diabetic patients with established chronic heart failure. *J Am Coll Cardiol* 2003;41(8):1394-8. **Oral medication is compared or added to insulin.**
- Taylor K G, Wright A D, John W G. A prospective study of sulphonylurea therapy and serum HDL-cholesterol in type 2 (insulin independent) diabetics. *DIABETOLOGIA* 81;21(5):514-515 **Not an original article. N<40.**
- Taylor R, Isles T E, McLaren S et al. A comparison of the metabolic profiles in type 2 diabetics during glipizide and glibenclamide treatment. *DIABETOLOGIA* 81;21(3):518 **Not an original article. N<40.**
- Testa M A, Simonson D C, Turner R R. Valuing quality of life and improvements in glycemic control in people with type 2 diabetes. *Diabetes Care* 98;21 Suppl 3C44-52. **Does not apply to the key questions.**
- Tomino Y, Shirato I, Horikoshi S et al. Effect of acarbose on blood glucose and proteinuria in patients with diabetic nephropathy. *Nephron* 2000;85(2):190. **N<40.**
- Trischitta V, Italia S, Mazzarino S et al. Addition of insulin or metformin after secondary failure to glyburide. *ANN. INTERN. MED.* 92;117(SUPPL. 2):46. **N<40.**
- Turner R C, Cull C A, Frighi V et al. Glycemic control with diet, sulfonylurea, metformin, or insulin in patients with type 2 diabetes mellitus: progressive requirement for multiple therapies (UKPDS 49). UK Prospective Diabetes Study (UKPDS) Group. *JAMA* 99;281(21):2005-12. **Does not apply to the key questions.**
- Turner R C, Holman R R. Metformin and risk of cardiovascular disease. *Cardiology* 99;91(3):203-4 **Not an original article**
- U.K. prospective diabetes study. II. Reduction in HbA1c with basal insulin supplement, sulfonylurea, or biguanide therapy in maturity-onset diabetes. A multicenter study. *Diabetes* 85;34(8):793-8. **Other ()**.
- Udezue E. Flexible glibenclamide dosage in Nigerian diabetic patients. *Trop Doct* 90;20(2):81-2. **N<40.**
- Vidhya S, Mohan V. Rosiglitazone--useful drug but has side effects. *J Assoc Physicians India* 2002;50615 **Not an original article**
- Vrijlandt PJWS, Huisman J. Acarbose improves glycaemic control and insulin sensitivity in obese type 2 diabetes patients with secondary failure on sulphonylureas. *The Netherlands Journal of Medicine* 2001;58A17 **Not an original article**
- Wagstaff A J, Goa K L. Spotlight on rosiglitazone in the management of type 2 diabetes mellitus. *Treat Endocrinol* 2002;1(6):411-4 **Not an original article**
- Wagstaff A J, Goa K L. Spotlight on rosiglitazone in the management of type 2 diabetes mellitus. *Treat Endocrinol* 2002;1(6):411-4. **Other (abstract).**
- Wajchenberg B J, Santomaro A T, Cherem J J et al. Effect of gliclazide on non-insulin dependent diabetes mellitus. *Adv Exp Med Biol* 88;246313-9. **Does not evaluate medications in this study. N<40.**
- Waters A K, Morgan D B, Wales J K. Blood lactate and pyruvate levels in diabetic patients treated with biguanides with and without sulphonylureas. *Diabetologia* 78;14(2):95-8. **Other (no clinical outcomes).**
- Weaver J U, Robertson D, Atkin S L. Nateglinide alone or with metformin safely improves glycaemia to target in patients up to an age of 84. *Diabetes Obes Metab* 2004;6(5):344-52. **Evaluates nateglinide or repaglinide added to any other oral medication in one arm.**
- Weitzman S, Maislos M, Bodner-Fishman B et al. Association of diabetic retinopathy, ischemic heart disease, and albuminuria with diabetic treatment in type 2 diabetic patients. A population-based study. *Acta Diabetol* 97;34(4):275-9. **Does not evaluate medications in this study.**
- Weitzman S, Maislos M, Bodner-Fishman B et al. Association of diabetic retinopathy, ischemic heart disease, and albuminuria with diabetic treatment in type 2 diabetic patients. A population-based study. *Acta Diabetol* 97;34(4):275-9. **Does not apply to the key questions.**
- Wolever T M, Radmard R, Chiasson J L et al. One-year acarbose treatment raises fasting serum acetate in diabetic patients. *Diabet Med* 95;12(2):164-72. **Does not apply to the key questions. Evaluates combinations of greater than 2 oral medications in one arm. Other (data available from another study).**
- Yang J, Di F, He R et al. Effect of addition of low-dose rosiglitazone to sulphonylurea therapy on glycemic control in type 2 diabetic patients. *Chin Med J (Engl)* 2003;116(5):785-7. **Not written in English**
- Yang JK, Di FS, He RH et al. Clinical study on rosiglitazone monotherapy of early type 2 diabetes. *China Pharmacy* 2002;13(10):608-610. **Not written in English**
- Yki-Jarvinen H, Nikkila K, Makimattila S. Metformin prevents weight gain by reducing dietary intake during insulin therapy in patients with type 2 diabetes mellitus. *Drugs* 99;58 Suppl 153-4; discussion 75-82. **N<40. Oral medication is compared or added to insulin.**
- Yudkin J S, Smits P. Effects of hypoglycemic agents on patients with diabetes [17]. *CIRCULATION* 97;96(10):3797-3798 **Not an original article**
- Zargar A H, Laway B A, Masoodi S R et al. Use of sulfonylureas during pregnancy: some incidental observations. *J Assoc Physicians India* 2004;52168-9. **Evaluates only pregnant women with diabetes. Does not apply to the key questions.**
- Zimmerman B R, Espenshade J, Fujimoto W Y et al. The pharmacological treatment of hyperglycemia in NIDDM. *DIABETES CARE* 96;19(SUPPL. 1):S54-S61 **Not an original article**

Appendix E: Sample Forms

Previewing Only: You cannot submit data from this form



Previewing at Level 1

Refid: 3597, Charles, B., Norris, R., Xiao, X., and Hague, W., Population Pharmacokinetics of Metformin in Late Pregnancy, *Ther Drug Monit*, 28(1), 2006, p.67-72
State: Excluded, Level: 1

Title Review

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Submit Data

1. Does this article **potentially apply** to any of our key questions?

- ☒ **Potentially** eligible
- ☐ Ineligible
- ☐ Not in English
- ☐ Ineligible, but includes inflammatory markers
- ☐ Van de Laar/Salpeter article

[Clear Selection](#)

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Previewing at Level 2

Refid: 3597, Charles, B., Norris, R., Xiao, X., and Hague, W., Population Pharmacokinetics of Metformin in Late Pregnancy, *Ther Drug Monit*, 28(1), 2006, p.67-72
State: Excluded, Level: 1

Abstract Review

Keywords:

No keywords available

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Abstract:

The pharmacokinetic disposition of metformin in late pregnancy was studied together with the level of fetal exposure at birth. Blood samples were obtained in the third trimester of pregnancy from women with gestational diabetes or type 2 diabetes; 5 had a previous diagnosis of polycystic ovary syndrome. A cord blood sample also was obtained at the delivery of some of these women, and also at delivery of others who had been taking metformin during pregnancy but from whom no blood had been taken. Plasma metformin concentrations were assayed by a new, validated, reverse-phase HPLC method. A 2-compartment, extravascular maternal model with transplacental partitioning of drug to a fetal compartment was fitted to the data. Nonlinear mixed-effects modeling was performed in NONMEM using FOCE with INTERACTION. Variability was estimated using logarithmic interindividual and additive residual variance models; the covariance between clearance and volume was modeled simultaneously. Mean (range) metformin concentrations in cord plasma and in maternal plasma were 0.81 (range, 0.1-2.6) mg/L and 1.2 (range, 0.1-2.9) mg/L, respectively. Typical population values (interindividual variability, CV%) for allometrically scaled maternal clearance and volume of distribution were 28 L/h/70 kg (17.1%) and 190 L/70 kg (46.3%), giving a derived population-wide half-life of 5.1 hours. The placental partition coefficient for metformin was 1.07 (36.3%). Neither maternal age nor weight significantly influenced the pharmacokinetics. The variability (SD) of observed concentrations about model-predicted concentrations was 0.32 mg/L. The pharmacokinetics were similar to those in nonpregnant patients and, therefore, no dosage adjustment is warranted. Metformin readily crosses the placenta, exposing the fetus to concentrations approaching those in the maternal circulation. The sequelae to such exposure, eg, effects on neonatal obesity and insulin resistance, remain unknown.

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1. Exclude article because... (check one or more)

☐ written in language other than

English

☐ subjects **<18 years old**

☐ no **original data** (e.g., is a meeting abstract, review, commentary, etc.)

☐ study evaluates outcomes in **animals only** (no humans evaluated)

☐ not evaluating people with **type 2 diabetes**, NIDDM (non-insulin dependent diabetes mellitus), or adult onset diabetes

☐ evaluates markers of **inflammation only** (e.g., tumor necrosis factor alpha (TNF-alpha), interleukin-1 (IL-1), etc.)

☐ study only evaluates a **first generation sulfonylurea** (tolazamide, tolbutamide, chlorpropamide)

☐ evaluates none of the **medications** in our review (see medication list posted on trialstat to see which medications we have included in the review)

☐ does not apply to any of the **key questions**

☐ other: specify _____

☐ Undecided; retrieve full article to decide

Below are specific questions to determine inclusion/exclusion if did not exclude based on a reason above. Skip options under questions if the article does not apply to that particular question.
CHECK TO SEE IF ARTICLE APPLIES TO Q2-6 BEFORE MARKING EXCLUDE FOR Q1.

2. Q1: **proximal clinical outcomes**: glycosylated hemoglobin, weight, systolic or diastolic blood pressure, serum lipid levels, and two hour postprandial glucose levels in adult patients with type 2 diabetes?

☐ exclude since study is **< 3 months**

☐ exclude since **NOT a randomized controlled trial**

☐ exclude since number of subjects in entire study is **≤ 40**

☐ include

3. Q2: **distal diabetes-related complications**

including mortality and the following macrovascular and microvascular complications: coronary artery disease, myocardial infarction, stroke, transient ischemic attack, retinopathy, nephropathy, neuropathy, peripheral arterial disease (PAD), or amputations?

☐ exclude since study is **≤ 3 months**

☐ exclude since number of subjects in entire study is **≤ 40**

☐ include but mark if deals with **PAD, amputations, or neuropathy**

☐ include

4. Q3: other health outcomes including **quality of life** and **functional status**?

☐ exclude since study is **≤ 3 months**

☐ exclude since **NO comparison group**

☐ exclude since number of subjects in entire study **≤ 40**

☐ include

5. Old Q4&5: safety for the following life-threatening and non life-threatening **adverse events**:

hypoglycemia, liver failure, congestive heart failure, lactic acidosis, cancer, anemia, thrombocytopenia, or leukopenia, allergic reactions requiring hospitalization or death, elevated aminotransferase levels, edema, hypervolemia, pancytopenia, weight gain and gastrointestinal problems and other adverse events?

See new revised Q4&5 below.

☐ (see below)

☐ (see below)

☐ (see below)

☐ (see below)

☐ (see below)

6. Q6: Are the safety and effectiveness different for particular adult populations such as those based on **demographic factors** (e.g., race/ethnicity, age>65 years, or gender) or **co-morbidities** (e.g., renal insufficiency, congestive heart failure, liver disease, obesity, depression, schizophrenia)?

☐ include

7. Evaluates an oral medication in our review and insulin. Check below if oral medication is compared to insulin (and there is **no** other oral comparison or placebo group). Examples to exclude are:

- oral + insulin compared to insulin
- oral + insulin compared to another oral medication **with no placebo or other oral medication arm**
- oral + insulin compared to oral + insulin
- oral compared to insulin **with no placebo or other oral medication arm**

☐ Exclude if oral medication is compared to insulin (and there is no other oral comparison or placebo group)

☐ Exclude for other reason (specify:)



8. Exclude if the following combinations are evaluated (and there is no other oral comparison groups and/or placebo groups).

☐ Exclude if study evaluates acarbose or miglitol added to any other oral medication in one arm

☐ Exclude if study evaluates nateglinide or repaglinide added to any other oral medication in one arm

☐ Exclude if study evaluates combinations of greater than 2 oral medications in one arm (e.g., metformin added to glyburide added to acarbose in one arm)


9. **Revised Q4&5:** safety for the following life-threatening and non life-threatening **adverse events:** hypoglycemia, liver failure, congestive heart failure, lactic acidosis, cancer, anemia, thrombocytopenia, or leukopenia, allergic reactions requiring hospitalization or death, elevated aminotransferase levels, edema, hypervolemia, pancytopenia, gastrointestinal problems and other adverse events?

Note: weight gain was removed from adverse events.

☐ Include if **RCT** >3 months AND N>40 AND is likely to have data on safety (i.e., those that mention safety or adverse events in the title or abstract) even if it does not have data on Q1

☐ Include if **cohort** >3 months AND N>40 AND is likely to have data on safety (i.e., those that mention safety or adverse events in the title or abstract) even if it does not have data on Q2, 3

☐ Include if **case control study** AND N>40 AND is likely to have data on safety (i.e., mentions safety or adverse events in the title or abstract)

	<div><input type="checkbox"/> Exclude if case report or case series (i.e., a series of case reports)</div> <div><input type="checkbox"/> Other study design AND is likely to have data on safety (i.e., mentions safety or adverse events in the title or abstract) (specify: </div> <div><input type="checkbox"/> Unable to tell study duration, number of subjects, or study design but is likely to have data on safety (i.e., those that mention safety or adverse events in the title or abstract); retrieve full article to decide</div> <div><input type="checkbox"/> Exclude if does not meet any of the inclusion criteria for Q4&5, such as N<40</div> <div><div>Save to finish later</div><div>Submit Data</div></div>
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Previewing at Level 3

Refid: 3597, Charles, B., Norris, R., Xiao, X., and Hague, W., Population Pharmacokinetics of Metformin in Late Pregnancy, *Ther Drug Monit*, 28(1), 2006, p.67-72
State: Excluded, Level: 1

Article Review

Keywords:

No keywords available

Increase Font Size

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Abstract:

The pharmacokinetic disposition of metformin in late pregnancy was studied together with the level of fetal exposure at birth. Blood samples were obtained in the third trimester of pregnancy from women with gestational diabetes or type 2 diabetes; 5 had a previous diagnosis of polycystic ovary syndrome. A cord blood sample also was obtained at the delivery of some of these women, and also at delivery of others who had been taking metformin during pregnancy but from whom no blood had been taken. Plasma metformin concentrations were assayed by a new, validated, reverse-phase HPLC method. A 2-compartment, extravascular maternal model with transplacental partitioning of drug to a fetal compartment was fitted to the data. Nonlinear mixed-effects modeling was performed in NONMEM using FOCE with INTERACTION. Variability was estimated using logarithmic interindividual and additive residual variance models; the covariance between clearance and volume was modeled simultaneously. Mean (range) metformin concentrations in cord plasma and in maternal plasma were 0.81 (range, 0.1-2.6) mg/L and 1.2 (range, 0.1-2.9) mg/L, respectively. Typical population values (interindividual variability, CV%) for allometrically scaled maternal clearance and volume of distribution were 28 L/h/70 kg (17.1%) and 190 L/70 kg (46.3%), giving a derived population-wide half-life of 5.1 hours. The placental partition coefficient for metformin was 1.07 (36.3%). Neither maternal age nor weight significantly influenced the pharmacokinetics. The variability (SD) of observed concentrations about model-predicted concentrations was 0.32 mg/L. The pharmacokinetics were similar to those in nonpregnant patients and, therefore, no dosage adjustment is warranted. Metformin readily crosses the placenta, exposing the fetus to concentrations approaching those in the maternal circulation. The sequelae to such exposure, eg, effects on neonatal obesity and insulin resistance, remain unknown.

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1. Exclude article because... (check one or more)


- ☐ not written in **English**
- ☐ subjects not **adults** (<18 years old)
- ☐ not an **original article** (e.g., is a meeting abstract, review, commentary, etc.)
- ☐ study evaluates outcomes in **animals only** (no humans evaluated)
- ☐ not evaluating people with **type 2 diabetes**. NIDDM (non-insulin dependent diabetes mellitus), or adult-onset diabetes (e.g. **exclude if** evaluates people with **impaired glucose tolerance, metabolic syndrome**, maturity onset diabetes of youth (MODY), gestational diabetes)
- ☐ evaluates **pregnant women** with diabetes only
- ☐ evaluates markers of **inflammation only** (e.g., tumor necrosis factor alpha (TNF-alpha), interleukin-1 (IL-1), etc.)
- ☐ study only evaluates a **first generation sulfonylurea** (tolazamide, tolbutamide, chlorpropamide) or is a head to head comparison with a first generation sulfonylurea only with no placebo or other comparison group to compare our medication of interest.
- ☐ evaluates none of the **medications** in our review (see medication list posted on trialstat to see which medications we have included in the review. Note: Exclude studies on **muraglitazar** unless data on other medications in the study. Exclude studies on **troglitazone, phenformin, and voglibose** even if its a head-to-head trial.)
- ☐ does not apply to any of the **key questions** (such as dealing with cost or adherence or results not broken down by type of medication or drug-drug interactions)
- ☐ **N<40**
- ☐ evaluates **acarbose or miglitol added** to any other oral medication in one arm (AND there is no other oral comparison or placebo groups)

☐ evaluates **nateglinide or repaglinide added** to any other oral medication in one arm (AND there is no other oral comparison or placebo groups)

☐ evaluates **combinations of greater than 2 oral medications in one arm** (e.g., metformin added to glyburide added to acarbose in one arm)

☐ oral medication is **compared or added to insulin** (AND there is no other oral comparison or placebo group). Examples to exclude are: oral + insulin compared to insulin, oral + insulin compared to another oral medication **with no placebo or other oral medication arm**, oral + insulin compared to oral + insulin, oral compared to insulin **with no placebo or other oral medication arm**

☐ the study is a **pharmacokinetic or dosing study** where there is no placebo or comparison group such as: acarbose 50mg compared to acarbose 100mg with no placebo or other oral medication comparison group.

☐ other: specify _____ 

2. Include:

☐ Include but do **NOT** review if this is a study with >2 trials reported in the article with **pooled results** eligible for one of the 6 questions.

Below are specific questions to determine inclusion/exclusion if did not exclude based on a reason above. Skip options under questions if the article does not apply to that particular question.
CHECK TO SEE IF ARTICLE APPLIES TO Q2-6 BEFORE MARKING EXCLUDE FOR Q1.

3.
 Q1: **proximal clinical outcomes**: glycosylated hemoglobin, weight, systolic or diastolic blood pressure, serum lipid levels, and two hour postprandial glucose levels in adult patients with type 2 diabetes? (NOTE: if only evaluates another measure of post prandial glucose (e.g., study evaluates one hour post prandial glucose AND there is no other relevant outcome), then mark "does not apply to key question above.")

☐ exclude since study is **< 3 months**

☐ exclude since **NOT a randomized controlled trial**

☐ include - **CONSIDER FOR INCLUSION FOR OTHER QUESTIONS THEN BEGIN DATA ABSTRACTION. COMPLETE ALL GENERAL FORMS, Q1 & Q3 OUTCOMES FORM, AND QUALITY FORM.**

4.
 Q2: **distal diabetes-related complications** including

mortality and the following macrovascular and microvascular complications: coronary artery disease, myocardial infarction, stroke, transient ischemic attack, retinopathy, nephropathy, neuropathy (microalbuminuria, urine albumin/creatinine ratio, serum creatinine, GFR, creatinine clearance, proteinuria/albuminuria, end stage renal disease, and renal replacement therapy or transplant), peripheral arterial disease (PAD), or amputations?

☐ exclude since study is < 3 months

☐ exclude if deals with **biological markers** of outcomes **such as vascular endothelial function or carotid intima media thickness**. (Mark "include" below if deals with clinical outcomes such as ventricular fibrillation, restenosis rates, or EKG abnormalities, such as QT prolongation.)

☐ include - **CONSIDER FOR INCLUSION FOR OTHER QUESTIONS THEN BEGIN DATA ABSTRACTION. COMPLETE ALL GENERAL FORMS, Q2 OUTCOMES FORM, AND QUALITY FORM**

5.

Q3: other health outcomes including quality of life and functional status?

☐ exclude since study is < 3 months

☐ exclude since **NO comparison group**

☐ include - **CONSIDER FOR INCLUSION FOR OTHER QUESTIONS THEN BEGIN DATA ABSTRACTION. COMPLETE ALL GENERAL FORMS, Q1 & Q3 OUTCOMES FORM, AND QUALITY FORM**

6.

Revised Q4&5: safety for the following life-threatening and non life-threatening **adverse events**: hypoglycemia, liver failure, congestive heart failure, lactic acidosis, cancer, anemia, thrombocytopenia, leukopenia, allergic reactions requiring hospitalization or death, elevated aminotransferase levels, edema, hypervolemia, pancytopenia, gastrointestinal problems and other adverse events?

Note: weight gain was removed from adverse events.

☐ Include if **RCT** >3 months AND is likely to have data on safety (i.e., those that mention safety or adverse events in the title or abstract) even if it does not have data on Q1 - **CONSIDER FOR INCLUSION FOR OTHER QUESTIONS THEN BEGIN DATA ABSTRACTION. COMPLETE ALL GENERAL FORMS, Q4&5 OUTCOMES FORM, AND QUALITY FORM**

☐ Include if **cohort** >3 months AND is likely to have data on safety (i.e., those that mention safety or adverse events in the title or abstract) even if it does not have data on Q2, 3 - **CONSIDER FOR INCLUSION FOR OTHER QUESTIONS THEN BEGIN DATA ABSTRACTION. COMPLETE**

**ALL GENERAL FORMS, Q4&5
OUTCOMES FORM, AND QUALITY
FORM**

☐ Include if **case control study** AND is likely to have data on safety (i.e., mentions safety or adverse events in the title or abstract) - **CONSIDER FOR INCLUSION FOR OTHER QUESTIONS THEN BEGIN DATA ABSTRACTION. COMPLETE STUDY DESIGN, ELIGIBILITY CRITERIA, POPULATION CHARACTERISTICS, Q4&5 CASE CONTROL OUTCOMES FORM**

☐ Exclude if **case report or case series** (i.e., a series of case reports)

☐ Include if other study design AND is likely to have data on safety (i.e., mentions safety or adverse events in the title or abstract) (specify:)

CONSIDER FOR INCLUSION FOR OTHER QUESTIONS THEN BEGIN DATA ABSTRACTION. COMPLETE ALL GENERAL FORMS, Q4&5 OUTCOMES FORM, AND QUALITY FORM

☐ Exclude if does not meet any of the inclusion criteria for Q4&5, such as N<40

7.

Q6: Are the safety and effectiveness different for particular adult populations such as those based on **demographic factors** (e.g., race/ethnicity, age>65 years, or gender) or **co-morbidities** (e.g., renal insufficiency, congestive heart failure, liver disease, obesity, depression, schizophrenia, etc...)?

☐ Include - **CONSIDER FOR INCLUSION FOR OTHER QUESTIONS THEN BEGIN DATA ABSTRACTION. COMPLETE ALL GENERAL FORMS AND QUALITY FORM**

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Previewing Only: You cannot submit data from this form



Previewing at Level 4

Refid: 3597, Charles, B., Norris, R., Xiao, X., and Hague, W., Population Pharmacokinetics of Metformin in Late Pregnancy, *Ther Drug Monit*, 28(1), 2006, p.67-72
State: Excluded, Level: 1

Study Design

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Submit Data

Oral Diabetes Medications

General Form

Study Design Characteristics

Fill out this form for ALL included studies.

1. In what country does the study occur? **(check all that apply)**

☐ United States

☐ Canada

☐ United Kingdom

☐ Other (specify:)

2. What study design is used? **(check only one response)**

☐ Randomized controlled trial

☐ Non-randomized trial

☐ Prospective or retrospective/non-concurrent cohort (e.g., post-marketing surveillance)

☐ Cross-sectional study

☐ Retrospective/non-concurrent case-control

☐ Nested case-control (e.g. conducted within a larger cohort study)

☐ Other

[Clear Selection](#)

3. If this is a trial, then please mark any of the following. **(check all that apply)**

☐ Factorial design

☐ Parallel arms

☐ Cross-over design

☐ Placebo-controlled

☐ Other (specify:)

☐ None of the above apply to the trial/Not applicable (not a trial)

4. If this is a crossover trial, was there a washout period? **(check only one response)**

☐ Yes (specify how long in days:)

☐ No

☐ Not reported

☐ NA[Clear Selection](#)

5. Is the source population of this study from one of the following studies? **(check only one response)**

- ☐ UKPDS (United Kingdom Prospective Diabetes Study)
- ☐ UGDP (University Group Diabetes Program)
- ☐ DPP (Diabetes Prevention Program)
- ☐ PROactive (Prospective pioglitazone clinical trial in macrovascular events)
- ☐ Other (specify:)
- ☐ None of the above

[Clear Selection](#)

6. Was pharmaceutical support (funding or drug given for free) received to conduct the study? **(check only one response)**

- ☐ Yes
- ☐ No
- ☐ Not reported

[Clear Selection](#)

7. Study period recruitment was from:

- ☐ Start year
- ☐ End year
- ☐ Not reported

The mean/median follow-up duration was: (Record your answer in weeks. If reported separately by groups then please list in other by group.)

- | | Weeks | Other (specify:) | Not reported |
|-----------|----------------------|----------------------|--------------------------|
| 8. Mean | <input type="text"/> | <input type="text"/> | <input type="checkbox"/> |
| 9. Median | <input type="text"/> | <input type="text"/> | <input type="checkbox"/> |

10. Was a subgroup analysis conducted?

- ☐ Yes (specify which subgroups were analyzed:)
- ☐ No

[Clear Selection](#)

11. Comments:

[Enlarge](#) [Shrink](#)

Thank you very much!

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Previewing Only: You cannot submit data from this form



Previewing at Level 5

Refid: 3597, Charles, B., Norris, R., Xiao, X., and Hague, W., Population Pharmacokinetics of Metformin in Late Pregnancy, *Ther Drug Monit*, 28(1), 2006, p.67-72
State: Excluded, Level: 1

Eligibility

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Oral Diabetes Medications

General Form

Eligibility Criteria

Fill out this form for ALL included studies. If the characteristic is listed as an exclusion criteria, please check the exclusion box. Otherwise, do not check the box. Please list all inclusion criteria as exclusions (i.e., if study includes patients with coronary artery disease, specify no coronary artery disease in "other" and click exclusion).

Eligibility criteria of participants (list as exclusion criteria)		
Characteristic	Specify criteria for exclusion (e.g., age<30)	Exclusion
Age	(Specify) <div> <input type="text"/> <input type="text"/> </div> <div>Enlarge Shrink</div>	<input type="checkbox"/>
Male		<input type="checkbox"/>
Female		<input type="checkbox"/>
Any liver disease (such as elevated aminotransferases (ALT, AST, SGOT, SGPT))		<input type="checkbox"/>
Any kidney disease (such as microalbuminuria, macroalbuminuria, or elevated creatinine, GFR, or creatinine clearance)		<input type="checkbox"/>
History of cardiovascular disease (e.g., myocardial infarction, stroke, transient ischemic attack, coronary artery disease, angina)		<input type="checkbox"/>
Treatment experienced (had been on oral hypoglycemics or insulin in the past)		<input type="checkbox"/>
Neuropathy		<input type="checkbox"/>
Retinopathy		<input type="checkbox"/>
HgbA1c	(Specify HgbA1c criteria used) <div> <input type="text"/> <input type="text"/> </div>	<input type="checkbox"/>

	Enlarge Shrink	
No type 2 diabetes		
Other	(Specify) Enlarge Shrink	
Other	(Specify) Enlarge Shrink	
Other	(Specify) Enlarge Shrink	
Other	(Specify) Enlarge Shrink	
Other	(Specify) Enlarge Shrink	
Other	(Specify) Enlarge Shrink	

26. Comments:

[Enlarge](#) [Shrink](#)

Thank you very much!

Save to finish later

Submit Data

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Previewing Only: You cannot submit data from this form



Previewing at Level 6

Refid: 3597, Charles, B., Norris, R., Xiao, X., and Hague, W., Population Pharmacokinetics of Metformin in Late Pregnancy, *Ther Drug Monit*, 28(1), 2006, p.67-72
State: Excluded, Level: 1

Intervention

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Submit Data

Oral Diabetes Medications

General Form

Intervention Description

Fill out this form for ALL included RCT, cohort, and cross-sectional studies.

Please indicate the intervention or medication for each arm of the study. **(check all that apply)**

(For crossover studies, record each portion of the crossover as a separate group.)

(For cohort or cross-sectional studies, please record each medication exposure as a separate group.)

(For case control studies, please fill out the Q4 & Q5 Case-Control Outcomes Form.)

	Group 1	Group 2
1. Placebo	<input type="checkbox"/>	<input type="checkbox"/>
<u>Non medication intervention</u>		
2. Diet	<input type="checkbox"/>	<input type="checkbox"/>
3. Exercise	<input type="checkbox"/>	<input type="checkbox"/>
4. Behavioral therapy	<input type="checkbox"/>	<input type="checkbox"/>
5. Education	<input type="checkbox"/>	<input type="checkbox"/>
6. Other non medication intervention (specify under checkbox)	<input type="checkbox"/>	<input type="checkbox"/>
7. Other non medication intervention (specify under checkbox)	<input type="checkbox"/>	<input type="checkbox"/>
<u>Glucophage (metformin)</u>		
8. metformin (Glucophage)	<input type="checkbox"/>	<input type="checkbox"/>
9. metformin extended release (Glucophage XR)	<input type="checkbox"/>	<input type="checkbox"/>
<u>Second generation sulfonylureas</u>		
10. glyburide (Micronase)	<input type="checkbox"/>	<input type="checkbox"/>
11. glyburide (Diabeta)	<input type="checkbox"/>	<input type="checkbox"/>
12. glyburide (Glynase PresTab)	<input type="checkbox"/>	<input type="checkbox"/>
13. glyburide (no trade drug specified)	<input type="checkbox"/>	<input type="checkbox"/>
14. glimepiride (Amaryl)	<input type="checkbox"/>	<input type="checkbox"/>

15. glipizide (Glucotrol)

☐☐

16. glypizide XL (Glucotrol XL)

☐☐

17. glibenclamide

☐☐

18. glyclazide

☐☐

19. unspecified sulfonylurea

☐☐**Alpha glucosidase inhibitors**

20. miglitol (Glyset)

☐☐

21. acarbose (Precose)

☐☐

22. voglibose

☐☐

23. unspecified alpha-glucosidase inhibitor

☐☐**Non-sulfonylurea secretagogues/metiglinides**

24. nateglinide (Starlix)

☐☐

25. repaglinide (Prandin)

☐☐**Thiazolidinediones**

26. rosiglitazone (Avandia)

☐☐

27. pioglitazone (Actos)

☐☐

28. troglitazone

☐☐

29. unspecified TZD

☐☐**Combined medications in one pill**

30. avandia + metformin (Avandamet)

☐☐

31. glyburide + metformin (Glucovance)

☐☐

32. metformin + glipizide (Metaglip)

☐☐

33. Other (specify under checkbox)

☐☐

<input type="checkbox"/>		<input type="checkbox"/>	
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34. Other (specify under checkbox)

☐☐

<input type="checkbox"/>		<input type="checkbox"/>	
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35. Other (specify under checkbox)

☐☐

<input type="checkbox"/>		<input type="checkbox"/>	
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36. Other (specify under checkbox)

☐☐

<input type="checkbox"/>		<input type="checkbox"/>	
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37. Other (specify under checkbox)

☐☐

<input type="checkbox"/>		<input type="checkbox"/>	
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38. Other (specify under checkbox)

☐☐



<input type="checkbox"/>		<input type="checkbox"/>	
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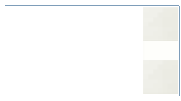

39. Other (specify under checkbox)




☐☐


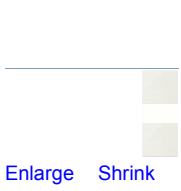
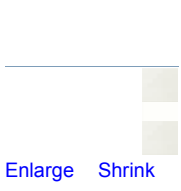
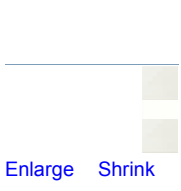
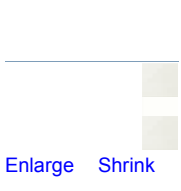
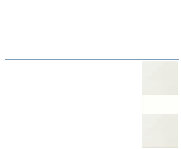
<input type="checkbox"/>		<input type="checkbox"/>	
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For each medication listed in Q1, please indicate the <u>initial</u> d		
Medication	Group 1	Group 2

<p>Please select medication</p> <p>Please Select</p> <div></div>	<p>Initial dose: <input type="text"/></p> <p>Unit:</p> <p><input type="radio"/> mg</p> <p><input type="radio"/> micronized tabs</p> <p><input type="radio"/> mcg</p> <p><input type="radio"/> IU</p> <p><input type="radio"/> Other <input type="text"/></p> <p><input type="radio"/> Not specified</p> <p>Clear Selection</p> <p>Was the dose:</p> <p><input type="radio"/> fixed</p> <p><input type="radio"/> escalated</p> <p><input type="radio"/> other <input type="text"/></p> <p><input type="radio"/> not reported</p> <p>Clear Selection</p> <p>If escalated, maximum dose: <input type="text"/></p>	<p>Initial dose: <input type="text"/></p> <p>Unit:</p> <p><input type="radio"/> mg</p> <p><input type="radio"/> micronized tabs</p> <p><input type="radio"/> mcg</p> <p><input type="radio"/> IU</p> <p><input type="radio"/> Other <input type="text"/></p> <p><input type="radio"/> Not specified</p> <p>Clear Selection</p> <p>Was the dose:</p> <p><input type="radio"/> fixed</p> <p><input type="radio"/> escalated</p> <p><input type="radio"/> other <input type="text"/></p> <p><input type="radio"/> not reported</p> <p>Clear Selection</p> <p>If escalated, maximum dose: <input type="text"/></p>
<p>Please select medication</p> <p>Please Select</p> <div></div>	<p>Initial dose: <input type="text"/></p> <p>Unit:</p> <p><input type="radio"/> mg</p> <p><input type="radio"/> micronized tabs</p> <p><input type="radio"/> mcg</p> <p><input type="radio"/> IU</p> <p><input type="radio"/> Other <input type="text"/></p> <p><input type="radio"/> Not specified</p> <p>Clear Selection</p> <p>Was the dose:</p> <p><input type="radio"/> fixed</p> <p><input type="radio"/> escalated</p> <p><input type="radio"/> other <input type="text"/></p> <p><input type="radio"/> not reported</p> <p>Clear Selection</p> <p>If escalated, maximum dose: <input type="text"/></p>	<p>Initial dose: <input type="text"/></p> <p>Unit:</p> <p><input type="radio"/> mg</p> <p><input type="radio"/> micronized tabs</p> <p><input type="radio"/> mcg</p> <p><input type="radio"/> IU</p> <p><input type="radio"/> Other <input type="text"/></p> <p><input type="radio"/> Not specified</p> <p>Clear Selection</p> <p>Was the dose:</p> <p><input type="radio"/> fixed</p> <p><input type="radio"/> escalated</p> <p><input type="radio"/> other <input type="text"/></p> <p><input type="radio"/> not reported</p> <p>Clear Selection</p> <p>If escalated, maximum dose: <input type="text"/></p>
	<p>Initial dose: <input type="text"/></p>	<p>Initial dose: <input type="text"/></p>

<p>Please select medication</p> <p>Please Select</p> <div></div> <p>Enlarge Shrink</p>	<p>Unit:</p> <p><input type="radio"/> mg</p> <p><input type="radio"/> micronized tabs</p> <p><input type="radio"/> mcg</p> <p><input type="radio"/> IU</p> <p><input type="radio"/> Other _____</p> <p><input type="radio"/> Not specified</p> <p>Clear Selection</p> <p>Was the dose:</p> <p><input type="radio"/> fixed</p> <p><input type="radio"/> escalated</p> <p><input type="radio"/> other _____</p> <p><input type="radio"/> not reported</p> <p>Clear Selection</p> <p>If escalated, maximum dose: _____</p>	<p>Unit:</p> <p><input type="radio"/> mg</p> <p><input type="radio"/> micronized tabs</p> <p><input type="radio"/> mcg</p> <p><input type="radio"/> IU</p> <p><input type="radio"/> Other _____</p> <p><input type="radio"/> Not specified</p> <p>Clear Selection</p> <p>Was the dose:</p> <p><input type="radio"/> fixed</p> <p><input type="radio"/> escalated</p> <p><input type="radio"/> other _____</p> <p><input type="radio"/> not reported</p> <p>Clear Selection</p> <p>If escalated, maximum dose: _____</p>
<p>Please select medication</p> <p>Please Select</p> <div></div> <p>Enlarge Shrink</p>	<p>Initial dose: _____</p> <p>Unit:</p> <p><input type="radio"/> mg</p> <p><input type="radio"/> micronized tabs</p> <p><input type="radio"/> mcg</p> <p><input type="radio"/> IU</p> <p><input type="radio"/> Other _____</p> <p><input type="radio"/> Not specified</p> <p>Clear Selection</p> <p>Was the dose:</p> <p><input type="radio"/> fixed</p> <p><input type="radio"/> escalated</p> <p><input type="radio"/> other _____</p> <p><input type="radio"/> not reported</p> <p>Clear Selection</p> <p>If escalated, maximum dose: _____</p>	<p>Initial dose: _____</p> <p>Unit:</p> <p><input type="radio"/> mg</p> <p><input type="radio"/> micronized tabs</p> <p><input type="radio"/> mcg</p> <p><input type="radio"/> IU</p> <p><input type="radio"/> Other _____</p> <p><input type="radio"/> Not specified</p> <p>Clear Selection</p> <p>Was the dose:</p> <p><input type="radio"/> fixed</p> <p><input type="radio"/> escalated</p> <p><input type="radio"/> other _____</p> <p><input type="radio"/> not reported</p> <p>Clear Selection</p> <p>If escalated, maximum dose: _____</p>
<p>Please select medication</p> <p>Please Select</p>	<p>Initial dose: _____</p> <p>Unit:</p> <p><input type="radio"/> mg</p>	<p>Initial dose: _____</p> <p>Unit:</p> <p><input type="radio"/> mg</p>

<div></div>	<div><input type="radio"/> micronized tabs</div> <div><input type="radio"/> mcg</div> <div><input type="radio"/> IU</div> <div><input type="radio"/> Other _____</div> <div><input type="radio"/> Not specified</div> <div>Clear Selection</div> <div>Was the dose:</div> <div><input type="radio"/> fixed</div> <div><input type="radio"/> escalated</div> <div><input type="radio"/> other _____</div> <div><input type="radio"/> not reported</div> <div>Clear Selection</div> <div>If escalated, _____</div> <div>maximum dose: _____</div>	<div><input type="radio"/> micronized tabs</div> <div><input type="radio"/> mcg</div> <div><input type="radio"/> IU</div> <div><input type="radio"/> Other _____</div> <div><input type="radio"/> Not specified</div> <div>Clear Selection</div> <div>Was the dose:</div> <div><input type="radio"/> fixed</div> <div><input type="radio"/> escalated</div> <div><input type="radio"/> other _____</div> <div><input type="radio"/> not reported</div> <div>Clear Selection</div> <div>If escalated, _____</div> <div>maximum dose: _____</div>
<div>Please select medication</div> <div><div>Please Select</div><div></div></div>	<div>Initial dose: _____</div> <div>Unit:</div> <div><input type="radio"/> mg</div> <div><input type="radio"/> micronized tabs</div> <div><input type="radio"/> mcg</div> <div><input type="radio"/> IU</div> <div><input type="radio"/> Other _____</div> <div><input type="radio"/> Not specified</div> <div>Clear Selection</div> <div>Was the dose:</div> <div><input type="radio"/> fixed</div> <div><input type="radio"/> escalated</div> <div><input type="radio"/> other _____</div> <div><input type="radio"/> not reported</div> <div>Clear Selection</div> <div>If escalated, _____</div> <div>maximum dose: _____</div>	<div>Initial dose: _____</div> <div>Unit:</div> <div><input type="radio"/> mg</div> <div><input type="radio"/> micronized tabs</div> <div><input type="radio"/> mcg</div> <div><input type="radio"/> IU</div> <div><input type="radio"/> Other _____</div> <div><input type="radio"/> Not specified</div> <div>Clear Selection</div> <div>Was the dose:</div> <div><input type="radio"/> fixed</div> <div><input type="radio"/> escalated</div> <div><input type="radio"/> other _____</div> <div><input type="radio"/> not reported</div> <div>Clear Selection</div> <div>If escalated, _____</div> <div>maximum dose: _____</div>
Medication	Group 1	Group 2
<div>Please select intervention or medication</div> <div><div>Please Select</div><div></div></div>	<div><input type="radio"/> 1x/day</div> <div><input type="radio"/> 2x/day</div>	<div><input type="radio"/> 1x/day</div> <div><input type="radio"/> 2x/day</div>

 <p>Enlarge Shrink</p>	<p><input type="radio"/> 3x/day</p> <p><input type="radio"/> Other (specify) _____</p> <p><input type="radio"/> Not specified</p> <p>Clear Selection</p>	<p><input type="radio"/> 3x/day</p> <p><input type="radio"/> Other (specify) _____</p> <p><input type="radio"/> Not specified</p> <p>Clear Selection</p>
<p>Please select intervention or medication</p> <p>Please Select</p>  <p>Enlarge Shrink</p>	<p><input type="radio"/> 1x/day</p> <p><input type="radio"/> 2x/day</p> <p><input type="radio"/> 3x/day</p> <p><input type="radio"/> Other (specify) _____</p> <p><input type="radio"/> Not specified</p> <p>Clear Selection</p>	<p><input type="radio"/> 1x/day</p> <p><input type="radio"/> 2x/day</p> <p><input type="radio"/> 3x/day</p> <p><input type="radio"/> Other (specify) _____</p> <p><input type="radio"/> Not specified</p> <p>Clear Selection</p>
<p>Please select intervention or medication</p> <p>Please Select</p>  <p>Enlarge Shrink</p>	<p><input type="radio"/> 1x/day</p> <p><input type="radio"/> 2x/day</p> <p><input type="radio"/> 3x/day</p> <p><input type="radio"/> Other (specify) _____</p> <p><input type="radio"/> Not specified</p> <p>Clear Selection</p>	<p><input type="radio"/> 1x/day</p> <p><input type="radio"/> 2x/day</p> <p><input type="radio"/> 3x/day</p> <p><input type="radio"/> Other (specify) _____</p> <p><input type="radio"/> Not specified</p> <p>Clear Selection</p>
<p>Please select intervention or medication</p> <p>Please Select</p>  <p>Enlarge Shrink</p>	<p><input type="radio"/> 1x/day</p> <p><input type="radio"/> 2x/day</p> <p><input type="radio"/> 3x/day</p> <p><input type="radio"/> Other (specify) _____</p> <p><input type="radio"/> Not specified</p> <p>Clear Selection</p>	<p><input type="radio"/> 1x/day</p> <p><input type="radio"/> 2x/day</p> <p><input type="radio"/> 3x/day</p> <p><input type="radio"/> Other (specify) _____</p> <p><input type="radio"/> Not specified</p> <p>Clear Selection</p>
<p>Please select intervention or medication</p> <p>Please Select</p>  <p>Enlarge Shrink</p>	<p><input type="radio"/> 1x/day</p> <p><input type="radio"/> 2x/day</p> <p><input type="radio"/> 3x/day</p> <p><input type="radio"/> Other (specify) _____</p> <p><input type="radio"/> Not specified</p> <p>Clear Selection</p>	<p><input type="radio"/> 1x/day</p> <p><input type="radio"/> 2x/day</p> <p><input type="radio"/> 3x/day</p> <p><input type="radio"/> Other (specify) _____</p> <p><input type="radio"/> Not specified</p> <p>Clear Selection</p>
<p>Please select intervention or medication</p> <p>Please Select</p> 	<p><input type="radio"/> 1x/day</p> <p><input type="radio"/> 2x/day</p> <p><input type="radio"/> 3x/day</p>	<p><input type="radio"/> 1x/day</p> <p><input type="radio"/> 2x/day</p> <p><input type="radio"/> 3x/day</p>

[Enlarge](#) [Shrink](#)
☐ Other
(specify) _____
☐ Not
specified

[Clear Selection](#)
☐ Other
(specify) _____
☐ Not
specified

[Clear Selection](#)



304. Please indicate if the duration of exposure to the medication was recorded as the mean duration or planned duration? (If both, please on

- ☐ Mean duration
- ☐ Planned duration
- ☐ Not reported
- ☐ Other _____


[Clear Selection](#)

For each intervention		
Medication	Group 1	
Please select intervention or medication Please Select _____ _____ _____ _____ Enlarge Shrink	weeks _____ months _____ years _____	weeks _____ months _____ years _____
Please select intervention or medication Please Select _____ _____ _____ _____ Enlarge Shrink	weeks _____ months _____ years _____	weeks _____ months _____ years _____
Please select intervention or medication Please Select _____ _____ _____ _____ Enlarge Shrink	weeks _____ months _____ years _____	weeks _____ months _____ years _____
Please select intervention or medication Please Select _____ _____ _____ _____ Enlarge Shrink	weeks _____ months _____ years _____	weeks _____ months _____ years _____
Please select intervention or medication Please Select _____ _____ _____ _____ Enlarge Shrink	weeks _____ months _____ years _____	weeks _____ months _____ years _____
Please select intervention or medication Please Select _____ _____ _____ _____ Enlarge Shrink	weeks _____ months _____ years _____	weeks _____ months _____ years _____

Group 1	Group 2	Group 3
Indicate which medications group was on prior to starting the study. (check all that apply)	Indicate which medications group was on prior to starting the study. (check all that apply)	Indicate which medications group was on prior to starting the study. (check all that apply)
<input type="checkbox"/> placebo	<input type="checkbox"/> placebo	<input type="checkbox"/> placebo
<input type="checkbox"/> diet	<input type="checkbox"/> diet	<input type="checkbox"/> diet
<input type="checkbox"/> exercise	<input type="checkbox"/> exercise	<input type="checkbox"/> exercise
<input type="checkbox"/> behavioral therapy	<input type="checkbox"/> behavioral therapy	<input type="checkbox"/> behavioral therapy
<input type="checkbox"/> education	<input type="checkbox"/> education	<input type="checkbox"/> education
<input type="checkbox"/> metformin (Glucophage)	<input type="checkbox"/> metformin (Glucophage)	<input type="checkbox"/> metformin (Glucophage)
<input type="checkbox"/> metformin extended release (Glucophage XR)	<input type="checkbox"/> metformin extended release (Glucophage XR)	<input type="checkbox"/> metformin extended release (Glucophage XR)
<input type="checkbox"/> glyburide (Micronase)	<input type="checkbox"/> glyburide (Micronase)	<input type="checkbox"/> glyburide (Micronase)
<input type="checkbox"/> glyburide (Diabeta)	<input type="checkbox"/> glyburide (Diabeta)	<input type="checkbox"/> glyburide (Diabeta)
<input type="checkbox"/> glyburide (Glynase PresTab)	<input type="checkbox"/> glyburide (Glynase PresTab)	<input type="checkbox"/> glyburide (Glynase PresTab)
<input type="checkbox"/> glyburide (no trade drug specified)	<input type="checkbox"/> glyburide (no trade drug specified)	<input type="checkbox"/> glyburide (no trade drug specified)
<input type="checkbox"/> glimepiride (Amaryl)	<input type="checkbox"/> glimepiride (Amaryl)	<input type="checkbox"/> glimepiride (Amaryl)
<input type="checkbox"/> glipizide (Glucotrol)	<input type="checkbox"/> glipizide (Glucotrol)	<input type="checkbox"/> glipizide (Glucotrol)
<input type="checkbox"/> glipizide XL (Glucotrol XL)	<input type="checkbox"/> glipizide XL (Glucotrol XL)	<input type="checkbox"/> glipizide XL (Glucotrol XL)
<input type="checkbox"/> glibenclamide	<input type="checkbox"/> glibenclamide	<input type="checkbox"/> glibenclamide
<input type="checkbox"/> glyclazide	<input type="checkbox"/> glyclazide	<input type="checkbox"/> glyclazide
<input type="checkbox"/> miglitol (Glyset)	<input type="checkbox"/> miglitol (Glyset)	<input type="checkbox"/> miglitol (Glyset)
<input type="checkbox"/> acarbose (Precose)	<input type="checkbox"/> acarbose (Precose)	<input type="checkbox"/> acarbose (Precose)
<input type="checkbox"/> voglibose	<input type="checkbox"/> voglibose	<input type="checkbox"/> voglibose
<input type="checkbox"/> nateglinide (Starlix)	<input type="checkbox"/> nateglinide (Starlix)	<input type="checkbox"/> nateglinide (Starlix)
<input type="checkbox"/> repaglinide (Prandin)	<input type="checkbox"/> repaglinide (Prandin)	<input type="checkbox"/> repaglinide (Prandin)
<input type="checkbox"/> rosiglitazone (Avandia)	<input type="checkbox"/> rosiglitazone (Avandia)	<input type="checkbox"/> rosiglitazone (Avandia)
<input type="checkbox"/> pioglitazone (Actos)	<input type="checkbox"/> pioglitazone (Actos)	<input type="checkbox"/> pioglitazone (Actos)
<input type="checkbox"/> troglitazone	<input type="checkbox"/> troglitazone	<input type="checkbox"/> troglitazone
<input type="checkbox"/> avandia + metformin (Avandamet)	<input type="checkbox"/> avandia + metformin (Avandamet)	<input type="checkbox"/> avandia + metformin (Avandamet)
<input type="checkbox"/> glyburide +	<input type="checkbox"/> glyburide +	<input type="checkbox"/> glyburide +

<input type="checkbox"/> metformin (Glucovance)	<input type="checkbox"/> metformin (Glucovance)	<input type="checkbox"/> metformin (Glucovance)
<input type="checkbox"/> metformin + glyburide (Metaglip)	<input type="checkbox"/> metformin + glyburide (Metaglip)	<input type="checkbox"/> metformin + glyburide (Metaglip)
<input type="checkbox"/> unspecified sulfonylurea	<input type="checkbox"/> unspecified sulfonylurea	<input type="checkbox"/> unspecified sulfonylurea
<input type="checkbox"/> unspecified alpha-glucosidase inhibitors	<input type="checkbox"/> unspecified alpha-glucosidase inhibitors	<input type="checkbox"/> unspecified alpha-glucosidase inhibitors
<input type="checkbox"/> unspecified TZD	<input type="checkbox"/> unspecified TZD	<input type="checkbox"/> unspecified TZD
<input type="checkbox"/> Other (specify below) _____ 	<input type="checkbox"/> Other (specify below) _____ 	<input type="checkbox"/> Other (specify below) _____

373. Comments:

[Enlarge](#) [Shrink](#)

374. If the dose is escalating, please record the mean dose for each medication for each group.

[Enlarge](#) [Shrink](#)

Thank you very much!

Form took 8.28125 seconds to render

Previewing Only: You cannot submit data from this form

**Previewing at Level 7**

Refid: 3597, Charles, B., Norris, R., Xiao, X., and Hague, W., Population Pharmacokinetics of Metformin in Late Pregnancy, *Ther Drug Monit*, 28(1), 2006, p.67-72
State: Excluded, Level: 1

Population

Save to finish later

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Oral Diabetes Medications

General Form

Study Population Characteristics

Fill out this form for ALL included studies.

Please fill in the study population characteristics (age, gender, race/ethnicity, BMI, HgbA1c, and duration of use). **need to record standard errors or standard deviations for these measures.**

Total N at Enrollment

	Group 1	Group 2	Group 3	Group 4
1. Total N for enrollment	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

Age




























	Group 1	Group 2	Group 3	Group 4
2. Mean age	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
3. Age range	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
4. Age, other (specify age categories below in Q5 and record results under each group:)	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
5. Specify other age classification for Q4.				

[Enlarge](#) [Shrink](#)**Male**

	Group 1	Group 2	Group 3	Group 4
6. N	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
7. %	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

Race/ethnicity

	Group 1	Group 2	Group 3	Group 4
8. African American (N)	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
9. African American (%)	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
10. Caucasian (N)	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

11. Caucasian (%)				
	Group 1	Group 2	Group 3	Group 4
12. Asian or Asian American (N)				
13. Asian or Asian American (%)				
14. Hispanic/Latino (N)				
15. Hispanic/Latino (%)				
16. Other race/ethnicity (N) (specify other race/ethnicity below in Q20 and record results under each group)				
17. Other race/ethnicity (%) (specify other race/ethnicity below in Q20 and record results under each group)				
18. Other race/ethnicity (N) (specify other race/ethnicity below in Q21 and record results under each group)				
19. Other race/ethnicity (%) (specify other race/ethnicity below in Q21 and record results under each group)				
20. Specify other race/ethnicity category for Q16 or Q17.				

[Enlarge](#) [Shrink](#)

21. Specify other race/ethnicity category for Q18 or Q19.

[Enlarge](#) [Shrink](#)**BMI/Weight**

	Group 1	Group 2	Group 3	Group 4
22. Mean BMI (kg/m ²)				
23. Other BMI measures (specify other BMI measures below in Q26 and record results under each group:)				
24. Mean weight (kg)				
25. Other weight measures (specify other weight measures below in Q27 and record results under each group:)				
26. Specify other BMI measures for Q23.				

[Enlarge](#) [Shrink](#)

27. Specify other weight measures for Q25.

[Enlarge](#) [Shrink](#)**HgbA1c**

	Group 1	Group 2	Group 3	Group 4
28. Mean HgbA1c(%)				
29. Other HgbA1c measures (specify HgbA1c measures below in Q33 and record results under each group:)				
30. Mean HgbA1 (%)				
31. Other HgbA1 measures (specify other HgbA1 measures below in Q34 and record results under each group:)				
32. Other hemoglobin measures (specify other hemoglobin measures below in Q35)				

and record
results under
each group:)

33. Specify other HgbA1c measures for Q29.

[Enlarge](#) [Shrink](#)

34. Specify other HgbA1 measures for Q31.

[Enlarge](#) [Shrink](#)

35. Specify other hemoglobin measures for Q32.

[Enlarge](#) [Shrink](#)

Duration of Diabetes

Group 1

Group 2

Group 3

Group 4

36. Mean
duration of
diabetes (in
years)



37. Other
duration of
diabetes
measures
(specify other
duration of
diabetes
measures
below in Q38
and record
results under
each group:)



38. Specify other duration of diabetes measures for Q37.

[Enlarge](#) [Shrink](#)

Other key characteristic that was different between randomized groups

Group 1

Group 2

Group 3

Group 4

39. Other key
characteristic
(specify key
characteristic
below in Q43
and record
results under
each group) -
mean



40. Other key
characteristic
(specify key
characteristic
below in Q43
and record
results under
each group) -
median



41. Other key
characteristic
(specify key
characteristic
below in Q43
and record



results under
each group) -
N

42. Other key
characteristic
(specify key
characteristic
below in Q43
and record
results under
each group) -
%



43. Specify other key characteristic for Q39, Q40, Q41, or Q42.

[Enlarge](#) [Shrink](#)

44. Comments:

[Enlarge](#) [Shrink](#)

Thank you very much!

Save to finish later

Submit Data

Form took 2.6875 seconds to render

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Previewing at Level 8

Refid: 3597, Charles, B., Norris, R., Xiao, X., and Hague, W., Population Pharmacokinetics of Metformin in Late Pregnancy, *Ther Drug Monit*, 28(1), 2006, p.67-72
State: Excluded, Level: 1

Q1 & Q3 Outcomes

Save to finish later

Submit Data

Oral Diabetes Medications

Q1 and Q3 (Proximal Clinical Outcomes and Quality of Life) Outcomes Form

Fill out this form only for proximal clinical outcomes and quality of life outcomes

1. Outcome of interest being reported on this form: (check only one response)

- ☐ LDL calculated
- ☐ LDL measured
- ☐ HDL
- ☐ HgbA1c
- ☐ Hemoglobin a1
- ☐ Total glycated hemoglobin
- ☐ Weight
- ☐ BMI
- ☐ Triglyceride
- ☐ Systolic blood pressure
- ☐ Diastolic blood pressure
- ☐ 2 hour postprandial glucose **Note: do not need to abstract area under the curve data or any other measure besides 2 hour ppg**
- ☐ Fasting plasma glucose (only report if 2 hour postprandial glucose is reported)
- ☐ QOL (quality of life): treatment satisfaction, well-being, or functional status
- ☐ Other (specify:)

[Clear Selection](#)

2. If quality of life assessed, what validated measure was used?

- ☐ Diabetes treatment satisfaction questionnaire from UKPDS
- ☐ Diabetes well-being questionnaire from UKPDS
- ☐ Medical outcomes study SF-36
- ☐ Euro-QoL (EQ-5D)
- ☐ ADL-activities of daily living
- ☐ IADL-instrumental activities of daily living
- ☐ WHO-DTSQ
- ☐ WHO-WBQ
- ☐ Other validated questionnaire or instrument (specify:)



☐ Other non-validated questionnaire or instrument (specify:) _____

3. What units were used? (check only one response)

☐ mmol/L

☐ umol/L

☐ mg/dL

☐ mmHg

☐ %

☐ kg/m2

☐ pounds

☐ kilograms













































☐ Other (specify:) _____ 





































[Clear Selection](#)

Please fill in the results below.

(Note: Please record the N for analysis by group at the bottom.

Please report mean difference from placebo and/or mean difference from other group. If these measures are available, you do not need to record the p-value if there are other measures of variability available (e.g., standard deviation, standard error, IQR, etc.).

	Group 1	Group 2	Group 3	Group 4
4. Baseline Mean				
5. Standard deviation (sd)				
6. Standard error (se)				
7. Baseline Median				
8. Lower limit of IQR (interquartile range) 25%				
9. Upper limit of IQR (interquartile range) 75%				
	Group 1	Group 2	Group 3	Group 4
10. Final Mean				
11. Standard deviation (sd)				
12. Standard error (se)				
13. Final Median				
14. Lower limit of IQR (interquartile range) 25%				
15. Upper limit of IQR (interquartile range) 75%				
16. Mean difference				

from baseline				
17. Mean difference from placebo				
18. Mean difference from other group (specify other group below:)				
19. 95% CI (lower limit)				
20. 95% CI (upper limit)				
21. p-value				
22. Other (specify below:)				
23. Other (specify below:)				
24. Other (specify below:)				
25. Other (specify below:)				

26. Specify other group for mean difference comparison.

[Enlarge](#) [Shrink](#)

27. Specify other measures.

[Enlarge](#) [Shrink](#)

28. Specify other measures.

[Enlarge](#) [Shrink](#)

29. Specify other measures.

[Enlarge](#) [Shrink](#)

30. Specify other measures.

[Enlarge](#) [Shrink](#)

31. Comments:

[Enlarge](#) [Shrink](#)

	Group 1		Group 2		Group 3		Group 4
32. N for the analysis							

Thank you very much!

Save to finish later

Submit Data

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Previewing at Level 19

Refid: 3597, Charles, B., Norris, R., Xiao, X., and Hague, W., Population Pharmacokinetics of Metformin in Late Pregnancy, *Ther Drug Monit*, 28(1), 2006, p.67-72
State: Excluded, Level: 1

Q2 Outcomes

Save to finish later

Submit Data

Oral Diabetes Medications

Q2 (Distal Diabetes-Related Complications) Outcomes Form

Fill out this form only for distal diabetes-related complications (e.g., mortality, attack, retinopathy, and nephropathy). Fill out one form for each distal diabetes

1. Outcome of interest being reported on this form: (check only one response)

- ☐ All cause mortality
- ☐ Cardiovascular disease mortality
- ☐ Cardiovascular disease morbidity
- ☐ Coronary heart diseases
- ☐ Cerebrovascular diseases
- ☐ Diabetic retinopathy
- ☐ Diabetic nephropathy (e.g. urinary albumin, micro or macroalbuminuria, creatinine, kidney disease, GFR)
- ☐ Peripheral arterial disease
- ☐ Neuropathy
- ☐ Other (specify:)

[Clear Selection](#)

2. Outcomes of Interest: All cause mortality

Indicate how the outcome was assessed. (check all that apply)

- ☐ Confirmed by National or State death certificate registry
- ☐ Other (Specify definition:)
- ☐ Other (Specify definition:)
- ☐ Present, but unclear definition

3. Outcomes of Interest: Cardiovascular Disease Mortality

Indicate how the outcome was assessed. (check all that apply)

- ☐ Fatal myocardial infarction
- ☐ Sudden cardiac death
- ☐ Fatal stroke
- ☐ Confirmed by death certificate registry
- ☐ Used ICD-9 codes to determine (specify:)

☐ Other (specify:) _____

☐ Other (specify:) _____

☐ Present, but unclear definition

Outcome(s) of Interest: C	
Outcome of Interest	Indicate how the outcome was ass
CVD Morbidity	<input type="checkbox"/> Use of nitrotyglycerine or oth
Coronary heart diseases	<input type="checkbox"/> Mycardial infarction (Non-fatal) <input type="checkbox"/> In absence of percutaneous coronary intervention or CABG had at least 2 of: a)Symptoms suggestive of myc more, b) EKG evidence of MI, c) Elevated cardiac enzymes (CPK-MB, or troponin) serum levels d) Survived >24h <input type="checkbox"/> Silent myocardial infarction <input type="checkbox"/> Angina <input type="checkbox"/> Ischemic heart disease <input type="checkbox"/> Coronary artery bypass surgery <input type="checkbox"/> Angioplasty or angiography showing at least 1 stenosis >50% <input type="checkbox"/> Used ICD-9 codes 410-414 <input type="checkbox"/> Used other ICD-9 codes (specify ICD-9 codes used:) <input type="checkbox"/> Used Patient Self-Report <input type="checkbox"/> Other (specify:) <input type="checkbox"/> Other (specify:) <input type="checkbox"/> Present, but unclear definition
Cerebrovascular diseases	<input type="checkbox"/> Stroke (defined as acute focal neurological deficit lasting for longer than 24h or resulting in death) <input type="checkbox"/> Transient ischemic attack (acute focal neurological deficit lasting for less than 24h) <input type="checkbox"/> Carotid endarterectomy <input type="checkbox"/> Used Patient self report <input type="checkbox"/> Used ICD-9 codes (specify ICD-9 codes used:) <input type="checkbox"/> Other (specify:) <input type="checkbox"/> Other (specify:) <input type="checkbox"/> Present, but unclear definition

10. Outcomes of Interest: Diabetic Retinopathy




Indicate how the outcome was assessed. (check all that apply)

☐ History of cataract extraction

☐ Macular edema




☐ Microaneurysms only

☐ Background retinopathy

- ☐ Proliferative retinopathy
- ☐ Mild non-proliferative diabetic retinopathy
- ☐ Moderate or severe non- proliferative diabetic retinopathy
- ☐ Visual Acuity
- ☐ ETDRS (Early Treatment Diabetic Retinopathy) criteria used
- ☐ Used ICD-9 codes: 362.0, 362.1, or 362.53
- ☐ Used other ICD-9 codes (specify ICD-9 codes used:) _____ 
- ☐ Used patient self-report
- ☐ Other (specify:) _____ 
- ☐ Other (specify:) _____ 
- ☐ Present, but unclear definition




11. Outcomes of Interest: Diabetic Nephropathy

Indicate how the outcome was assessed. (check all that apply)

- ☐ Proteinuria/Albuminuria
- ☐ Change in GFR/Creatinine clearance
- ☐ Change serum creatinine
- ☐ ESRD
- ☐ Renal Replacement Therapy or Transplant
- ☐ Used ICD-9 codes (specify ICD-9 codes used:) _____ 
- ☐ Other (specify:) _____ 
- ☐ Other (specify:) _____ 
- ☐ Present, but unclear definition

12. Outcomes of Interest: PAD

Indicate how the outcome was assessed. (check all that apply)

- ☐ Claudication
- ☐ Peripheral revascularization procedure – angioplasty, bypass surgery or stenting
- ☐ Gangrene
- ☐ Limb amputation
- ☐ Decreased ankle-brachial index
- ☐ Decreased systolic arm-toe gradient
- ☐ Patient self report of (specify:) _____ 
- ☐ Other (specify:) _____ 
- ☐ Other (specify:) _____ 
- ☐ Present, but unclear definition

13. Outcomes of Interest: Neuropathy

Indicate how the outcome was assessed. (check all that apply)

- ☐ Peripheral, assessed by monofilament test
- ☐ Peripheral, assessed by other means (specify:)
- ☐ Autonomic (specify test:)
- ☐ Used ICD-9 codes 250.6 for peripheral
- ☐ Used other ICD-9 codes (specify ICD-9 codes used:)
- ☐ Other (specify:)
- ☐ Other (specify:)
- ☐ Present, but unclear definition

14. Is analysis adjusted for confounders?


























































- ☐ Yes
- ☐ No
- ☐ Not reported
- ☐ Not applicable (e.g., RCT)

15. What covariates/confounders were adjusted? ****List all covariates here**** (Choose all applicable)

- ☐ Age
- ☐ Gender
- ☐ Race
- ☐ BMI
- ☐ Other (specify:)
- ☐ Other (specify:)
- ☐ Other (specify:)
- ☐ Other (specify:)
- ☐ Other (specify:)
- ☐ Other (specify:)
- ☐ Other (specify:)
- ☐ Other (specify:)
- ☐ Other (specify:)
- ☐ Other (specify:)
- ☐ Other (specify:)
- ☐ Not applicable (e.g., RCT)

Please report results of the most fully adjusted model if there is more than one model.

	Group 1	Group 2	Group 3	Group 4
16. Number of people in the analysis for each group	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
17. Numerator: # of events	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
18. Numerator: %	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

with events				
19. Demoninator: # Time Unit				
20. Demoninator: Record the units that was used for Q19 (days, weeks, months, years, person- years)				
21. Incidence rate				
22. 95% CI: Lower limit				
23. 95% CI: Upper limit				
24. Difference in incidence rates				
25. 95% CI: Lower limit				
26. 95% CI: Upper limit				
27. p-value				
28. Relative risk				
29. Relative hazard/hazard ratio				
30. Odds ratio				
31. 95% CI: Lower limit				
32. 95% CI: Upper limit				
33. p-value				
34. Relative risk reduction				
35. Other (specify below:)				
36. Other (specify below:)				
37. Other (specify below:)				
38. Specify other analysis:				

[Enlarge](#) [Shrink](#)

39. Specify other analysis:

[Enlarge](#) [Shrink](#)

40. Specify other analysis:

[Enlarge](#) [Shrink](#)

41. Comments:

[Enlarge](#) [Shrink](#)

Thank you very much!

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Previewing at Level 24

Refid: 3597, Charles, B., Norris, R., Xiao, X., and Hague, W., Population Pharmacokinetics of Metformin in Late Pregnancy, *Ther Drug Monit*, 28(1), 2006, p.67-72
State: Excluded, Level: 1

Q4 & Q5 Outcomes

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Oral Diabetes Medications

Q4 & Q5 (Safety & Adverse Events) Outcomes Form

Fill out this form only for safety & adverse events outcomes (e.g., hypoglycemia, thrombocytopenia, leukopenia, allergic reactions requiring hospitalization or cpancytopenia, gastrointestinal problems, and other adverse events). Fill out o




















































Choose the outcome of interest (choose one only) and then specify h	
	Adverse Event
	<input type="checkbox"/> hypoglycemia
	<input type="checkbox"/> elevated aminotransferase levels
	<input type="checkbox"/> cholestatic abnormality
	<input type="checkbox"/> liver failure
	<input type="checkbox"/> congestive heart failure

<input type="checkbox"/> lactic acidosis
<input type="checkbox"/> cancer
<input type="checkbox"/> anemia
<input type="checkbox"/> thrombocytopenia
<input type="checkbox"/> leukopenia
<input type="checkbox"/> allergic reactions
<input type="checkbox"/> edema/hypervolemia
<input type="checkbox"/> gastrointestinal problems

<input type="checkbox"/> mortality (Please record mortality on Q2 form unless cross-sectional study)
<input type="checkbox"/> Other (specify:) or number withdrawn due to unspecified adverse events

Serious event = comprised any experience that was fatal, life-threatening, permanently or substantially d
ER visit, or an important medical event that jeopardized the patient or required intervention such as trans

	Group 1	Group 2	Group 3	Group 4
31. Number of people in the analysis for each group	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
32. Number WITHDRAWN from study due to adverse events	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
33. Numerator: # with FIRST SERIOUS event	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
34. Numerator: % with FIRST SERIOUS events	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
35. Numerator: # with TOTAL FIRST events	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
36. Numerator: % with TOTAL FIRST events	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
37. Numerator: Other (specify below in Q38)	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
38. Specify other numerator.	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
39. Numerator: Other (specify below in Q40)	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
40. Specify other numerator.	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
41. Denominator: # Time Unit	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
42. Denominator: Record the	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

units that was used for Q41 (days, weeks, months, years, person-years)				
43. Incidence rate				
44. 95% CI: Lower limit				
45. 95% CI: Upper limit				
46. Difference in incidence rates				
47. 95% CI: Lower limit				
48. 95% CI: Upper limit				
49. p-value				
50. Relative risk				
51. Relative hazard/hazard ratio				
52. Odds ratio				
53. 95% CI: Lower limit				
54. 95% CI: Upper limit				
55. p-value				
56. Relative risk reduction				
57. Other (specify below:)				
58. Other (specify below:)				
59. Other (specify below:)				
60. Specify other analysis:				

[Enlarge](#) [Shrink](#)

61. Specify other analysis:

[Enlarge](#) [Shrink](#)

62. Specify other analysis:

[Enlarge](#) [Shrink](#)

63. Is analysis adjusted for confounders?

☐ Yes☐ No

☐ Not reported☐ Not applicable (e.g., RCT)

64. What covariates/confounders were adjusted? ****List all covariates here**** (Choose all applicable)

☐ Age☐ Gender☐ Race☐ BMI☐ Other (specify:)☐ Other (specify:)☐ Other (specify:)☐ Other (specify:)☐ Other (specify:)☐ Other (specify:)☐ Other (specify:)☐ Other (specify:)☐ Other (specify:)☐ Other (specify:)☐ Other (specify:)☐ Not applicable (e.g., RCT)

65. Comments:

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Thank you very much!

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Previewing at Level 33

Refid: 3597, Charles, B., Norris, R., Xiao, X., and Hague, W., Population Pharmacokinetics of Metformin in Late Pregnancy, *Ther Drug Monit*, 28(1), 2006, p.67-72
State: Excluded, Level: 1

Quality

Keywords:

No keywords available

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Abstract:

The pharmacokinetic disposition of metformin in late pregnancy was studied together with the level of fetal exposure at birth. Blood samples were obtained in the third trimester of pregnancy from women with gestational diabetes or type 2 diabetes; 5 had a previous diagnosis of polycystic ovary syndrome. A cord blood sample also was obtained at the delivery of some of these women, and also at delivery of others who had been taking metformin during pregnancy but from whom no blood had been taken. Plasma metformin concentrations were assayed by a new, validated, reverse-phase HPLC method. A 2-compartment, extravascular maternal model with transplacental partitioning of drug to a fetal compartment was fitted to the data. Nonlinear mixed-effects modeling was performed in NONMEM using FOCE with INTERACTION. Variability was estimated using logarithmic interindividual and additive residual variance models; the covariance between clearance and volume was modeled simultaneously. Mean (range) metformin concentrations in cord plasma and in maternal plasma were 0.81 (range, 0.1-2.6) mg/L and 1.2 (range, 0.1-2.9) mg/L, respectively. Typical population values (interindividual variability, CV%) for allometrically scaled maternal clearance and volume of distribution were 28 L/h/70 kg (17.1%) and 190 L/70 kg (46.3%), giving a derived population-wide half-life of 5.1 hours. The placental partition coefficient for metformin was 1.07 (36.3%). Neither maternal age nor weight significantly influenced the pharmacokinetics. The variability (SD) of observed concentrations about model-predicted concentrations was 0.32 mg/L. The pharmacokinetics were similar to those in nonpregnant patients and, therefore, no dosage adjustment is warranted. Metformin readily crosses the placenta, exposing the fetus to concentrations approaching those in the maternal circulation. The sequelae to such exposure, eg, effects on neonatal obesity and insulin resistance, remain unknown.

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Oral Diabetes Medications

Quality Form

**Fill out this form for all clinical trials.
Do not need to fill this out for cohort,
case-control, or cross-sectional studies.**

1. Was the study described as randomized (this includes the use of words such as randomly, random, and randomization)?

☐ Yes (1)☐ No (0)☐ Not Reported/Can't Tell (0)[Clear Selection](#)

2. If yes to q1, was the randomization scheme described AND appropriate?

☐ Yes: (1) appropriate randomization is if each study participant is allowed to have the same chance of receiving each intervention and the investigators could not predict which treatment was next.☐ No: (-1) randomization described AND inappropriate (e.g. methods of allocation using date of birth, date of admission, hospital numbers, or alteration should not be regarded as appropriate)☐ No: (0) randomization methods not described[Clear Selection](#)

3. Was the study described as double blind?

☐ Yes (1)☐ No (0)☐ Not reported/Can't tell (0)[Clear Selection](#)

4. If yes to Q3, was the method of double blinding described AND appropriate?

☐ Yes: (1) appropriate double blinding is if neither the person doing the assessments nor the study participant could identify the intervention being assessed OR if the use of active placebos, identical placebos or dummies is mentioned☐ No: (-1) the study was described as double blind AND inappropriate (e.g. comparison of tablet vs lifestyle with no double dummy or fake tablet given to the lifestyle group)

☐ No: (0) no description of double blinding available and unable to tell if appropriate or not.

[Clear Selection](#)

5. Was there a description of withdrawals and drop-outs?

☐ Yes: (1) the number and the reasons for withdrawals in each group must be stated or state that there were no withdrawals. If subjects were not included in the analysis, they must state the number and reasons for not including them in the analysis.

☐ No (0)

[Clear Selection](#)

6. Comments:

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Thank you very much!

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Appendix F: Evidence Tables

Appendix F: Evidence Table 1. Quality of systematic reviews

Author, year	Question clearly stated	Search methods described / comprehensive	Inclusion criteria reported / appropriate	Study quality assessed / appropriate	Reproducible methodology demonstrated	Variation in results discussed	Results combined appropriately	Conclusions supported by data
Saenz, 2005 ¹⁷	Yes	Yes / Yes	Yes / Yes	Yes / Yes	Yes	Yes	Yes	Yes
Van de Laar, 2005 ³⁸	Yes	Yes / Yes	Yes / Yes	Yes / Partially	Yes	Yes	Yes	Yes
Chiquette, 2004 ³⁰¹	Yes	Yes / Partially	Yes / Yes	Partially / Partially	Can't tell	Yes	Yes	Yes
Wulfele, 2004 ³⁰²	Yes	Yes / Partially	Yes / Yes	Yes / Yes	Can't tell	Partially	Yes	Yes
Meriden, 2004 ³⁰³	Partially	Partially / Partially	Partially / No	No / Can't tell	Can't tell	No	No	Partially
Czoski-Murray, 2004 ³⁰⁴	Yes	Yes / Yes	Yes / Yes	Yes / Yes	Can't tell	Partially	Yes	Yes
Buse, 2004 ²⁵	Yes	Yes / Partially	Yes / Yes	No / Can't tell	Can't tell	Partially	No	Partially
Stades, 2004 ³⁰⁵	Yes	Yes / Yes	Yes / Yes	Yes / Partially	Partially	Yes	Yes	Yes
Salpeter, 2003 ³⁰⁶	Yes	Yes / Yes	Yes / Yes	Yes / Yes	Yes	Yes	Yes	Yes
van Wijk, 2003 ³⁰⁷	Yes	Yes / Partially	Yes / Yes	No / Can't tell	Can't tell	Yes	Yes	Yes
Salas, 2002 ³⁰⁸	Yes	Partially / Partially	Partially / Yes	No / Can't tell	Can't tell	Partially	Yes	Yes
Inzucchi, 2002 ²⁶⁶	Yes	Partially / Partially	Yes / Partially	No / Can't tell	Can't tell	Yes	Yes	Yes
Chilcott, 2001 ²⁶⁷	Yes	Partially / Partially	Yes / Yes	Yes / Yes	Can't tell	Yes	Yes	Yes
Levien, 2001 ³⁰⁹	Partially	Partially / Partially	No / Can't tell	No / No	Can't tell	Partially	No	Partially
Chilcott, 2001 ³¹⁰	Yes	Yes / Yes	Yes / Yes	Yes / Yes	Can't tell	Yes	Yes	Yes
Culy, 2001 ³¹¹	No	Yes / Partially	Partially / Yes	No / Can't tell	Can't tell	No	Can't tell	Partially
Campbell, 2000 ³¹²	Partially	Partially / No	Yes / Partially	No / Can't tell	Can't tell	No	Yes	Yes

Appendix F: Evidence Table 1. Quality of systematic reviews

Author, year	Question clearly stated	Search methods described / comprehensive	Inclusion criteria reported / appropriate	Study quality assessed / appropriate	Reproducible methodology demonstrated	Variation in results discussed	Results combined appropriately	Conclusions supported by data
Johansen, 1999 ³¹³	Yes	Yes / Yes	Partially / Can't tell	No / Can't tell	Can't tell	Partially	Yes	Yes
Chan, 1999 ³¹⁴	Partially	Partially / Partially	No / Can't tell	No / Can't tell	Can't tell	No	Can't tell	Partially
McCartney, 1999 ³¹⁵	Partially	Yes / Yes	No / Can't tell	No / Can't tell	Can't tell	No	No	No
Campbell, 1998 ³¹⁶	Yes	Yes / Partially	No / No	No / No	Can't tell	No	Can't tell	Yes
Campbell, 1996 ³¹⁷	Yes	No / Can't tell	Yes / Yes	No / No	Can't tell	No	No	No
Melchior, 1996 ³¹⁸	Yes	Partially / Partially	Yes / Yes	No / Can't tell	Can't tell	No	No	Yes
Campbell, 1995 ³¹⁹	Yes	Yes / Partially	Yes / Yes	No / Can't tell	Can't tell	No	Yes	Yes
Campbell, 1985 ³²⁰	Yes	Partially / Partially	Partially / Can't tell	No / Can't tell	Can't tell	No	Can't tell	Yes
Vreven, 2005 ³²¹	Yes	Partially / Partially	Partially / Can't tell	No / Can't tell	Can't tell	No	Can't tell	Yes
Kimmel, 2005 ³⁹	Partially	Partially / Partially	Yes / Yes	No / Can't tell	Can't tell	No	Partially	Yes
Chandler, 2005 ¹⁹	Yes	Yes / Partially	Yes / Yes	Yes / Yes	Can't tell	Partially	Partially	Yes

Appendix F: Evidence Table 2. Study design characteristics table for studies reporting on proximal clinical outcomes (Key Question 1)

Author, year	Study design	Country	Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Ramachandran, 2004 ⁵⁵	RCT	India	NR	14 weeks (planned duration)	Age <30 or >60, treatment experienced, HbA1c >11%, no type 2 diabetes, other
Rosenbaum, 2002 ¹⁵³	RCT	Brazil	NR	24 weeks (planned duration)	Age <40 or >65, any liver disease, any kidney disease, treatment experienced, no type 2 diabetes, other
Nishio, 2006 ¹⁵¹	RCT	Japan	NR	6 months (planned duration)	Any liver disease, any kidney disease, no type 2 diabetes, other
Weissman, 2005 ¹⁰⁰	RCT	US	Yes	24 weeks (planned duration)	Age <18 or >75, any liver disease, any kidney disease, history of CVD, HbA1c <6.5 or >8.5 for patients having received prior combination treatment; <7 or >10 prior monotherapy or drug naive patients, no type 2 diabetes, other
Rosenstock, 2006 ¹²⁴	RCT	US, Canada	NR	NR	Age <60, history of CVD, no type 2 diabetes, other
Bailey, 2005 ¹⁰¹	RCT	UK, 14 European countries	Yes	24 weeks (planned duration)	Age <18 or >70, history of CVD, no type 2 diabetes, other
Pfutzner, 2006 ¹²³	RCT	Germany	Yes	16 weeks (planned duration)	NR
Betteridge, 2005 ¹⁵⁷	RCT	UK	Yes	104 weeks (planned duration)	Age<35 or >75, HbA1c <7.5 or >11, no type 2 diabetes
Kardas, 2005 ¹¹⁴ DIACOM	RCT	Poland	NR	NR	Age <40 or >75, HbA1c >9.0%, no type 2 diabetes, other
Forst, 2005 ¹⁴⁵	RCT	Germany	Yes	24 weeks (planned duration)	Age <40 or >75, any liver disease, any kidney disease, history of CVD, HbA1c <6.6 or >9.9, no type 2 diabetes, other
Yamanouchi, 2005 ⁵⁷	RCT	Japan	NR	12 months (planned duration)	Any liver disease, any kidney disease, history of CVD, treatment experienced, neuropathy, retinopathy, HbA1c <7.0, no type 2 diabetes, other

Appendix F: Evidence Table 2. Study design characteristics table for studies reporting on proximal clinical outcomes (Key Question 1)

Author, year	Study design	Country	Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Goldberg, 2005 ⁵²	RCT	US, Puerto Rico, Mexico, and Columbia	Yes	24 weeks (planned duration)	Age <35, any liver disease, any kidney disease, history of CVD, treatment experienced, HbA1c <7 or >11.5, if naive to antihyperglycemic therapy; <7 or >9.5 if previously treated with oral antihyperglycemic therapy, no type 2 diabetes, other
Pfutzner, 2005 ⁶⁸	RCT	Germany	Yes	26 weeks (planned duration)	Age <40 or >75, any liver disease, any kidney disease, history of CVD, HbA1c <6.6% or >9.9%, other
Derosa, 2005 ⁵³	RCT	Italy	NR	NR	Any liver disease, any kidney disease, history of CVD, neuropathy, retinopathy, HbA1c <7.5%, no type 2 diabetes, other
Derosa, 2005 ⁷²	RCT	Italy	NR	12 months (planned duration)	Age <18, any liver disease, any kidney disease, history of CVD, neuropathy, retinopathy, HbA1c <7.5, no type 2 diabetes, other
Inukai, 2005 ¹¹¹	RCT	Japan	NR	6 months (planned duration)	NR
Brunetti, 2004 ³²²	RCT, cross-over	Italy	NR	3 months (planned duration)	Age <35 or >70, any liver disease, any kidney disease, history of CVD, HbA1c <8.5, no type 2 diabetes, other
Langenfeld, 2005 ¹⁴⁶	RCT	Germany	Yes	24 weeks (planned duration)	Age <40 or >75, any liver disease, any kidney disease, history of CVD, HbA1c <6.6 or >9.9, no type 2 diabetes, other
Feinglos, 2005 ¹⁰⁴	RCT	US	Yes	16 weeks (planned duration)	Age <30 or >81, any liver disease, any kidney disease, history of CVD, HbA1c <7.0 or >8.5, no type 2 diabetes, other
Mari, 2005 ²⁶²	RCT	12 unspecified countries	Yes	24 weeks (planned duration)	Age <31, any liver disease, history of CVD, treatment experienced, no type 2 diabetes, other
Goke, 2002 ⁷⁵ German Pioglitazone Study Group	RCT	Germany	Yes	26 weeks (planned duration)	Any liver disease, any kidney disease, history of CVD, HbA1c <7.5 or >11.5, no type 2 diabetes, other

Appendix F: Evidence Table 2. Study design characteristics table for studies reporting on proximal clinical outcomes (Key Question 1)

Author, year	Study design	Country	Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Charbonnel, 2005 ⁶³	RCT	14 European countries, Australia, Canada, South Africa and Israel	Yes	52 weeks (planned duration)	Age <35 or >75, treatment experienced, HbA1c <7.5 or >11, no type 2 diabetes, other
Tan, 2005 ⁶¹ One year extension study for Quartet study group	RCT	Canada, UK, Australia, Finland, Poland, The Slovak Republic and South Africa	Yes	104 weeks (planned duration)	Age <35 or >75, treatment experienced, HbA1c <7.5 or >11 with diet alone, no type 2 diabetes, other
McCluskey, 2004 ⁷⁶	RCT	US	Yes	30 weeks (planned duration)	Age <18 or >80, treatment experienced, HbA1c <7.5 or >9.5, no type 2 diabetes, other
Kim, 2005 ¹⁵²	RCT	Korea	NR	12 weeks (planned duration)	Any liver disease, any kidney disease, treatment experienced, HbA1c <7.5, no type 2 diabetes, other
Schernthaner, 2004 ⁵⁶	RCT	Europe	NR	12 months (planned duration)	Age <35 or >75, treatment experienced, HbA1c <7.5 or >11, no type 2 diabetes
Smith, 2005 ¹⁶¹	RCT	US	Yes	24 weeks (planned duration)	Age <35 or >75, any liver disease, any kidney disease, history of CVD, treatment experienced, no type 2 diabetes, other
Choi, 2004 ⁷⁷	RCT	Korea	NR	6 months (planned duration)	Any liver disease, any kidney disease, other
Matthews, 2005 ⁷⁰	RCT	Europe and Australia	Yes	52 months (planned duration)	Age <35 or >75, history of CVD, HbA1c <7.5 or >11, no type 2 diabetes, other
Derosa, 2004 ⁹⁰	RCT	Italy	NR	12 months (planned duration)	Age <46 or >67, any liver disease, any kidney disease, history of CVD, treatment experienced, no type 2 diabetes, other

Appendix F: Evidence Table 2. Study design characteristics table for studies reporting on proximal clinical outcomes (Key Question 1)

Author, year	Study design	Country	Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Schemthaner, 2004 ¹⁰⁶	RCT	Austria, Belgium, Czech Republic, France, Germany, Hungary, Italy, Netherlands, Poland, Slovakia, Spain, and United Kingdom	NR	27 weeks (planned duration)	Age <35, any liver disease, any kidney disease, HbA1c <6.9 or >11.5, no type 2 diabetes, other
Tan, 2004 ⁶⁵	RCT	Denmark, Finland, Norway, and Sweden	Yes	52 weeks (planned duration)	Treatment experienced, HbA1c <7.5 or >11 for patients not receiving ODM, <7.5 or >9.5 for patients receiving ODM, no type 2 diabetes, other
Baksi, 2004 ¹²⁶	RCT	7 European countries	Yes	26 weeks (planned duration)	Age <35 or >80, any liver disease, history of CVD, treatment experienced, neuropathy, no type 2 diabetes, other
Tan, 2004 ⁶⁹	RCT	Mexico	Yes	NR	Any liver disease, any kidney disease, history of CVD, HbA1c <7.5 or >11 in patients who were not receiving ODMs, and <7.5 or >9.5 in patients who were receiving ODM monotherapy, no type 2 diabetes, other
Natali, 2004 ¹⁴⁴	RCT	London and Italy	Yes	16 weeks (planned duration)	Age <40 or >80, any liver disease, any kidney disease, history of CVD, neuropathy, retinopathy, HbA1c >10 after washout, other
Saad, 2004 ¹⁶⁴	RCT	US	Yes	12 weeks (planned duration)	Age <18 or >73, any liver disease, any kidney disease, history of CVD, treatment experienced, other
Rosenstock, 2004 ¹³¹	RCT	US	Yes	16 weeks (planned duration)	Age <18, females, treatment experienced, no type 2 diabetes, other
Raskin, 2004 ⁷⁴	RCT	US	Yes	12 titration and 12 maintenance weeks (planned duration)	Age <18, HbA1c <7 or >12 during previous monotherapy with sulfonylurea or metformin at 50% or more of maximal recommended dose for at least 3 months, no type 2 diabetes, other
Yanagawa, 2004 ⁶²	RCT	Japan	NR	12 weeks (planned duration)	Age <40 or >80, any liver disease, HbA1c <7 or >10, no type 2 diabetes, other
Manzella, 2004 ¹⁴⁸	RCT	Italy	NR	4 months (planned duration)	History of CVD, treatment experienced, neuropathy, no type 2 diabetes, other

Appendix F: Evidence Table 2. Study design characteristics table for studies reporting on proximal clinical outcomes (Key Question 1)

Author, year	Study design	Country	Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Feinbock, 2003 ¹³⁰	RCT	Austria	Yes	26 weeks (planned duration)	Age <36 or >80, any liver disease, any kidney disease, treatment experienced, HbA1c <7.8, no type 2 diabetes, other
Kerenyi, 2004 ¹²⁵	RCT	15 countries	Yes	26 weeks (planned duration)	Age <35 or >80, any liver disease, any kidney disease, history of CVD, no type 2 diabetes, other
Jovanovic, 2004 ⁷³	RCT	US	Yes	12 titration and 12 maintenance weeks (planned duration)	Age <18, HbA1c <7 or >12, no type 2 diabetes, other
Hanefeld, 2004 ⁶⁰ QUARTET study group	RCT	Canada, UK, Hungary, Finland, Slovak Republic, Belgium, Estonia, Lithuania, Denmark, Italy, Greece, Sweden, and the Netherlands	Yes	NR	Age <35 or >75, history of CVD, HbA1c <7.5 or >11, no type 2 diabetes, other
Lawrence, 2004 ⁵⁴	RCT	UK	Yes	12 titration and 12 maintenance weeks (planned duration)	Age <45 or >80, any liver disease, any kidney disease, history of CVD, HbA1c for diet treated diabetes: <7% or >10% and for low-dose oral hypoglycemic therapy: >7.5, no type 2 diabetes, other
Garber, 2003 ⁸⁰	RCT	US	Yes	16 weeks (planned duration)	Age <20 or >79, any liver disease, any kidney disease, treatment experienced, HbA1c >7 or <12, no type 2 diabetes, other
Takagi, 2003 ⁷⁸	RCT	Japan	NR	NR	Any liver disease, any kidney disease, no type 2 diabetes, other
Tosi, 2003 ⁹⁵	RCT, cross-over	Italy	Yes	6 months (planned duration)	Any liver disease, any kidney disease, history of CVD, treatment experienced, HbA1c <6.3, no type 2 diabetes, other
Goldstein, 2003 ⁸²	RCT	US	Yes	18 weeks (planned duration)	Any liver disease, any kidney disease, history of CVD, HbA1c <7.5 and >12.0, other
Herz, 2003 ¹⁶³	RCT	Canada and Spain	Yes	16 weeks (planned duration)	Any liver disease, any kidney disease, treatment experienced, HbA1c <6.5 or >9.8, no type 2 diabetes, other

Appendix F: Evidence Table 2. Study design characteristics table for studies reporting on proximal clinical outcomes (Key Question 1)

Author, year	Study design	Country	Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Bech, 2003 ¹⁹⁷	RCT	Australia, Croatia, Czech Republic, France, Greece, Israel, Macedonia, Poland, Russia, Slovenia, and Spain	Yes	NR	Age<40 years, any liver disease, history of CVD, treatment experienced, no type 2 diabetes, other
Derosa, 2003 ⁹⁷	RCT	Italy	NR	12 months (planned duration)	Any kidney disease, history of CVD, treatment experienced, HbA1c <7, no type 2 diabetes, other
Barnett, 2003 ¹⁷²	RCT	UK	NR	26 weeks (planned duration)	Age<30 or >80, any liver disease, HbA1c <7.5, no type 2 diabetes, other
Fujioka, 2003 ¹⁰⁵	RCT	US	Yes	24 weeks (planned duration)	Any liver disease, any kidney disease, history of CVD, HbA1c >8.5 and FPG>200 mg/dl while on metformin immediate release for >=8 weeks, no type 2 diabetes, other
Derosa, 2003 ¹¹⁸	RCT	Italy	NR	12 months (planned duration)	Any kidney disease, history of CVD, HbA1c <7.0%, no type 2 diabetes, other
Zhu, 2003 ¹⁸⁸	RCT	China	Yes	24 weeks (planned duration)	Age<40 or >70, any liver disease, any kidney disease, history of CVD, neuropathy, retinopathy, HbA1c <7.5, no type 2 diabetes, other
Del Prato, 2003 ¹⁴⁹	RCT	France, Italy, Netherlands	NR	29 weeks (planned duration)	Age<35 or >70, HbA1c <7.5 or >10 after run-in period, no type 2 diabetes, other
Pavo, 2003 ⁵⁹	RCT	Russia and Hungary	Yes	32 weeks (planned duration)	Age<40, any liver disease, any kidney disease, history of CVD, treatment experienced, HbA1c <7.5 or >11.0, no type 2 diabetes, other
Luis Bautista, 2003 ¹⁹³	RCT	US	Yes	14 weeks (planned duration)	Age<35 or >80, HbA1c <8.0 or >10.5, no type 2 diabetes, other
Bakris, 2003 ⁶⁶	RCT	US and UK	Yes	52 weeks (planned duration)	NR

Appendix F: Evidence Table 2. Study design characteristics table for studies reporting on proximal clinical outcomes (Key Question 1)

Author, year	Study design	Country	Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Vongthavaravat, 2002 ¹⁷⁰	RCT	India, Thailand, Philippines, Tunisia, Argentina, and Brazil	Yes	26 weeks (planned duration)	Age <40 or >80, any liver disease, any kidney disease, history of CVD, treatment experienced, neuropathy, retinopathy, no type 2 diabetes, other
Virtanen, 2003 ¹⁴³	RCT	Finland	Yes	26 weeks (planned duration)	Age <45 or >75, any liver disease, any kidney disease, history of CVD, treatment experienced, neuropathy, retinopathy, no type 2 diabetes, other
Vakkilainen, 2002 ¹²²	RCT	Finland	Yes	12 weeks (planned duration)	Age<18 or >75, any liver disease, any kidney disease, HbA1c <6.5 or >10, no type 2 diabetes, other
Cefalu, 2002 ³²³	RCT	US	NR	18 weeks (planned duration)	Age<35 or >70, HbA1c <7, no type 2 diabetes, other
Hallsten, 2002 ⁵⁸	RCT	Finland	Yes	26 weeks (planned duration)	Any liver disease, any kidney disease, history of CVD, no type 2 diabetes, other
Scherbaum, 2002 ¹⁴¹	RCT	Germany	Yes	26 weeks (planned duration)	Age<35 or >70, any liver disease, history of CVD, HbA1c <7.5 or >12, no type 2 diabetes, other
Blonde, 2002 ⁸¹	RCT	US	Yes	16 weeks (planned duration)	Age<30 or >75, any liver disease, any kidney disease, history of CVD, HbA1c <7.4, no type 2 diabetes, other
St John Sutto, 2002 ⁶⁷	RCT	US	Yes	52 weeks (planned duration)	Age<40 or >80, any liver disease, any kidney disease, history of CVD, no type 2 diabetes, other
Rachmani, 2002 ¹⁵⁰	RCT	Israel	NR	4 years (planned duration)	Age <40 or >75, no type 2 diabetes, other
Saloranta, 2002 ²⁴¹	RCT	Argentina, Australia, Belgium, Canada, Finland, France, Germany, Italy, Netherlands, New Zealand, Sweden, and US	Yes	24 weeks (planned duration)	Age <30, any liver disease, any kidney disease, history of CVD, no type 2 diabetes, other

Appendix F: Evidence Table 2. Study design characteristics table for studies reporting on proximal clinical outcomes (Key Question 1)

Author, year	Study design	Country	Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Marre, 2002 ⁸⁴	RCT	Netherlands, Denmark, Portugal, France, Belgium	Yes	4 months (planned duration)	Age<18, any liver disease, any kidney disease, history of CVD, other
Garber, 2002 ⁹	RCT	US	Yes	20 weeks (planned duration)	Any liver disease, any kidney disease, treatment experienced, HbA1c <7% or >11%, no type 2 diabetes, other
Gomez-Perez, 2002 ¹⁰²	RCT	Mexico	Yes	26 weeks (planned duration)	Age <40 or >80, any liver disease, any kidney disease, history of CVD, treatment experienced, no type 2 diabetes, other
Khan, 2002 ⁵¹	RCT	US	NR	16 weeks (planned duration)	Any liver disease, other
Charpentier, 2001 ⁸⁹	RCT	France	Yes	20 weeks (planned duration)	Age <= 34 or >= 71, any kidney disease, history of CVD, no type 2 diabetes, other
Rosenblatt, 2001 ¹⁶²	RCT	US	Yes	16 weeks (planned duration)	Any liver disease, any kidney disease, history of CVD, treatment experienced, neuropathy, retinopathy, HbA1c <8.0, no type 2 diabetes, other
Madsbad, 2001 ¹¹⁹	RCT	Denmark and Scandinavia	Yes	12 months (planned duration)	Age <=39 or >=76, any liver disease, any kidney disease, HbA1c <6.5 or >10, no type 2 diabetes, other
Kipnes, 2001 ¹⁶⁶	RCT	US	Yes	NR	Age <30 or >75, any liver disease, any kidney disease, history of CVD, neuropathy, retinopathy, HbA1c <8, no type 2 diabetes, other
Amador-Licona, 2000 ⁸⁵	RCT	Mexico	NR	12 weeks (planned duration)	Age >65, any liver disease, history of CVD, other
Lebovitz, 2001 ¹⁶⁹	RCT	US	NR	26 weeks (planned duration)	Age <36 or >81, any liver disease, any kidney disease, history of CVD, no type 2 diabetes, other
Patel, 1999 ¹⁶⁷	RCT	US	NR	12 weeks (planned duration)	Age <30 or >80, any liver disease, any kidney disease, history of CVD, no type 2 diabetes, other

Appendix F: Evidence Table 2. Study design characteristics table for studies reporting on proximal clinical outcomes (Key Question 1)

Author, year	Study design	Country	Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Phillips, 2001 ¹⁶⁸	RCT	US	Yes	26 weeks (planned duration)	Age <40 or >80, any liver disease, any kidney disease, neuropathy, no type 2 diabetes, other
Moses, 2001 ²¹⁸	RCT	13 countries	Yes	16 weeks (planned duration)	Age <40, any liver disease, history of CVD, treatment experienced, no type 2 diabetes, other
Einhorn, 2000 ¹⁶⁰	RCT	US	Yes	16 weeks (planned duration)	Any liver disease, any kidney disease, history of CVD, neuropathy, retinopathy, HbA1c <8.0, no type 2 diabetes, other
Fonseca, 2000 ¹⁰³	RCT	US	NR	26 weeks (planned duration)	Age <40 or >80, any liver disease, any kidney disease, history of CVD, treatment experienced, neuropathy, no type 2 diabetes, other
Nakamura, 2000 ⁶⁴	RCT	Japan	NR	3 months (planned duration)	Any liver disease, history of CVD, treatment experienced, HbA1c <6.5, no type 2 diabetes, other
Horton, 2000 ⁹⁶	RCT	US	Yes	24 weeks (planned duration)	Age <30, any kidney disease, HbA1c <6.8 or >11, no type 2 diabetes, other
Aronoff, 2000 ¹⁶⁵	RCT	US	Yes	26 weeks (planned duration)	Any liver disease, any kidney disease, history of CVD, neuropathy, retinopathy, HbA1c <7, no type 2 diabetes, other
Hanefeld, 2000 ¹⁹⁰	RCT	Europe	Yes	12 weeks (planned duration)	Age <30 or >75, any kidney disease, history of CVD, neuropathy, retinopathy, HbA1c mean level of two tests <6.8 or >10.5, no type 2 diabetes, other
Hasche, 1999 ¹³⁸	RCT	Germany	NR	104 weeks (planned duration)	Age <40 or >80, any liver disease, any kidney disease, history of CVD, treatment experienced, retinopathy, HbA1c <7.5 or >9.5%, no type 2 diabetes, other
Wolffenbuttel, 2000 ¹⁷¹	RCT	Italy, UK, France, Spain, Holland, and Switzerland	Yes	26 weeks (planned duration)	Age <30 or >80, any liver disease, any kidney disease, neuropathy, HbA1c <7.5%, no type 2 diabetes, other
Gregorio, 1999 ¹²⁹	RCT	Italy	NR	18 weeks (planned duration)	Age <70, any liver disease, any kidney disease, history of CVD, HbA1c <9, no type 2 diabetes, other

Appendix F: Evidence Table 2. Study design characteristics table for studies reporting on proximal clinical outcomes (Key Question 1)

Author, year	Study design	Country	Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Jovanovic, 2000 ¹⁹⁴	RCT	US	Yes	24 weeks (planned duration)	Age <40 or >75, any liver disease, any kidney disease, history of CVD, HbA1c with ODM (naïve): <6.5%; with ODM-treatment: >12%, no type 2 diabetes, other
Willms, 1999 ⁹⁹	RCT	Germany	Yes	12 weeks (planned duration)	Age <18, any liver disease, any kidney disease, history of CVD, HbA1c <7% or >13%, no type 2 diabetes, other
Erle, 1999 ¹²⁷	RCT	US and Italy	Yes	6 months (planned duration)	No type 2 diabetes, other
Landgraf, 1999 ¹²¹	RCT	Germany, Austria, and Netherlands	Yes	14 weeks (planned duration)	Any liver disease, any kidney disease, history of CVD, treatment experienced, no type 2 diabetes, other
Marbury, 1999 ¹¹⁶	RCT	US and Canada	Yes	12 months (planned duration)	Age >37 or <75, any liver disease, any kidney disease, history of CVD, treatment experienced, retinopathy, HbA1c <6.5% or 14.6%, no type 2 diabetes, other
Wolffenbuttel, 1999 ¹¹⁷	RCT	Germany, Austria, and Netherlands	NR	12 months (planned duration)	Age <40 or >75, any liver disease, any kidney disease, history of CVD, treatment experienced, HbA1c <6.5 if treated with diet only; >12 if treated with diet plus ODM, other
Testa, 1998 ¹⁹⁸	RCT	US	Yes	15 weeks (planned duration)	Age <30, no type 2 diabetes, other
Goldberg, 1998 ¹³⁹	RCT	US	Yes	18 weeks (planned duration)	Age <40 or >75, no type 2 diabetes, other
1998, ¹⁶ UKPDS	RCT	UK	Yes	NR	Age <25 or >65, any kidney disease, history of CVD, treatment experienced, retinopathy, no type 2 diabetes, other
Schade, 1998 ¹³⁵	RCT	US	Yes	12 weeks (planned duration)	Age <30 or >75, any liver disease, any kidney disease, history of CVD, treatment experienced, no type 2 diabetes, other
1998, ¹²⁸ UKPDS	RCT	UK	Yes	3 years (planned duration)	Age <25 or >65, any kidney disease, history of CVD, other

Appendix F: Evidence Table 2. Study design characteristics table for studies reporting on proximal clinical outcomes (Key Question 1)

Author, year	Study design	Country	Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Lee, 1998 ²³⁹	RCT	US	NR	NR	Males, any liver disease, any kidney disease, history of CVD, no type 2 diabetes, other
Garber, 1997 ²¹⁷	RCT	US	Yes	14 weeks (planned duration)	Age <30, treatment experienced, no type 2 diabetes, other
Simonson, 1997 ¹³⁶	RCT	US	Yes	16 weeks (planned duration)	Age <30, any liver disease, any kidney disease, history of CVD, treatment experienced, retinopathy, HbA1c <6% at the end of week 2 of placebo administration, no type 2 diabetes, other
Rosenstock, 1996 ¹⁸⁹	RCT	US	Yes	14 weeks (planned duration)	No type 2 diabetes, other
Dills, 1996 ¹⁰⁷	RCT	US	Yes	12 months (planned duration)	Age <30 or >80, any liver disease, any kidney disease, no type 2 diabetes, other
Draeger, 1996 ¹¹²	RCT	UK, Europe, Asia, South Africa and South America	NR	12 months (planned duration)	Age <40 or >80, any liver disease, any kidney disease, treatment experienced, no type 2 diabetes, other
Goldberg, 1996 ¹³⁴	RCT	US	Yes	14 weeks (planned duration)	Age <30 or >75, any liver disease, any kidney disease, no type 2 diabetes, other
Grant, 1996 ¹⁵⁴	RCT	UK	Yes	24 weeks (planned duration)	No type 2 diabetes, other
Vray, 1995 ¹³⁷	RCT, factorial	France, China	Yes	3 months (planned duration)	Age <40 or >70, any liver disease, any kidney disease, treatment experienced, no type 2 diabetes, other
DeFronzo, 1995 ⁸⁸	RCT	US	NR	29 weeks (planned duration)	Age <40 or >70, any liver disease, any kidney disease, history of CVD, treatment experienced, no type 2 diabetes, other
1995, ⁹² UKPDS	RCT	UK	Yes	3 years (planned duration)	Age <25 or >65, any liver disease, any kidney disease, history of CVD, treatment experienced, retinopathy, no type 2 diabetes, other

Appendix F: Evidence Table 2. Study design characteristics table for studies reporting on proximal clinical outcomes (Key Question 1)

Author, year	Study design	Country	Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Hermann, 1994 ⁸⁷	RCT	Sweden	Yes	6 months (planned duration)	No type 2 diabetes, other
Campbell, 1994 ⁸³	RCT	UK	NR	52 weeks (planned duration)	Age <40 or >69, any liver disease, any kidney disease, history of CVD, no type 2 diabetes, other
Birkeland, 1994 ¹¹⁰	RCT	Norway	Yes	15 months (planned duration)	Any liver disease, any kidney disease, history of CVD, treatment experienced, HbA1c <7 or >11, no type 2 diabetes, other
Rosenstock, 1993 ¹⁰⁹	RCT	US	Yes	4 months (planned duration)	Age <65, any liver disease, any kidney disease, treatment experienced, no type 2 diabetes, other
Carlson, 1993 ¹⁰⁸	RCT	US	Yes	12 weeks (planned duration)	Age <30 or >75, any liver disease, any kidney disease, no type 2 diabetes, other
Wolffenbuttel, 1993 ¹²⁰	RCT	Netherlands	Yes	12 (4 week titration, 8 week treatment) (planned duration)	Any liver disease, any kidney disease, HbA1c <7.0 or >12.0, no type 2 diabetes, other
Leonhardt, 1991 ²⁶³	RCT	Germany	Yes	24 weeks (planned duration)	Age <43 or >70, no type 2 diabetes, other
Teupe, 1991 ¹⁵⁵	RCT	Germany	NR	2 years (planned duration)	Age >70, any liver disease, any kidney disease, history of CVD, no type 2 diabetes, other
Noury, 1991 ⁸⁶	RCT	France	NR	3 months (planned duration)	Any liver disease, any kidney disease, no type 2 diabetes, other
Hermann, 1991 ⁹⁴	RCT	Sweden	Yes	6 months (planned duration)	Any liver disease, any kidney disease, history of CVD, no type 2 diabetes, other
Schneider, 1991 ¹⁷³	RCT	Germany	NR	12 weeks (planned duration)	Age <37 or >77, any liver disease, any kidney disease, history of CVD, no type 2 diabetes, other

Appendix F: Evidence Table 2. Study design characteristics table for studies reporting on proximal clinical outcomes (Key Question 1)

Author, year	Study design	Country	Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Hermann, 1991 ¹⁵⁹	RCT	Sweden	NR	6 months (planned duration)	No type 2 diabetes, other
Dorman, 1991 ²⁶⁰	RCT	UK	Yes	8 months (planned duration)	Any liver disease, any kidney disease, history of CVD, treatment experienced, no type 2 diabetes, other
Kilo, 1988 ¹⁴⁷	RCT	US	NR	3 months (planned duration)	Treatment experienced, no type 2 diabetes, other
1985, ⁹¹ UKPDS	RCT	UK	Yes	12 months (planned duration)	Age <25 or >65, any kidney disease, history of CVD, retinopathy, no type 2 diabetes, other
Harrower, 1985 ¹¹³	RCT	UK and Scotland	NR	1 year (planned duration)	No type 2 diabetes, other
Baba, 1983 ¹³³	RCT	Japan	NR	24 weeks (planned duration)	No type 2 diabetes, other
Tseng, 2005 ¹⁴⁰	RCT	Taiwan	NR	12 weeks (planned duration)	No type 2 diabetes, other
Wolever, 2000 ⁹⁸	RCT	Canada	Yes	9 months (planned duration)	Age <40, any liver disease, history of CVD, treatment experienced, HbA1c <7.2 or >9.1, no type 2 diabetes, other
Cefalu, 1998 ²⁶¹	RCT	US	NR	8 months (planned duration)	Age <30 or >73, any liver disease, any kidney disease, HbA1c ≥11 at time of screening; ≥7.8% in normal time, no type 2 diabetes, other
Turner, 1998 ⁹³ UKPDS	RCT	UK	Yes	6 years (planned duration)	Age <25 or ≥65, any kidney disease, history of CVD, treatment experienced, retinopathy, no type 2 diabetes, other
Garber, 2006 ⁷¹	RCT	US	Yes	24 weeks (planned duration)	Age <20 or >78, any liver disease, any kidney disease, history of CVD, HbA1c ≤7.0 or ≥12.0, no type 2 diabetes, other

RCT = randomized controlled trial; NR = not reported; HbA1c = hemoglobin A1c; CVD = cardiovascular disease; US = United States; UK = United Kingdom; ODM = oral diabetic medicine; FPG = fasting plasma glucose; UKPDS = United Kingdom Prospective Diabetes Study; DIACOM = effect of Dosing frequency of oral Antidiabetic agents on the COMpliance and biochemical control of type 2 diabetes

Appendix F: Evidence Table 2. Study design characteristics table for studies reporting on proximal clinical outcomes (Key Question 1)

Author, year		Mean age in years (age range)			Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes in years
Study group	Group, n		Male, n (%)	Race, n (%)				
Ramachan-dran, 2004 ⁵⁵	Diet + exercise, 15	43.5	13	AA: 0; C: 0; Asian: 0; H: 0; O: 100	26.1	71.2	7.5	0
	Diet + glimepiride, 18	45.3	14	AA: 0; C: 0; Asian: 0; H: 0; O: 100	24.6	65.7	10.2	0
	Diet + metformin, 21	44.4	15	AA: 0; C: 0; Asian: 0; H: 0; O: 100	25.7	67.7	9.6	0
	Diet + pioglitazone, 23	45.1	17	AA: 0; C: 0; Asian: 0; H: 0; O: 100	25.5	68.9	9.3	0
Rosenbaum, 2002 ¹⁵³	Placebo, 20	62	8	NR	31.7	80.2	6.3	NR
	Acarbose, 20	59.8	6	NR	30.3	75.1	6.4	NR
Nishio, 2006 ¹⁵¹	Control group (no placebo), 28	67.5	20 (71.4)	AA: 0; C: 0; Asian: 0; H: 0; O: (100)	24.6	NR	6.9	NR
	Pioglitazone, 26	66.2	19 (73.1)	AA: 0; C: 0; Asian: 0; H: 0; O: (100)	24.6	NR	7.7	NR
Weissman, 2005 ¹⁰⁰	Metformin + rosiglitazone, 358	55.5	NR	NR	34.4	98.2	8.05	NR
	Metformin, 351	55.7	NR	NR	33.8	96.7	7.97	NR
Rosenstock, 2006 ¹²⁴	Glipizide + rosiglitazone, 116	68.7	(74.8)	NR	30.2	NR	7.72	6.8
	Placebo + glipizide, 111	68.2	(71.8)	NR	30.5	NR	7.65	6.6
Bailey, 2005 ¹⁰¹	Metformin + rosiglitazone, 288	58.1	168 (58)	AA: 2 (1); C: 280 (97); Asian: 3 (1); H: 0; O: 3 (1)	32.2	90.9	7.4	6
	Metformin, 280	57.6	159 (57)	AA: 1 (<1); C: 273 (98); Asian: 3 (1); H: 0; O: 3 (1)	32.1	89.5	7.5	6.1

Appendix F: Evidence Table 3. Study population table for studies reporting on proximal clinical outcomes (Key Question 1)

Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes in years
Pfutzner, 2006 ¹²³	Placebo + glimepiride, 30	63.7	15	NR	30	NR	7.7	7.3
	Glimepiride + rosiglitazone, 31	59.8	15	NR	27.7	NR	8.3	5.9
	Glimepiride + rosiglitazone, 41	62.2	22	NR	29.3	NR	8	6.4
Betteridge, 2005 ¹⁵⁷	Metformin + pioglitazone, 317	NR	NR	NR	NR	NR	NR	NR
	Metformin + glyclazide, 313	NR	NR	NR	NR	NR	NR	NR
	Unspecified sulfonylurea + pioglitazone, 319	NR	NR	NR	NR	NR	NR	NR
	Metformin + unspecified sulfonylurea, 320	NR	NR	NR	NR	NR	NR	NR
Kardas, 2005 ¹¹⁴ DIACOM	Glyclazide, 55	60.9	(53)	NR	27.1	79	7.1	2.2
	Glibenclamide, 50	62.4	(38)	NR	26.3	75	7.2	3.5
Forst, 2005 ¹⁴⁵	Glimepiride, 84	63 (SD 7.4)	52	NR	31.8	NR	7.44	6.9
	Pioglitazone, 89	62.2 (SD 8.4)	55	NR	31.7	NR	7.52	7.4
Yamanouchi, 2005 ⁵⁷	Diet + exercise + pioglitazone, 38	55.2 (46 - 64.4)	18	AA: 0; C: 0; Asian: 0; H: 0; O: (100)	25.8	NR	10.2	3.2 months
	Diet + exercise + metformin, 39	54.7 (44.9 - 64.5)	20	AA: 0; C: 0; Asian: 0; H: 0; O: (100)	26.2	NR	9.9	3 months
	Diet + exercise + glimepiride, 37	55.6 (46.3 - 64.9)	19	AA: 0; C: 0; Asian: 0; H: 0; O: (100)	25.6	NR	9.8	3.3 months
Goldberg, 2005 ⁵²	Diet + pioglitazone, 369	55.9	199 (53.9)	AA: 9 (2.4); C: 239 (64.8); Asian: 10 (2.7); H: 105 (28.5); O: 6 (1.6)	33.7	93.7	7.6	3.9

Appendix F: Evidence Table 3. Study population table for studies reporting on proximal clinical outcomes (Key Question 1)

Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes in years
	Diet + rosiglitazone, 366	56.3	201 (54.9)	AA: 10 (2.7); C: 219 (59.8); Asian: 12 (3.3); H: 118 (32.2); O: 7 (1.9)	32.6	92.5	7.5	4
Pfutzner, 2005 ⁶⁸	Pioglitazone, 89	62.2	58 (61.8)	AA: 0; C: 88 (98.8); Asian: 0; H: 0; O: 1 (1.1)	31.7	NR	7.52	7.4
	Glimepiride, 84	63	52 (61.9)	AA: 0; C: 81 (96.4); Asian: 0; H: 0; O: 3 (3.7)	31.8	NR	7.44	6.9
Derosa, 2005 ⁵³	Diet + exercise + glimepiride + pioglitazone, 45	53 (47 - 59)	21	AA: 0; C: 0; Asian: 0; H: 0; O: (100)	24.4	68.9	8.2	5
	Diet + exercise glimepiride + rosiglitazone, 42	54 (49 - 59)	22	AA: 0; C: 0; Asian: 0; H: 0; O: (100)	24.3	67.8	8	6
Derosa, 2005 ⁷²	Diet + exercise + behavioral therapy + metformin + glimepiride, 47	52 (47 - 57)	23	NR	26.8	NR	7.9	4
	Diet + exercise + behavioral therapy metformin + rosiglitazone, 48	54 (50 - 58)	25	NR	26.6	NR	8	5
Inukai, 2005 ¹¹¹	Glibenclamide + glyclazide, 52	60.7 (49.2 - 72.2)	24 (46.15)	NR	24.9	62.9	7.46	NR
	Glimepiride, 120	61.9 (50.8 - 72.0)	56 (46.67)	NR	24.8	62.2	7.64	NR
Langenfeld, 2005 ¹⁴⁶	Pioglitazone, 89	62	55 (61.8)	AA: 0; C: 88 (98.9); Asian: 0; H: 0; O: (1.1)	31.7	NR	7.52	7.4
	Glimepiride, 84	63	52 (61.9)	AA: 0; C: 81 (96.4); Asian: 0; H: 0; O: (3.6)	31.8	NR	7.44	6.9
Feinglos, 2005 ¹⁰⁴	Metformin + glipizide, 61	57.7 (30-80)	28	AA: 5 (8.2); C: 48 (78.7); Asian: 2 (3.3); H: 5 (8.2); O: 1 (1.6)	31.7	90	7.45	6.5
	Placebo + metformin, 61	58.8 (40-81)	25	AA: 10 (16.4); C: 42 (68.9); Asian: 2 (3.3); H: 5 (8.2); O: 2 (3.3)	32.1	90.8	7.64	4.6

Appendix F: Evidence Table 3. Study population table for studies reporting on proximal clinical outcomes (Key Question 1)

Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes in years
Mari, 2005 ²⁶²	Placebo, 30	60	19	NR	28.3	NR	6.5	4.5
	Nateglinide, 26	56	14	NR	28.8	NR	6.5	2.9
	Nateglinide, 27	61	19	NR	27.8	NR	6.6	4.3
	Nateglinide, 25	62	15	NR	28.4	NR	6.6	5.2
Goke, 2002 ⁷⁵ German Pioglitazone Study Group	Pioglitazone, 129	58.9	69 (53.5)	NR	30.9	NR	8.98	57.0 months
	Acarbose, 136	58.8	74 (54.5)	NR	30.8	NR	9.03	59.1 months
Charbonnel, 2005 ⁶³	Pioglitazone, NR (Total 1270)	NR	NR	NR	NR	NR	8.7	NR
	Glyclazide, NR (Total 1270)	NR	NR	NR	NR	NR	8.7	NR
Tan, 2005 ⁶¹ One year extension study for Quartet study group	Pioglitazone, 270	57	171 (63.3)	AA: 0; C: 253 (93.7); Asian: 0; H: 0; O: 17 (6.3)	32	91.7	NR	2.7
	Glyclazide, 297	56	182 (61.3)	AA: 0; C: 275 (92.6); Asian: 0; H: 0; O: 22 (7.4)	32	89.2	NR	2.9
McCluskey, 2004 ⁷⁶	Glimepiride + rosiglitazone, 25	60.2 (46 - 76)	11 (44%)	AA: 0; C: 24 (96); Asian: 0; H: 0; O: 0	NR	100.5	7.9	7.2
	Placebo + rosiglitazone, 15	50.8 (35 - 69)	6 (40%)	AA: 0; C: 12 (80); Asian: 0; H: 0; O: 0	NR	99.4	8.4	4.6
Kim, 2005 ¹⁵²	Diet + exercise + rosiglitazone, 63	58.8 (50.0 - 67.6)	NR	NR	23.9	61.5	9.7	12
	Diet + exercise, 62	58.1 (48.6 - 67.6)	NR	NR	24.5	62.3	9.3	10.1
Schemthaner, 2004 ⁵⁶	Placebo + diet + pioglitazone, 597	57	314 (52.6)	NR	31.2	88.2	8.7	3.4
	Placebo + diet + metformin, 597	56	345 (57.8)	NR	31.4	89.7	8.7	3.1
Smith, 2005 ¹⁶¹	Placebo + diet, 21	53.1	10	AA: 0; C: 16; Asian: 0; H: 0; O: 5	31.9	91.5	6.46	NR

Appendix F: Evidence Table 3. Study population table for studies reporting on proximal clinical outcomes (Key Question 1)

Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes in years
	Diet + pioglitazone, 21	56.2	9	AA: 0; C: 15; Asian: 0; H: 0; O: 6	32.1	93.5	6.88	NR
Choi, 2004 ⁷⁷	Rosiglitazone, 38	60.9	24	NR	24.9	67.6	7.79	7.5
	Uptitration of existing medications, 45	59.9	34	NR	24.8	68.1	7.72	7.2
Matthews, 2005 ⁷⁰	Diet + pioglitazone + metformin, 317	56	161 (50.8)	AA: 0; C: 315 (99.4); Asian: 2 (0.6); H: 0; O: 0	32.6	NR	8.71	5.8
	Diet + glycazide + metformin, 313	57	154 (49.2)	AA: 0; C: 313 (100); Asian: 0; H: 0; O: 0	32.6	NR	8.53	5.5
Derosa, 2004 ⁹⁰	Placebo + diet + exercise + glimepiride, 81	56	38	NR	27.6	NR	8.5	NR
	Placebo + diet + exercise + metformin, 83	58	42	NR	28.1	NR	8.4	NR
Schemthaner, 2004 ¹⁰⁶	Glyclazide, 405	60.5	(51)	NR	30.5	83.1	8.4	5.6
	Glimepiride, 440	60.6	(52)	NR	30.6	83.8	8.2	5.8
Tan, 2004 ⁶⁵	Glibenclamide, 109	57.9	80 (73)	AA: 0; C: 109 (100); Asian: 0; H: 0; O: 0	29.6	89	8.5	62.6 months
	Pioglitazone, 91	60	56 (62)	AA: 0; C: 90 (99); Asian: 0; H: 0; O: 1 (1)	30.2	88.4	8.4	57.1 months
Baksi, 2004 ¹²⁶	Glyclazide, 241	61.9	151 (62.7)	AA: 1 (0.4); C: 235 (97.5); Asian: 1 (0.4); H: 0; O: 4 (1.7)	29.7	NR	8.6	6.9
	Glyclazide + rosiglitazone, 225	61.1	129 (57.3)	AA: 1 (0.4); C: 219 (97.3); Asian: 3 (1.3); H: 0; O: 2 (0.9)	30.2	NR	8.5	6.5
Tan, 2004 ⁶⁹	Diet + exercise + pioglitazone, 121	55.1	54 (45)	AA: 0; C: 0 (0); Asian: 0; H: 121 (100); O: 0	29.3	74.2	8.54	77.8 months
	Diet + exercise + glimepiride, 123	55.7	65 (53)	AA: 0; C: 1 (1); Asian: 0; H: 122 (99); O: 0	28.8	74.5	8.45	81.2 months
Natali, 2004 ¹⁴⁴	Placebo, 22	58	18	NR	30.2	NR	7.6	3.4
	Metformin, 28	58	22	NR	28	NR	7.8	6.3
	Rosiglitazone, 24	59	22	NR	27.6	NR	7.7	6.5

Appendix F: Evidence Table 3. Study population table for studies reporting on proximal clinical outcomes (Key Question 1)

Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes in years
Saad, 2004 ¹⁶⁴	Placebo, 30	54	18	NR	31	NR	8.1	NR
	Pioglitazone, 28	55	11	NR	31	NR	8.5	NR
Rosenstock, 2004 ¹³¹	Repaglinide, 76	50.9	41	AA: 6; C: 60; Asian: 0; H: 9; O: 1	33	NR	8.9	3.5
	Nateglinide, 74	54	42	AA: 3; C: 59; Asian: 1; H: 9; O: 2	32.9	NR	8.9	4.3
Raskin, 2004 ⁷⁴	Repaglinide, 63	58.5	39	AA: 10; C: (40); Asian: 0; H: 1; O: 12	NR	NR	NR	7.2
	Rosiglitazone, 62	56.6	33	AA: 8; C: (42); Asian: 0; H: 0; O: 12	NR	NR	NR	7.4
	Repaglinide + rosiglitazone, 127	57.5	65	AA: 21; C: (83); Asian: 0; H: 4; O: 19	NR	NR	NR	7.3
Yanagawa, 2004 ⁶²	Glyclazide, 21	54	15	NR	24	NR	8.3	6
	Pioglitazone, 19	54	13	NR	24.6	NR	8.3	6.7
Manzella, 2004 ¹⁴⁸	Placebo + diet, 60	57 (all patients)	33	NR	29.2	NR	8.1	NR
	Diet + metformin, 60	57 (all patients)	31	NR	29.5	NR	8	NR
Feinbock, 2003 ¹³⁰	Glimepiride, 111	57.7	66	AA: 0; C: 110; Asian: 1; H: 0; O: 0	29.2	85	9.1	36.3 months
	Acarbose, 108	57.1	58	AA: 0; C: 107; Asian: 1; H: 0; O: 0	29.1	83	9.4	43.1 months
Kerenyi, 2004 ¹²⁵	Diet + glibenclamide, 170	59.9	105	AA: 2; C: 163; Asian: 4; H: 0; O: 1	29.2	NR	8.1	6.7
	Diet + glibenclamide + rosiglitazone, 165	60	91	AA: 1; C: 160; Asian: 3; H: 0; O: 1	30.7	NR	7.9	5.6
Jovanovic, 2004 ⁷³	Repaglinide, 61	57.8	36	AA: 7; C: 46; Asian: 0; H: 3; O: 5	31.2	NR	9	6.9
	Pioglitazone, 62	56.2	31	AA: 7; C: 51; Asian: 0; H: 2; O: 2	32.1	NR	9.1	6.1
Hanefeld, 2004 ⁶⁰ QUARTET Study	Placebo + unspecified sulfonylurea + pioglitazone, 31	60	171 (53.6)	AA: 2 (0.6); C: 317 (99.4); Asian: 0; H: 0; O: 0 (0)	30.2	85.3	8.82	7

Appendix F: Evidence Table 3. Study population table for studies reporting on proximal clinical outcomes (Key Question 1)

Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes in years
Group	Placebo + metformin + unspecified sulfonylurea, 320	60	175 (54.7)	AA: 3 (0.9); C: 315 (98.4); Asian: 0; H: 0; O: 2 (0.6)	30	84.9	8.8	7.1
Lawrence, 2004 ⁵⁴	Metformin, 20	59.5	12	NR	(Median 29.2)	NR	8.04	NR
	Glyclazide, 20	63.5	13	NR	(Median 28.7)	NR	7.85	NR
	Pioglitazone, 20	60.4	14	NR	(Median 30.6)	NR	7.43	NR
Garber, 2003 ⁸⁰	Metformin + glyburide, 171	55.6	76 (44)	AA: 18 (10.5); C: 132 (77.2); Asian: 0; H: 15 (8.8); O: 6 (3.5)	31.4	91.9	8.8	3
	Metformin, 164	54.7	71 (43.3)	AA: 11 (6.7); C: 132 (80.5); Asian: 0; H: 15 (9.1); O: 6 (3.7)	31.4	92.8	8.5	2.6
	Glyburide, 151	55.3	66 (43.7)	AA: 11 (7.3); C: 123 (81.5); Asian: 0; H: 12 (7.9); O: 5 (3.3)	31.1	91	8.7	3
Takagi, 2003 ⁷⁸	Pioglitazone, 23	64	20	NR	25.6	NR	6.8	NR
	Control, 21	65	14	NR	24.5	NR	6.7	NR
Tosi, 2003 ⁹⁵	Glibenclamide, 20	NR	NR	NR	NR	NR	NR	NR
	Metformin + glibenclamide, 41	NR	NR	NR	NR	NR	NR	NR
	Metformin, 19	NR	NR	NR	NR	NR	NR	NR
	Glibenclamide, 21	NR	NR	NR	NR	NR	NR	NR
	Metformin + glibenclamide, 39	NR	NR	NR	NR	NR	NR	NR
	Metformin, 20	NR	NR	NR	NR	NR	NR	NR
Goldstein, 2003 ⁸²	Metformin + glipizide, 87	54.6	(58.6)	AA: (11.5); C: (72.4); Asian: (0); H: (16.1); O: 0	31.7	94	8.7	5.9
	Glipizide, 84	57.4	(64.3)	AA: (11.9); C: (71.4); Asian: (2.4); H: (14.3); O: 0	30.6	89.9	8.9	6.5
	Metformin, 76	56.6	(61.8)	AA: (15.8); C: (65.8); Asian: (1.3); H: (17.1); O: 0	31.6	93.8	8.7	7.3
Herz, 2003 ¹⁶³	Placebo, 99	58 (33 - 85)	49 (49.5%)	AA: 0 (0); C: 96 (97); Asian: 3 (3); H: 0 (0); O: 0	31.7	86.3	7.5	NR

Appendix F: Evidence Table 3. Study population table for studies reporting on proximal clinical outcomes (Key Question 1)

Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes in years
	Pioglitazone, 99	59 (24 - 79)	59 (59.6)	AA: 0 (0); C: 97 (98); Asian: 1 (1); H: 1 (1); O: 0	31.7	86.6	7.5	NR
	Pioglitazone, 99	58.1 (24 -84)	52 (52.5)	AA: 0 (0); C: 93 (93.9); Asian: 1 (3); H: 3 (3); O: 0	30.8	84.1	7.6	NR
Bech, 2003 ¹⁹⁷	Repaglinide, 164	56.9 (40 -81)	(57.3)	AA: 1 (0.6); C: 161 (98.2); Asian: 0 (0); H: 0; O: 2 (1.2)	NR	NR	7.8	2.77
	Placebo, 89	57.3 (40 -76)	(58.4)	AA: 0 (0); C: 88 (98); Asian: 0 (0); H: 0; O: 1 (1.1)	NR	NR	7.6	2.81
Derosa, 2003 ⁹⁷	Diet + exercise + repaglinide, 56	55	29	NR	25.2	70.2	7.6	4
	Diet + exercise + metformin, 56	52	27	NR	24.7	72.3	7.4	5
Barnett, 2003 ¹⁷²	Placebo + unspecified sulfonylurea, 87	54.1 (32 -78)	(75)	AA: 0 (0); C: 0 (0); Asian: 0 (0); H: 0 (0); O: (100)	26.4	NR	9.06	6.5
	Unspecified sulfonylurea + rosiglitazone, 84	54.3 (28 -76)	(80)	AA: 0 (0); C: 0 (0); Asian: 0 (0); H: 0 (0); O: (100)	26.8	NR	9.21	6.5
Fujioka, 2003 ¹⁰⁵	Placebo + diet + metformin XR, 75	54	34	NR	32	92	7	3
	Placebo + diet + metformin XR, 71	55	28	NR	31	88	7	3
	Placebo + diet + metformin, 71	54	31	NR	33	96	7.1	3
Derosa, 2003 ¹¹⁸	Placebo + repaglinide, 62	56	31	NR	26.1	76.4	8	NR
	Placebo + glimepiride, 62	54	30	NR	26.4	77.1	7.8	NR
Zhu, 2003 ¹⁸⁸	Placebo + unspecified sulfonylurea, 105	58.8	(46)	AA: 0; C: 0; Asian: 100; H: 0; O: 0	25.1	NR	9.8	7.6
	Unspecified sulfonylurea + rosiglitazone, 215	59	(41)	AA: 0; C: 0; Asian: 100; H: 0; O: 0	24.8	NR	9.8	7.2

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Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes in years
	Unspecified sulfonylurea + rosiglitazone, 210	58.9	(48)	AA: 0; C: 0; Asian: 100; H: 0; O: 0	24.9	NR	9.9	7.9
Del Prato, 2003 ¹⁴⁹	Placebo, 144	56	91	NR	29.9	NR	NR	NR
	Placebo + metformin, 284	56	68	NR	29.7	NR	NR	NR
Pavo, 2003 ⁵⁹	Placebo + pioglitazone, 105	54.2	(43.8)	NR	31.3	86.6	8.6	0.47
	Placebo + metformin, 100	55.8	(56)	NR	31.1	88.9	8.6	0.53
Luis Bautista, 2003 ¹⁹³	Diet + exercise + glimepiride, 48	48.4	27 (56.3)	AA: 0; C: 0; Asian: 0; H: (100); O: 0	NR	83.3	10	4.2
	Placebo + diet + exercise, 22	50.7	11 (50)	AA: 0; C: 0; Asian: 0; H: (100); O: 0	NR	76.3	10.5	5.7
Bakris, 2003 ⁶⁶	Glyburide, 64	56.1	(71)	NR	NR	NR	9.5	NR
	Rosiglitazone, 57	5.1	(75)	NR	NR	NR	9.1	NR
Vongthavara-vat, 2002 ¹⁷⁰	Diet + unspecified sulfonylurea + rosiglitazone, 164	54.6 (30 -76)	75 (45.7)	AA: 6 (3.7); C: 66 (40.2); Asian: 91 (55.5); H: 0; O: 1 (0.6)	27.1	69	9.1	5
	Diet + unspecified sulfonylurea, 170	57.3 (37 -77)	72 (42.4)	AA: 4 (2.4); C: 62 (36.5); Asian: 101 (59.4); H: 0; O: 3 (1.8)	27.1	68.8	8.9	6
Virtanen, 2003 ¹⁴³	Placebo + diet, 14	58	10	NR	30.3	88.3	6.3	NR
	Diet + rosiglitazone, 14	58	10	NR	29.1	83.7	6.8	NR
	Diet + metformin, 13	58	8	NR	29.9	88.8	6.9	NR
Vakkilainen, 2002 ¹²²	Placebo + nateglinide, 23	63	NR	AA: 0; C: (100); Asian: 0; H: 0; O: 0	27.8	NR	7.6	NR
	Placebo + glibenclamide, 20	63	NR	AA: 0; C: (100); Asian: 0; H: 0; O: 0	28.8	NR	7.6	NR
Hallsten, 2002 ⁵⁸	Placebo + diet, 14	57.7	10	NR	30.3	NR	6.3	NR
	Diet + metformin, 13	57.8	8	NR	29.9	NR	6.9	NR

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Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes in years
	Diet + rosiglitazone, 14	58.6	10	NR	29.3	NR	6.8	NR
Scherbaum, 2002 ¹⁴¹	Placebo + diet, 84	59.1	47	NR	29.2	84.8	8.75	5.6
	Diet + pioglitazone, 89	58	56	NR	29.9	87.2	9.33	5.4
	Diet + pioglitazone, 78	59.6	32	NR	29.3	82	9.06	4.6
Blonde, 2002 ⁸¹	Glyburide, 164	55.8	94 (57.3)	AA: 20 (12.2); C: 109 (66.5); Asian: 0; H: 28 (17.1); O: 7 (4.3)	30.3	88	9.64	7.01
	Metformin, 153	57.6	95 (62.1)	AA: 16 (10.5); C: 105 (69.3); Asian: 0; H: 26 (17); O: 5 (3.3)	30.6	89.5	9.51	8.18
	Metformin + glyburide, 160	55.4	89 (55.6)	AA: 20 (12.5); C: 112 (70); Asian: 0; H: 25 (15.6); O: 3 (1.9)	30.7	89.4	9.41	7.36
	Metformin + glyburide, 162	55.6	103 (63.6)	AA: 15 (9.3); C: 110 (67.9); Asian: 0; H: 31 (19.1); O: 6 (3.7)	30.6	89.6	9.42	6.97
St John Sutto, 2002 ⁶⁷	Glyburide, 99	56.1 (40 -76)	(71)	AA: (3); C: (76); Asian: 0; H: 0; O: (21)	(% BMI \geq 27: 65.7%)	NR	9.5	6.2
	Rosiglitazone, 104	55.1 (40 -77)	(75)	AA: (5); C: (73); Asian: 0; H: 0; O: (22)	(% BMI \geq 27: 67.3%)	NR	9.1	5.3
Rachmani, 2002 ¹⁵⁰	Diet + metformin stopped, 198	64	102	NR	28.4	NR	8.6	14
	Diet + metformin continued, 195	65	103	NR	28.7	NR	8.6	15
Saloranta, 2002 ²⁴¹	Nateglinide, 166	61	105 (63.3)	AA: 2 (1.2); C: 162 (97.6); Asian: 1 (0.6); H: 0; O: 1 (0.6)	28.95	NR	6.55	3.8
	Nateglinide, 175	61.1	107 (61.1)	AA: 1 (0.6); C: 163 (93.1); Asian: 3 (4.6); H: 0; O: 8 (4.6)	28.92	NR	6.53	3.6
	Nateglinide, 171	59.6	112 (65.5)	AA: 2 (1.2); C: 163 (95.3); Asian: 4 (1.2); H: 0; O: 2 (1.2)	29.12	NR	6.57	3.7

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Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes in years
	Placebo, 163	59.1	98 (60.1)	AA: 2 (1.2); C: 157 (96.3); Asian: 1 (1.8); H: 0; O: 3 (1.8)	28.78	NR	6.45	3.2
Marre, 2002 ⁸⁴	Metformin, 104	57.5	62	NR	29.9	84.9	8.09	5.4
	Glibenclamide, 103	58.7	57	NR	29.3	82.5	7.88	6.6
	Metformin + glibenclamide, 101	58	50	NR	30.1	84.7	7.89	5.9
	Metformin + glibenclamide, 103	60.7	56	NR	29.7	83.1	7.62	6.7
Garber, 2002 ⁷⁹	Placebo, 161	55.4	76	AA: 122; C: 122; Asian: 0; H: 17; O: 6	30.2	86.2	8.21	2.76
	Glyburide, 161	56.5	82	AA: 126; C: 126; Asian: 0; H: 14; O: 6	30.3	87.2	8.21	2.81
	Metformin, 161	56	93	AA: 130; C: 130; Asian: 0; H: 20; O: 4	30.4	88.6	8.26	2.98
	Metformin + glyburide, 158	56.9	91	AA: 117; C: 117; Asian: 0; H: 18; O: 3	30.1	88.8	8.25	3.52
	Metformin + glyburide, 165	58.1	96	AA: 131; C: 131; Asian: 0; H: 16; O: 8	29.6	86.7	8.18	3.3
Gomez-Perez, 2002 ¹⁰²	Placebo + metformin, 34	53.4 (40 -68)	10	AA: 0; C: 1; Asian: 0; H: 26; O: 7	28.5	NR	NR	9.1
	Metformin + rosiglitazone, 35	51.7 (40 -73)	10	AA: 0; C: 0; Asian: 0; H: 28; O: 7	28	NR	NR	11.1
	Metformin + rosiglitazone, 36	54.2 (42 -76)	7	AA: 0; C: 4; Asian: 0; H: 26; O: 6	27.6	NR	NR	10.7
Khan, 2002 ⁵¹	Rosiglitazone, 60	57.1	27	NR	35.6	NR	7.9	NR
	Pioglitazone, 67	57.8	35	NR	35.2	NR	8	NR
Charpentier, 2001 ⁸⁹	Placebo + metformin, 75	56.7 (36 -69)	45 (60)	NR	29.2	82.2	6.8	7
	Placebo + glimepiride, 150	55.4 (35 -70)	87 (58)	NR	29.3	81	6.5	5.3
	Metformin + glimepiride, 147	56.8 (36 -70)	87 (59)	NR	29.5	81.2	6.4	5.6

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Rosenblatt, 2001 ¹⁶²	Placebo, 96	55.2	(46.2)	AA: (11.5); C: (61.5); Asian: 0; H: (24); O: (3.1)	30.7	87.2	10.42	NR
	Pioglitazone, 101	53.8	(50.5)	AA: (8.9); C: (69.3); Asian: 0; H: (19.8); O: (2)	31.5	89.8	10.65	NR
Madsbad, 2001 ¹¹⁹	Repaglinide, 175	60.2	107	NR	28	82.9	7.3	8.1
	Placebo + glipizide, 81	62	52	NR	28	83.6	7.2	7
Kipnes, 2001 ¹⁶⁶	Placebo + unspecified sulfonylurea, 187	56.9	109	AA: 25; C: 141; Asian: 3; H: 18; O: 0	32	NR	9.9	19
	Unspecified sulfonylurea + pioglitazone, 184	56.5	109	AA: 20; C: 146; Asian: 3; H: 15; O: 0	31.4	NR	10	29
	Unspecified sulfonylurea + pioglitazone, 189	56.6	113	AA: 17; C: 156; Asian: 3; H: 13; O: 0	32.4	NR	9.9	26
Amador-Licona, 2000 ⁸⁵	Glibenclamide, 23	48.2	7	NR	30.4	73.2	8.4	4
	Metformin, 28	49.3	11	NR	26.8	70.7	8.5	4.5
Lebovitz, 2001 ¹⁶⁹	Placebo, 158	59	104	NR	29.9	NR	9.0	4.6
	Rosiglitazone, 166	60	107	NR	30.2	NR	9.0	4.8
	Rosiglitazone, 169	61	113	NR	29.1	NR	8.8	5.4
Patel, 1999 ¹⁶⁷	Placebo, 75	56.8 (34 -83)	52 (69.3)	AA: 2; C: 55; Asian: 0; H: 0; O: 18	28.9	NR	9.1	4.2
	Rosiglitazone, 74	56.7 (30 -76)	49 (66.2)	AA: 4; C: 55; Asian: 0; H: 0; O: 15	29.4	NR	9.1	4.9
	Rosiglitazone, 72	55.8 (31 -74)	51 (70.8)	AA: 6; C: 53; Asian: 0; H: 0; O: 13	28.6	NR	8.9	6.7
	Rosiglitazone, 79	59.8 (37 -79)	51 (64.6)	AA: 4; C: 63; Asian: 0; H: 0; O: 12	29.5	NR	9	4.4
	Rosiglitazone, 80	59.7 (41 -81)	55 (68.8)	AA: 5; C: 58; Asian: 0; H: 0; O: 17	28.4	NR	9	5.8
Phillips, 2001 ¹⁶⁸	Placebo, 173	57.7	119 (68.8)	AA: 16 (9.2); C: 137 (79.2); Asian: 0; H: 0; O: 20 (11.6)	29.1	NR	8.9	6.6

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	Rosiglitazone, 181	57.5	106 (58.6)	AA: 23 (12.7); C: 138 (76.2); Asian: 0; H: 0; O: 20 (11)	29.9	NR	8.9	5.4
	Rosiglitazone, 186	56.8	110 (59.1)	AA: 15 (8.1); C: 145 (78); Asian: 0; H: 0; O: 26 (14)	30	NR	8.9	5.5
	Rosiglitazone, 181	58.9	119 (65.7)	AA: 13 (7.2); C: 145 (80.1); Asian: 0; H: 0; O: 23 (12.7)	30	NR	8.9	6.1
	Rosiglitazone, 187	56.5	122 (65.2)	AA: 20 (10.7); C: 133 (71.1); Asian: 0; H: 0; O: 34 (18.2)	29.9	NR	9	5.9
Moses, 2001 ²¹⁸	Repaglinide, 260	57.5	(53.5)	AA: (0.4); C: (98.8); Asian: (0); H: 0; O: (0.8)	30	84	7.8	2.99
	Placebo, 134	57.4	(57.5)	AA: (0); C: (98.5); Asian: (0); H: 0; O: (1.5)	30.9	86.6	7.6	3.07
Einhom, 2000 ¹⁶⁰	Diet + metformin + pioglitazone, 168	55.5	92 (54.8)	AA: 14 (8.3); C: 136 (81); Asian: 0; H: 17 (10.1); O: 1 (0.6)	32.11	NR	9.86	NR
	Placebo + diet + metformin, 160	55.7	96 (60)	AA: 10 (6.3); C: 139 (86.9); Asian: 0; H: 6 (3.8); O: 5 (3.1)	32.12	NR	9.75	NR
Fonseca, 2000 ¹⁰³	Placebo + metformin, 113	58.8	74.3	AA: (3.5); C: (81.4); Asian: 0; H: 0; O: (15)	30.3	NR	8.6	7.3
	Metformin + rosiglitazone, 116	57.5	62.1	AA: (6.9); C: (80.2); Asian: 0; H: 0; O: (12.9)	30.2	NR	8.9	7.5
	Metformin + rosiglitazone, 110	58.3	68.2	AA: (10); C: (77.3); Asian: 0; H: 0; O: (12.7)	29.8	NR	8.9	8.3
Nakamura, 2000 ⁶⁴	Pioglitazone, 15	60	7	NR	NR	NR	7.7	16
	Glibenclamide, 15	61	8	NR	NR	NR	7.8	14
	Voglibose, 15	56	8	NR	NR	NR	7.6	15
Horton, 2000 ⁹⁶	Nateglinide, 179	58.6	110	AA: (9.5); C: (82.1); Asian: (2.8); H: 0; O: 5.6	29.6	NR	8.3	4.7
	Metformin, 178	56.8	121	AA: (9.6); C: (79.2); Asian: (2.2); H: 0; O: 9	29.6	NR	8.4	7.5
	Metformin + nateglinide, 172	58.4	101	AA: (11.6); C: (82.6); Asian: (0.6); H: 0; O: 5.2	30	NR	8.4	4.5

Appendix F: Evidence Table 3. Study population table for studies reporting on proximal clinical outcomes (Key Question 1)

Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes in years
	Placebo, 172	59.6	104	AA: (16.9); C: (78.5); Asian: (0.6); H: 0; O: 4.1	29.2	NR	8.3	4.6
Aronoff, 2000 ¹⁶⁵	Placebo, 79	53.7 overall (29 - 75 overall)	(58 overall)	AA: (8) overall; C: (78) overall; Asian: (2) overall; H: (12) overall; O: (1) overall	NR	90.4	10.4	NR
	Pioglitazone, 81	53.7 overall (29 - 75 overall)	(58 overall)	AA: (8) overall; C: (78) overall; Asian: (2) overall; H: (12) overall; O: (1) overall	NR	93.5	10	NR
	Pioglitazone, 81	53.7 overall (29 - 75 overall)	(58 overall)	AA: (8) overall; C: (78) overall; Asian: (2) overall; H: (12) overall; O: (1) overall	NR	91.2	10.2	NR
	Pioglitazone, 87	53.7 overall (29 - 75 overall)	(58 overall)	AA: (8) overall; C: (78) overall; Asian: (2) overall; H: (12) overall; O: (1) overall	NR	90.3	10.2	NR
	Pioglitazone, 80	53.7 overall (29 - 75 overall)	(58 overall)	AA: (8) overall; C: (78) overall; Asian: (2) overall; H: (12) overall; O: (1) overall	NR	90.8	10.3	NR
Hanefeld, 2000 ¹⁹⁰	Placebo, 60	57.4	36	NR	28.3	NR	8.5	5.4
	Nateglinide, 51	58	36	NR	29	NR	8.4	4.5
	Nateglinide, 58	56.1	41	NR	28.1	NR	8.3	6.2
	Nateglinide, 63	54.4	44	NR	28.6	NR	8.3	4.4
	Nateglinide, 57	56.5	36	NR	28.8	NR	8.5	3.7
Hasche, 1999 ¹³⁸	Diet + acarbose, 36	63.8	17	NR	26.1	74.3	8.5	1
	Placebo + diet, 38	63.1	19	NR	26.7	75.5	8.3	1
Wolffenbuttel, 2000 ¹⁷¹	Placebo + unspecified sulfonylurea, 192	61.9	110	AA: 2; C: 186; Asian: 0; H: 0; O: 4	28.1	NR	9.21	8
	Unspecified sulfonylurea + rosiglitazone, 19	61	125	AA: 2; C: 190; Asian: 0; H: 0; O: 7	28.0	NR	9.2	7
	Unspecified sulfonylurea + rosiglitazone, 18	60.6	101	AA: 2; C: 180; Asian: 0; H: 0; O: 1	28.3	NR	9.23	7

Appendix F: Evidence Table 3. Study population table for studies reporting on proximal clinical outcomes (Key Question 1)

Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes in years
Gregorio, 1999 ¹²⁹	Glibenclamide + glyclazide, 85	75.73	40	NR	NR	76.61	10.32	14.67
	Metformin + glibenclamide + glyclazide, 89	75.42	42	NR	NR	76.44	10.33	15.11
Jovanovic, 2000 ¹⁹⁴	Placebo, 75	58.5	49 (65)	AA: 11 (15); C: 51 (68); Asian: 1 (1); H: 0; O: 12 (16)	29.8	NR	8.6	6.8
	Repaglinide, 140	57.9	96 (69)	AA: 14 (10); C: 107 (76); Asian: 0 (0); H: 0; O: 19 (14)	29.4	NR	8.9	6.6
	Repaglinide, 146	57.6	87 (60)	AA: 18 (12); C: 110 (75); Asian: 2 (1); H: 0; O: 16 (11)	29.5	NR	8.7	6.3
Willms, 1999 ⁹⁹	Acarbose, 31	60.3	15	NR	NR	86.1	10.6	134.8 months
	Placebo, 29	59.2	17	NR	NR	90.2	10.6	119.6 months
	Metformin, 27	53.4	13	NR	NR	88.6	10.6	111.9 months
Erle, 1999 ¹²⁷	Glyburide, 20	60 overall	21 overall	NR	30.5 overall	85.2	7.37	NR
	Metformin + glyburide, 20	60 overall	21 overall	NR	30.5 overall	85.5	7.67	NR
Landgraf, 1999 ¹²¹	Repaglinide, 94	61	56	AA: 0; C: 90; Asian: 0; H: 0; O: 4	27.6	80	7.8	10
	Placebo + glibenclamide, 100	63	57	AA: 6; C: 93; Asian: 0; H: 0; O: 1	27.5	79	8	10
Marbury, 1999 ¹¹⁶	Repaglinide, 362	58.3	242 (67)	AA: 33 (9); C: 279 (77); Asian: 0; H: 0; O: 50 (14)	29.4	NR	8.7	7.2
	Placebo + glyburide, 182	58.7	120 (66)	AA: 16 (9); C: 144 (79); Asian: 0; H: 0; O: 22 (12)	29.1	NR	8.9	8.3
Wolffenbuttel, 1999 ¹¹⁷	Repaglinide, 286	61	(62)	NR	28.4	81.5	7.1	(Median 6)
	Placebo + glyburide, 139	61	(68)	NR	28	81.3	7	(Median 6)

Appendix F: Evidence Table 3. Study population table for studies reporting on proximal clinical outcomes (Key Question 1)

Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes in years
Testa, 1998 ¹⁹⁸	Placebo + diet, 192	58.4 (30 -82)	(58.9)	AA: (15.6); C: (72.9); Asian: 0; H: 0; O: (11.5)	30.3	NR	8.7	4.7
	Diet + glipizide GITS, 377	58.7 (30 -85)	(54.9)	AA: (16.7); C: (71.9); Asian: 0; H: 0; O: (11.4)	30.1	NR	8.5	5.6
Goldberg, 1998 ¹³⁹	Placebo, 33	56.4	25 (76)	AA: 0; C: 29 (88); Asian: 0; H: 0; O: 4 (12)	30	NR	8.1	5.1
	Repaglinide, 67	58.7	49 (74)	AA: 0; C: 58 (88); Asian: 0; H: 0; O: 8 (12)	30.6	NR	8.3	5.6
1998 ¹⁵ UKPDS	Diet, 411	53	193 (47)	AA: 0; C: (86); Asian: (6); H: 0; O: (8)	31.8	87	7.1	NR
	Diet + metformin, 342	53	157 (46)	AA: 0; C: (85); Asian: (4); H: 0; O: (11)	31.6	87	7.3	NR
	Diet + glibenclamide, 277	53	127 (46)	AA: 0; C: (87); Asian: (4); H: 0; O: (9)	31.5	86	7.2	NR
	Diet + unspecified sulfonylurea, 269	58	164 (61)	AA: 0; C: (77); Asian: (13); H: 0; O: (10)	29.4	82	7.6	NR
	Diet + metformin + unspecified sulfonylurea, 268	59	158 (59)	AA: 0; C: (77); Asian: (11); H: 0; O: (12)	29.7	83	7.5	NR
1998 ¹⁶ UKPDS	Diet, 896	54	555	AA: 0; C: (83); Asian: 0; H: 0; O: (16)	27.5	77	6.2	NR
	Diet + glibenclamide, 615	54	381	AA: 0; C: (84); Asian: 0; H: 0; O: (15)	27.4	77	6.3	NR
Schade, 1998 ¹³⁵	Glimepiride, 123	52	NR	NR	NR	86.8	9.1	3.1
	Placebo, 126	54	NR	NR	NR	87.3	8.9	3.1
1998 ¹²⁸ UKPDS	Diet + metformin + glibenclamide, 291	59	(59)	AA: (14); C: (78); Asian: (8); H: 0; O: 0	29.2	81	(Median 7.4)	NR
	Diet + glibenclamide, 300	58	(60)	AA: (11); C: (78); Asian: (11); H: 0; O: 0	29.1	81	(Median 7.3)	NR
Lee, 1998 ²⁵⁹	Placebo + diet + metformin, 24	59 (56 - 62)	0	NR	40	112.8	8.3	4
	Placebo + diet, 24	61 (59 - 63)	0	NR	39.6	108.6	8.1	3

Appendix F: Evidence Table 3. Study population table for studies reporting on proximal clinical outcomes (Key Question 1)

Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes in years
Garber, 1997 ²¹⁷	Placebo, 79	55	(56)	AA: (22); C: (66); Asian: 0; H: (11); O: (1)	NR	90.9	9.9	NR
	Metformin, 73	57	(62)	AA: (11); C: (62); Asian: 0; H: (14); O: (1)	NR	90	10.1	NR
	Metformin, 73	55	(55)	AA: (12); C: (55); Asian: 0; H: (10); O: (1)	NR	90	10	NR
	Metformin, 76	59	(63)	AA: (12); C: (63); Asian: 0; H: (15); O: (2)	NR	89.6	9.7	NR
	Metformin, 73	60	(53)	AA: (14); C: (53); Asian: 0; H: (12); O: (4)	NR	89.1	10.1	NR
	Metformin, 77	59	(65)	AA: (10); C: (65); Asian: 0; H: (10); O: (0)	NR	94.5	10	NR
Simonson, 1997 ¹³⁶	Glipizide, 68	57.4 (33 -81)	40	AA: 10; C: 50; Asian: 0; H: 0; O: 8	29	185 pounds	8.5	6.9
	Glipizide, 42	58.7 (34 -78)	25	AA: 4; C: 32; Asian: 0; H: 0; O: 6	28.4	181 pounds	8.8	8.8
	Glipizide, 42	55.5 (130 - 271)	26	AA: 4; C: 30; Asian: 0; H: 0; O: 8	29.5	187.3 pounds	8.6	6.5
	Glipizide, 69	59.3 (128 - 312)	47	AA: 7; C: 54; Asian: 0; H: 0; O: 8	28.8	186.7 pounds	8.7	7.8
	Glipizide, 28	61.7 (144 - 267)	17	AA: 1; C: 25; Asian: 0; H: 0; O: 2	29.6	196.2 pounds	8.4	6.6
	Glipizide, 29	56.9 (142 - 270)	23	AA: 1; C: 24; Asian: 0; H: 0; O: 4	30.5	201.1 pounds	8.6	5.3
	Placebo, 69	60.2 (125 - 280)	53	AA: 8; C: 50; Asian: 0; H: 0; O: 11	29.78	191.7 pounds	8.3	7.5
Rosenstock, 1996 ¹⁸⁹	Placebo, 79	61.1	(67)	NR	NR	85.9	8	median 6
	Glimepiride, 88	61.8	(74)	NR	NR	82.9	8.1	median 7
	Glimepiride, 81	58.8	(70)	NR	NR	86.3	8.1	median 6
	Glimepiride, 83	59.6	(66)	NR	NR	84.2	8	median 5
	Glimepiride, 85	61.7	(72)	NR	NR	86.8	8.3	median 7
Dills, 1996 ¹⁰⁷	Glimepiride, 289	59	(61)	AA: 0; C: (86); Asian: 0; H: 0; O: (14)	NR	192 pounds	8.5	5

Appendix F: Evidence Table 3. Study population table for studies reporting on proximal clinical outcomes (Key Question 1)

Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes in years
	Glyburide, 288	60	(58)	AA: 0; C: (87); Asian: 0; H: 0; O: (13)	NR	192 pounds	8.5	5
Draeger, 1996 ¹¹²	Glibenclamide, 520	60.7 (26 -81)	340	AA: 0; C: 0; Asian: 74; H: 0; O: (26)	26.5	NR	8.1	5
	Glimepiride, 524	59.7 (27 -81)	325	NR	26.5	NR	8.1	5
Goldberg, 1996 ¹³⁴	Placebo, 74	60.4	48	AA: 0; C: 60; Asian: 0; H: 0; O: 14	NR	85	7.8	6
	Glimepiride, 78	58.9	56	AA: 0; C: 65; Asian: 0; H: 0; O: 13	NR	83.9	7.8	7
	Glimepiride, 76	57.8	41	AA: 0; C: 60; Asian: 0; H: 0; O: 16	NR	86.1	7.7	5
	Glimepiride, 76	59.6	43	AA: 0; C: 64; Asian: 0; H: 0; O: 12	NR	85.3	7.8	6
Grant, 1996 ¹⁵⁴	Placebo, 23	NR	NR	NR	NR	NR	NR	NR
	Metformin, 25	NR	NR	NR	NR	NR	NR	NR
	Metformin, 27	NR	NR	NR	NR	NR	NR	NR
Vray, 1995 ¹³⁷	Placebo, 56	56.8	(36)	NR	F 23.7; M 23.8	NR	10	3.9
	Glibenclamide, 56	55.8	(36)	NR	F 24.5; M 23.7	NR	9.6	2.4
DeFronzo, 1995 ⁸⁸	Metformin, 143	53	62	NR	29.9	94.4	8.4	6
	Placebo, 53	53	62	NR	29.2	92.2	8.2	6
	Placebo + metformin, 210	55	96	NR	29.4	92.6	8.9	8.4
	Placebo + glyburide, 209	56	103	NR	29.1	92.6	8.5	8.7
	Metformin + glyburide, 213	55	98	NR	29	92.1	8.8	7.8
1995 ⁹² UKPDS	Diet, 664	NR	NR	NR	NR	NR	NR	NR
	Diet + glibenclamide, 472	NR	NR	NR	NR	NR	NR	NR
	Diet + metformin, 262	NR	NR	NR	NR	NR	NR	NR

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Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes in years
Hermann, 1994 ⁸⁷	Diet + metformin, 25	60 (34 - 74)	(63%)	NR	NR	78.6	6.9	4
	Diet + glibenclamide, 21	NR	NR	NR	NR	82.6	6.7	NR
	Diet + metformin + glibenclamide, 54	NR	NR	NR	NR	80.2	6.8	NR
	Diet + metformin + glibenclamide, 13	NR	NR	NR	NR	84.6	7.8	NR
	Diet + metformin + glibenclamide, 13	NR	NR	NR	NR	76	7.8	NR
	Diet + metformin + glibenclamide, 18	NR	NR	NR	NR	83.2	8.4	NR
Campbell, 1994 ⁸³	Metformin, 24	57	8	NR	29.6	78.2	11.5	2.3
	Glipizide, 24	57	8	NR	31.2	82.2	11.8	2.8
Birkeland, 1994 ¹¹⁰	Diet + glipizide, 46	59	22	NR	26.4	NR	8	3.5
	Diet + glyburide	NR	NR	NR	NR	NR	8	NR
	Placebo + diet	NR	NR	NR	NR	NR	8.1	NR
Rosenstock, 1993 ¹⁰⁹	Glyburide, 70	71.4	39	AA: 0; C: 65; Asian: 0; H: 2; O: 3	NR	79.6	5.7	11
	Glyclazide, 69	70.2	48	AA: 0; C: 64; Asian: 0; H: 2; O: 3	NR	80.5	5.8	11
Carlson, 1993 ¹⁰⁸	Glyburide, 104	59.2 (33 -80)	61	AA: 11; C: 81; Asian: 0; H: 7; O: 5	NR	NR	7.6	N=15/32/57 for <1/1-5/>5 years
	Glyburide, 102	60.3 (38 -78)	62	AA: 13; C: 81; Asian: 0; H: 4; O: 4	NR	NR	7.6	N=6/42/54 for <1/1-5/>5 years
Wolffenbuttel, 1993 ¹²⁰	Repaglinide, 29	62 (45 - 75)	25	NR	26.1	74	(Range 7.0 - 12.0)	9
	Glibenclamide, 15	62 (45 - 75)	25	NR	26.1	70.9	(Range 7.0 - 12.0)	9
Leonhardt,	Acarbose, 47	NR	NR	NR	NR	NR	NR	NR

Appendix F: Evidence Table 3. Study population table for studies reporting on proximal clinical outcomes (Key Question 1)

Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes in years
1991 ²⁶³	Placebo, 47	NR	NR	NR	NR	NR	NR	NR
Teupe, 1991 ¹⁵⁵	Diet, 50	56	20	NR	NR	86.1	9.6	6.4
	Diet + metformin, 50	51.5	20	NR	NR	89.1	10	8.1
Noury, 1991 ⁸⁶	Metformin, 30	55	16	NR	29.1	80.4	9.75	3
	Glyclazide, 27	54.9	12	NR	28	79	9.72	3
Hermann, 1991 ⁹⁴	Diet + metformin, 16	60 overall (38 - 73 overall)	(64 overall)	NR	27	76.5	6.7	NR
	Diet + glibenclamide, 17	60 overall (38 - 73 overall)	(64 overall)	NR	29.2	84.1	6.6	NR
	Diet + metformin + glibenclamide, 12	60 overall (38 - 73 overall)	(64 overall)	NR	30	87.3	7.7	NR
	Diet + metformin + glibenclamide, 11	60 overall (38 - 73 overall)	(64 overall)	NR	26.1	74.4	7.8	NR
Schneider, 1991 ¹⁷³	Placebo, 16	61.5	9	NR	27.1	NR	6.48	NR
	Metformin, 18	60.4	8	NR	26.1	NR	6.76	NR
Hermann, 1991 ¹⁵⁹	Diet + metformin + glibenclamide, 72	60 (34 - 74)	79	NR	28.4	82.3	NR	NR
	Diet + metformin, 38	NR	NR	NR	NR	NR	NR	NR
	Diet + glibenclamide, 34	NR	NR	NR	NR	NR	NR	NR
	Diet, 14	NR	NR	NR	NR	NR	NR	NR
Doman, 1991 ²⁶⁰	Metformin, 30	55	(53)	NR	30	NR	11.7	NR
	Placebo, 30	55	(30)	NR	30	NR	11.8	NR
Kilo, 1988 ¹⁴⁷	Glyburide, 47	NR	66 overall	NR	NR	NR	NR	NR
	Glipizide, 52	NR	NR	NR	NR	NR	NR	NR
1985 ⁹¹ UKPDS	Diet	52	(64%)	NR	NR	overall N=77 >120% ideal weight	NR	0

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Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes in years
	Diet + unspecified sulfonylurea	NR	NR	NR	NR	overall N=77 >120% ideal weight	NR	0
	Diet + metformin	NR	NR	NR	NR	overall N=77 >120% ideal weight	NR	0
Harrower, 1985 ¹¹³	Glipizide, 24	62	NR	NR	NR	NR	10	2.6
	Glyclazide, 22	60	NR	NR	NR	NR	13	3.5
	Glibenclamide, 23	60	NR	NR	NR	NR	11	3.5
Baba, 1983 ¹³³	Glyclazide, 146	Age categories (N) <39: 11 40-49: 25 50-59: 46 60-69: 52 >70: 12	78 (53.42)	NR	Obesity Index: <119%: 71.9%; >120%: 28.1%	NR	NR	Duration categories (N) <1: 35 1-4: 25 5-9: 39 >10: 47
	Glibenclamide, 131	Age categories (N) <39: 13 40-49: 24 50-59: 46 60-69: 35 >70: 13	55 (41.98)	NR	Obesity Index: <119%: 71%; >120%: 29%	NR	NR	Duration categories (N) <1: 30 1-4: 35 5-9: 34 >10: 35
Tseng, 2005 ¹⁴⁰	Unspecified sulfonylurea + pioglitazone, 23	58	8	AA: 0; C: 0; Asian: 0; H: 0; O: (100)	NR	61.3	NR	NR
	Placebo + unspecified sulfonylurea, 25	54	9	NR	NR	62.6	NR	NR
Wolever, 2000 ⁹⁸	Placebo, 45	58.5	27	NR	30.8	NR	7.8	4.5
	Metformin, 62	58.7	45	NR	30.5	NR	8.2	7.3
	Miglitol, 45	56.8	39	NR	30.7	NR	7.9	4.7

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Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes in years
	Metformin + miglitol, 47	59.5	42	NR	29.9	NR	8.2	5.2
Cefalu, 1998 ²⁶¹	Placebo, 20	58.7	15 (75)	NR	NR	91	NR	NR
	Glipizide GITS, 20	56.7	13 (65)	NR	NR	84	NR	NR
Turner, 1998 ⁹³ UKPDS	Diet + metformin	NR	NR	NR	NR	NR	NR	NR
	Diet + glyburide or chlorpropamide	NR	NR	NR	NR	NR	NR	NR
Garber, 2006 ⁷¹	Diet + metformin + glibenclamide, 160	56 (31 - 78)	90	AA: 8 (5); C: 128 (80); Asian: 4 (3); H: 17 (11); O: 3 (2)	32	93	8.5	5
	Diet + metformin + rosiglitazone, 158	56 (24 - 78)	102	AA: 9 (6); C: 125 (79); Asian: 4 (3); H: 16 (10); O: 4 (3)	32	94	8.4	6

BMI = body mass index; kg = kilograms; HbA1c = hemoglobin A1c; AA = African American; C = Caucasian; H = Hispanic; O = Other; NR = not reported; SD = standard deviation; XR = extended release; GITS = gastrointestinal therapeutic system; F = females; M = males; UKPDS = United Kingdom Prospective Diabetes Study; DIACOM = effect of Dosing frequency of oral Antidiabetic agents on the COMpliance and biochemical control of type 2 diabetes

Appendix F: Evidence Table 4. Grading of the Body of Evidence for Proximal Clinical Outcome Measures

Grading of the quality of evidence of the efficacy/effectiveness of oral diabetes medications: Thiazolidinedione vs. Metformin

	Key Question 1 Comparative Effectiveness of Short Term Outcomes and Quality of Life				
	HbA1c/2hr PPG	BMI/Weight	SBP/DBP	Lipids	QOL
Quantity of Evidence: Number of studies	7/1	4/6	5/5	6/8/8	0
Total number of patients studied	2194/36	268/2152	1546	1630	0
Quality and Consistency of Evidence: Were study designs mostly randomized trials (high quality), non-randomized controlled trials (medium quality), observational studies (low quality), or about a 50:50 mix of experimental and observational (medium quality) ?	high	High	High	High	
Did the studies have serious (-1) or very serious (-2) limitations in quality? (Enter 0 if none)	-1	-1	0	-1	
Did the studies have important inconsistency? (-1)	0	0	0	0	
Was there some (-1) or major (-2) uncertainty about the directness (i.e. extent to which the people, interventions and outcomes are similar to those of interest? <u>Reminder: we're looking for head to head comparisons of different diabetes meds to get full credit for directness in addressing our question.</u>	0	0	0	0	
Were data imprecise or sparse? (-1) (i.e. lack of data or very wide confidence intervals that may change conclusions)	0	-1	-1	0	
Did the studies have high probability of reporting bias? (-1)	0	0	0	0	
Did the studies show strong evidence of association between intervention and recruitment outcome? ("strong" if significant relative risk or odds ratio > 2 based on consistent evidence from 2 or more studies with no plausible confounders (+1); "very strong" if significant relative risk or odds ratio > 5 based on direct evidence with no major threats to validity (+2))- <u>use your clinical judgement for absolute differences.</u>	+1	+1	0	0	
Did the studies have evidence of a dose-response gradient? (+1)	+1	0	0	0	

Appendix F: Evidence Table 4. Grading of the Body of Evidence for Proximal Clinical Outcome Measures

Did the studies have unmeasured plausible confounders that most likely reduced the magnitude of the observed association? (+1)	0	0	0	0	
Overall grade of evidence (high, moderate, low, very low)	High	Moderate	Low	Moderate	

High = further research is very unlikely to change our confidence in the estimates; moderate = further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low = further research is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; very low = any estimate of effect is very uncertain.

Grading of the quality of evidence of the efficacy/effectiveness of oral diabetes medications: Thiazolidinediones vs Second Generation Sulfonylureas

	Key Question 1 Comparative Effectiveness of Short Term Outcomes and Quality of Life				
	HbA1c/2hr PPG	BMI/Weight	SBP/DBP	Lipids	QOL
Quantity of Evidence: Number of studies	12/1	5/5	6/6	7/7/7	2 indirect studies only
Total number of patients studied	2957/41	438/1911	820	1968	611
Quality and Consistency of Evidence: Were study designs mostly randomized trials (high quality), non-randomized controlled trials (medium quality), observational studies (low quality), or about a 50:50 mix of experimental and observational (medium quality) ?	high	High	High	High	high
Did the studies have serious (-1) or very serious (-2) limitations in quality? (Enter 0 if none)	-1	-1	-1	-2	-0.5
Did the studies have important inconsistency? (-1)	0	-1	0	0	0
Was there some (-1) or major (-2) uncertainty about the directness (i.e. extent to which the people, interventions and outcomes are similar to those of interest? Reminder: we're looking for head to head comparisons of different diabetes meds to get full credit for directness in addressing our question.	0	0	0	0	-2
Were data imprecise or sparse? (-1) (i.e. lack of data or very wide confidence intervals that may change conclusions)	0	-1	0	0	-1
Did the studies have high probability of reporting bias? (-1)	0	0	0	0	0
Did the studies show strong evidence of association between intervention and recruitment outcome? ("strong" if significant relative risk or odds ratio > 2 based on consistent evidence from 2 or more studies with no plausible confounders (+1); "very strong" if significant relative risk or odds ratio > 5 based on direct evidence with no major threats to validity (+2))- use your clinical judgement for absolute differences.	+1	0	0	0	0
Did the studies have evidence of a dose-response gradient? (+1)	+0.5	0	0	0	0

Appendix F: Evidence Table 4. Grading of the Body of Evidence for Proximal Clinical Outcome Measures

Did the studies have unmeasured plausible confounders that most likely reduced the magnitude of the observed association? (+1)	0	0	0	0	0
Overall grade of evidence (high, moderate, low, very low)	Moderate	Low	Moderate	Low	Very low

High = further research is very unlikely to change our confidence in the estimates; moderate = further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low = further research is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; very low = any estimate of effect is very uncertain.

Grading of the quality of evidence of the efficacy/effectiveness of oral diabetes medications: Metformin vs Second Generation Sulfonylureas

	Key Question 1 Comparative Effectiveness of Short Term Outcomes and Quality of Life				
	HbA1c/2hr PPG	BMI/Weight	SBP/DBP	Lipids	QOL
Quantity of Evidence: Number of studies	18/7	7/14	6/6	10/13/14	0
Total number of patients studied	2494/1570	598/2445	957	2323	0
Quality and Consistency of Evidence: Were study designs mostly randomized trials (high quality), non-randomized controlled trials (medium quality), observational studies (low quality), or about a 50:50 mix of experimental and observational (medium quality) ?	high	High	High	High	
Did the studies have serious (-1) or very serious (-2) limitations in quality? (Enter 0 if none)	-1	0	-1	-1	
Did the studies have important inconsistency? (-1)	0	0	0	-1	
Was there some (-1) or major (-2) uncertainty about the directness (i.e. extent to which the people, interventions and outcomes are similar to those of interest? Reminder: we're looking for head to head comparisons of different diabetes meds to get full credit for directness in addressing our question.	0	0	0	0	
Were data imprecise or sparse? (-1) (i.e. lack of data or very wide confidence intervals that may change conclusions)	0	0	0	0	
Did the studies have high probability of reporting bias? (-1)	0	0	0	0	
Did the studies show strong evidence of association between intervention and recruitment outcome? ("strong" if significant relative risk or odds ratio > 2 based on consistent evidence from 2 or more studies with no plausible confounders (+1); "very strong" if significant relative risk or odds ratio > 5 based on direct evidence with no major threats to validity (+2)	+1	+1	0	0	
Did the studies have evidence of a dose-response gradient? (+1)	+0.5	0	0	0	

Appendix F: Evidence Table 4. Grading of the Body of Evidence for Proximal Clinical Outcome Measures

Did the studies have unmeasured plausible confounders that most likely reduced the magnitude of the observed association? (+1)	0	0	0	0	
Overall grade of evidence (high, moderate, low, very low)	high	High	Low	Moderate to Low	

High = further research is very unlikely to change our confidence in the estimates; moderate = further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low = further research is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; very low = any estimate of effect is very uncertain.

Grading of the quality of evidence of the efficacy/effectiveness of oral diabetes medications: Second Generation Sulfonylureas vs Meglitinides

	Key Question 1 Comparative Effectiveness of Short Term Outcomes and Quality of Life				
	HbA1c/2hr PPG	BMI/Weight	SBP/DBP	Lipids	QOL
Quantity of Evidence: Number of studies	7/3	1/5	2/2	3/6/5	2 indirect studies only
Total number of patients studied	1486/358	124/1256	444	1514	822
Quality and Consistency of Evidence: Were study designs mostly randomized trials (high quality), non-randomized controlled trials (medium quality), observational studies (low quality), or about a 50:50 mix of experimental and observational (medium quality) ?	high	High	High	High	high
Did the studies have serious (-1) or very serious (-2) limitations in quality? (Enter 0 if none)	0	0	0	0	0
Did the studies have important inconsistency? (-1)	0	0	0	0	0
Was there some (-1) or major (-2) uncertainty about the directness (i.e. extent to which the people, interventions and outcomes are similar to those of interest? <u>Reminder: we're looking for head to head comparisons of different diabetes meds to get full credit for directness in addressing our question.</u>	0	0	0	0	-2
Were data imprecise or sparse? (-1) (i.e. lack of data or very wide confidence intervals that may change conclusions)	-0.5	-1	-1	0	-1
Did the studies have high probability of reporting bias? (-1)	0	0	0	0	0
Did the studies show strong evidence of association between intervention and recruitment outcome? ("strong" if significant relative risk or odds ratio > 2 based on consistent evidence from 2 or more studies with no plausible confounders (+1); "very strong" if significant relative risk or odds ratio > 5 based on direct evidence with no major threats to validity (+2)	+1	0	0	0	0
Did the studies have evidence of a dose-response gradient? (+1)	+0.5	0	0	0	0

Appendix F: Evidence Table 4. Grading of the Body of Evidence for Proximal Clinical Outcome Measures

Did the studies have unmeasured plausible confounders that most likely reduced the magnitude of the observed association? (+1)	0	0	0	0	0
Overall grade of evidence (high, moderate, low, very low)	Moderate	Low	Very low	Moderate	Very low

High = further research is very unlikely to change our confidence in the estimates; moderate = further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low = further research is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; very low = any estimate of effect is very uncertain.

Grading of the quality of evidence of the efficacy/effectiveness of oral diabetes medications: Metformin vs Metformin + Second Generation Sulfonylureas

	Key Question 1 Comparative Effectiveness of Short Term Outcomes and Quality of Life				
	HbA1c/2hr PPG	BMI/Weight	SBP/DBP	Lipids	QOL
Quantity of Evidence: Number of studies	11/4	4/10	2/2	7/10/8	0
Total number of patients studied	2631/1516	494/2186	645	2007	0
Quality and Consistency of Evidence: Were study designs mostly randomized trials (high quality), non-randomized controlled trials (medium quality), observational studies (low quality), or about a 50:50 mix of experimental and observational (medium quality) ?	high	High	High	High	
Did the studies have serious (-1) or very serious (-2) limitations in quality? (Enter 0 if none)	-1	0	0	-1	
Did the studies have important inconsistency? (-1)	0	0	0	-1	
Was there some (-1) or major (-2) uncertainty about the directness (i.e. extent to which the people, interventions and outcomes are similar to those of interest? Reminder: we're looking for head to head comparisons of different diabetes meds to get full credit for directness in addressing our question.	0	0	0	0	
Were data imprecise or sparse? (-1) (i.e. lack of data or very wide confidence intervals that may change conclusions)	0	0	-1	0	
Did the studies have high probability of reporting bias? (-1)	0	0	0	0	
Did the studies show strong evidence of association between intervention and recruitment outcome? ("strong" if significant relative risk or odds ratio > 2 based on consistent evidence from 2 or more studies with no plausible confounders (+1); "very strong" if significant relative risk or odds ratio > 5 based on direct evidence with no major threats to validity (+2)	+1	+2	0	0	
Did the studies have evidence of a dose-response gradient? (+1)	+1	+1	0	0	

Appendix F: Evidence Table 4. Grading of the Body of Evidence for Proximal Clinical Outcome Measures

Did the studies have unmeasured plausible confounders that most likely reduced the magnitude of the observed association? (+1)	0	0	0	0	
Overall grade of evidence (high, moderate, low, very low)	High	High	Very low	Low	

High = further research is very unlikely to change our confidence in the estimates; moderate = further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low = further research is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; very low = any estimate of effect is very uncertain.

Grading of the quality of evidence of the efficacy/effectiveness of oral diabetes medications: Second Generation Sulfonylureas vs Metformin + Second Generation Sulfonylureas

	Key Question 1 Comparative Effectiveness of Short Term Outcomes and Quality of Life				
	HbA1c/2hr PPG	BMI/Weight	SBP/DBP	Lipids	QOL
Quantity of Evidence: Number of studies	13/5	3/13	5/5	7/8/9	0
Total number of patients studied	3457/1622	398/3513	1485	2835	
Quality and Consistency of Evidence: Were study designs mostly randomized trials (high quality), non-randomized controlled trials (medium quality), observational studies (low quality), or about a 50:50 mix of experimental and observational (medium quality) ?	high	High	High	High	
Did the studies have serious (-1) or very serious (-2) limitations in quality? (Enter 0 if none)	-1	0	-1	-1	
Did the studies have important inconsistency? (-1)	0	0	0	0	
Was there some (-1) or major (-2) uncertainty about the directness (i.e. extent to which the people, interventions and outcomes are similar to those of interest? <u>Reminder: we're looking for head to head comparisons of different diabetes meds to get full credit for directness in addressing our question.</u>	0	0	0	0	
Were data imprecise or sparse? (-1) (i.e. lack of data or very wide confidence intervals that may change conclusions)	0	0	0	0	
Did the studies have high probability of reporting bias? (-1)	0	0	0	0	
Did the studies show strong evidence of association between intervention and recruitment outcome? ("strong" if significant relative risk or odds ratio > 2 based on consistent evidence from 2 or more studies with no plausible confounders (+1); "very strong" if significant relative risk or odds ratio > 5 based on direct evidence with no major threats to validity (+2))- <u>use your clinical judgement for absolute differences.</u>	+1	0	0	0	

Appendix F: Evidence Table 4. Grading of the Body of Evidence for Proximal Clinical Outcome Measures

Did the studies have evidence of a dose-response gradient? (+1)	+1	0	0	0	
Did the studies have unmeasured plausible confounders that most likely reduced the magnitude of the observed association? (+1)	0	0	0	0	
Overall grade of evidence (high, moderate, low, very low)	High	Moderate	Low	Moderate	

High = further research is very unlikely to change our confidence in the estimates; moderate = further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low = further research is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; very low = any estimate of effect is very uncertain.

Grading of the quality of evidence of the efficacy/effectiveness of oral diabetes medications: Metformin vs Metformin +Thiazolidinediones

	Key Question 1				
	Comparative Effectiveness of Short Term Outcomes and Quality of Life				
	HbA1c/2hr PPG	BMI/Weight	SBP/DBP	Lipids	QOL
Quantity of Evidence:	4/0	0/2	0/0	4/4/4	1
Number of studies					
Total number of patients studied	1423/0	890	0	1311	528
Quality and Consistency of Evidence:	High	High		High	High
Were study designs mostly randomized trials (high quality), non-randomized controlled trials (medium quality), observational studies (low quality), or about a 50:50 mix of experimental and observational (medium quality) ?					
Did the studies have serious (-1) or very serious (-2) limitations in quality? (Enter 0 if none)	0	0		0	0
Did the studies have important inconsistency? (-1)	0	0		0	0
Was there some (-1) or major (-2) uncertainty about the directness (i.e. extent to which the people, interventions and outcomes are similar to those of interest? <u>Reminder: we're looking for head to head comparisons of different diabetes meds to get full credit for directness in addressing our question.</u>	0	0		0	0
Were data imprecise or sparse? (-1) (i.e. lack of data or very wide confidence intervals that may change conclusions)	-1	-1		-1	-1
Did the studies have high probability of reporting bias? (-1)	0	0		0	0
Did the studies show strong evidence of association between intervention and recruitment outcome? ("strong" if significant relative risk or odds ratio > 2 based on consistent evidence from 2 or more studies with no plausible confounders (+1); "very strong" if significant relative risk or odds ratio > 5 based on direct evidence with no major threats to validity (+2))- <u>use your clinical judgement for absolute differences.</u>	1	0		1	1

Appendix F: Evidence Table 4. Grading of the Body of Evidence for Proximal Clinical Outcome Measures

Did the studies have evidence of a dose-response gradient? (+1)	0	1		1	0
Did the studies have unmeasured plausible confounders that most likely reduced the magnitude of the observed association? (+1)	0	0		0	0
Overall grade of evidence (high, moderate, low, very low)	Moderate	Low		Moderate to low	Very low

High = further research is very unlikely to change our confidence in the estimates; moderate = further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low = further research is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; very low = any estimate of effect is very uncertain.

Grading of the quality of evidence of the efficacy/effectiveness of oral diabetes medications: Second Generation Sulfonylurea versus Second generation Sulfonylurea + Thiazolidinediones

	Key Question 1 Comparative Effectiveness of Short Term Outcomes and Quality of Life				
	HbA1c/2hr PPG	BMI/Weight	SBP/DBP	Lipids	QOL
Quantity of Evidence:	4/0	1/2	1/1	3/3/3	1
Number of studies					
Total number of patients studied	1061	95/598	95	785	237
Quality and Consistency of Evidence:	High	High	High	High	High
Were study designs mostly randomized trials (high quality), non-randomized controlled trials (medium quality), observational studies (low quality), or about a 50:50 mix of experimental and observational (medium quality) ?					
Did the studies have serious (-1) or very serious (-2) limitations in quality? (Enter 0 if none)	0	0	0	0	0
Did the studies have important inconsistency? (-1)	0	-1	0	0	0
Was there some (-1) or major (-2) uncertainty about the directness (i.e. extent to which the people, interventions and outcomes are similar to those of interest? Reminder: we're looking for head to head comparisons of different diabetes meds to get full credit for directness in addressing our question.	0	0	0	0	0
Were data imprecise or sparse? (-1) (i.e. lack of data or very wide confidence intervals that may change conclusions)	-1	-1	-1	-1	-1
Did the studies have high probability of reporting bias? (-1)	0	0	0	0	0
Did the studies show strong evidence of association between intervention and recruitment outcome? ("strong" if significant relative risk or odds ratio > 2 based on consistent evidence from 2 or more studies with no plausible confounders (+1); "very strong" if significant relative risk or odds ratio > 5 based on direct evidence with no major threats to validity (+2)	1	0	0	0	0

Appendix F: Evidence Table 4. Grading of the Body of Evidence for Proximal Clinical Outcome Measures

Did the studies have evidence of a dose-response gradient? (+1)	0	0	0	0	0
Did the studies have unmeasured plausible confounders that most likely reduced the magnitude of the observed association? (+1)	0	0	0	0	0
Overall grade of evidence (high, moderate, low, very low)	Moderate	Very low	Very low	Low to very low	Very low

High = further research is very unlikely to change our confidence in the estimates; moderate = further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low = further research is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; very low = any estimate of effect is very uncertain.

Grading of the quality of evidence of the efficacy/effectiveness of oral diabetes medications: Pioglitazone vs Rosiglitazone

	Key Question 1				
	Comparative Effectiveness of Short Term Outcomes and Quality of Life				
	HbA1c/2hr PPG	BMI/Weight	SBP/DBP	Lipids	QOL
Quantity of Evidence: Number of studies	3/1 (direct); 8 (placebo-controlled trials each)	1(direct)	1/1(direct)	3/3/3 (direct); 6-8 (placebo-controlled trials each)	0
Total number of patients studied	933/87	87	735	933	
Quality and Consistency of Evidence: Were study designs mostly randomized trials (high quality), non-randomized controlled trials (medium quality), observational studies (low quality), or about a 50:50 mix of experimental and observational (medium quality) ?	High	High	High	High	
Did the studies have serious (-1) or very serious (-2) limitations in quality? (Enter 0 if none)	0	0	0	0	
Did the studies have important inconsistency? (-1)	0	0	0	0	
Was there some (-1) or major (-2) uncertainty about the directness (i.e. extent to which the people, interventions and outcomes are similar to those of interest? <u>Reminder: we're looking for head to head comparisons of different diabetes meds to get full credit for directness in addressing our question.</u>	-1	0	0	-1	
Were data imprecise or sparse? (-1) (i.e. lack of data or very wide confidence intervals that may change conclusions)	-1	-1	-1	-1	
Did the studies have high probability of reporting bias? (-1)	0	0	0	0	
Did the studies show strong evidence of association between intervention and recruitment outcome? ("strong" if significant relative risk or odds ratio > 2 based on consistent evidence from 2 or more studies with no plausible confounders (+1); "very strong" if significant relative risk or odds ratio > 5 based on direct evidence with no major threats to validity (+2)	0	0	0	1	

Appendix F: Evidence Table 4. Grading of the Body of Evidence for Proximal Clinical Outcome Measures

Did the studies have evidence of a dose-response gradient? (+1)	0	0	0	0	
Did the studies have unmeasured plausible confounders that most likely reduced the magnitude of the observed association? (+1)	0	0	0	0	
Overall grade of evidence (high, moderate, low, very low)	Moderate to low	Very low	Very low	Moderate to low	

High = further research is very unlikely to change our confidence in the estimates; moderate = further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low = further research is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; very low = any estimate of effect is very uncertain.

Grading of the quality of evidence of the efficacy/effectiveness of oral diabetes medications: Thiazolidinediones vs Alpha-glucosidase inhibitors

	Key Question 1 Comparative Effectiveness of Short Term Outcomes and Quality of Life				
	HbA1c/2hr PPG	BMI/Weight	SBP/DBP	Lipids	QOL
Quantity of Evidence: Number of studies	2/0(direct); 8, 8, & 28 (placebo-controlled trials)	0/1(direct); 6, 4, & 16 (placebo-controlled trials)	2/2	1/1/1 (direct); 6, 8 & 4(placebo-controlled trials for LDL), 4,6,&6 (for TG)	0
Total number of patients studied	295(direct)	265(direct)	295	265(direct)	
Quality and Consistency of Evidence: Were study designs mostly randomized trials (high quality), non-randomized controlled trials (medium quality), observational studies (low quality), or about a 50:50 mix of experimental and observational (medium quality) ?	High	High	High	High	
Did the studies have serious (-1) or very serious (-2) limitations in quality? (Enter 0 if none)	-1	-1	-1	-1	
Did the studies have important inconsistency? (-1)	0	0	0	0	
Was there some (-1) or major (-2) uncertainty about the directness (i.e. extent to which the people, interventions and outcomes are similar to those of interest? <u>Reminder: we're looking for head to head comparisons of different diabetes meds to get full credit for directness in addressing our question.</u>	-2	-2	0	-2	
Were data imprecise or sparse? (-1) (i.e. lack of data or very wide confidence intervals that may change conclusions)	0	0	-1	0	
Did the studies have high probability of reporting bias? (-1)	-1	-1	-1	-1	

Appendix F: Evidence Table 4. Grading of the Body of Evidence for Proximal Clinical Outcome Measures

Did the studies show strong evidence of association between intervention and recruitment outcome? (“strong” if significant relative risk or odds ratio > 2 based on consistent evidence from 2 or more studies with no plausible confounders (+1); “very strong” if significant relative risk or odds ratio > 5 based on direct evidence with no major threats to validity (+2)	0	0	0	0	
Did the studies have evidence of a dose-response gradient? (+1)	0	0	0	0	
Did the studies have unmeasured plausible confounders that most likely reduced the magnitude of the observed association? (+1)	0	0	0	0	
Overall grade of evidence (high, moderate, low, very low)	Low	Low	Very Low	Low	

High = further research is very unlikely to change our confidence in the estimates; moderate = further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low = further research is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; very low = any estimate of effect is very uncertain.

Grading of the quality of evidence of the efficacy/effectiveness of oral diabetes medications: Metformin vs Alpha-glucosidase inhibitors

	Key Question 1				
	Comparative Effectiveness of Short Term Outcomes and Quality of Life				
	HbA1c/2hr PPG	BMI/Weight	SBP/DBP	Lipids	QOL
Quantity of Evidence: Number of studies	3/1 (direct); 15 and 28/ 1 and 23 (placebo-controlled trials)	0/3 (direct); 8 and 16 (placebo-controlled trials)	0/0	1/2/2(direct); 4 and 4 (placebo-controlled trials for LDL); 7 and 4 (for TG)	0
Total number of patients studied	227(direct)	281(direct)		120 (direct)	
Quality and Consistency of Evidence: Were study designs mostly randomized trials (high quality), non-randomized controlled trials (medium quality), observational studies (low quality), or about a 50:50 mix of experimental and observational (medium quality) ?	High	High		High	
Did the studies have serious (-1) or very serious (-2) limitations in quality? (Enter 0 if none)	-1	-1		-1	
Did the studies have important inconsistency? (-1)	0	0		0	
Was there some (-1) or major (-2) uncertainty about the directness (i.e. extent to which the people, interventions and outcomes are similar to those of interest? <u>Reminder: we're looking for head to head comparisons of different diabetes meds to get full credit for directness in addressing our question.</u>	-2	-2		-2	
Were data imprecise or sparse? (-1) (i.e. lack of data or very wide confidence intervals that may change conclusions)	0	0		0	
Did the studies have high probability of reporting bias? (-1)	-1	-1		-1	

Appendix F: Evidence Table 4. Grading of the Body of Evidence for Proximal Clinical Outcome Measures

Did the studies show strong evidence of association between intervention and recruitment outcome? ("strong" if significant relative risk or odds ratio > 2 based on consistent evidence from 2 or more studies with no plausible confounders (+1); "very strong" if significant relative risk or odds ratio > 5 based on direct evidence with no major threats to validity (+2))	0	0		0	
Did the studies have evidence of a dose-response gradient? (+1)	0	0		0	
Did the studies have unmeasured plausible confounders that most likely reduced the magnitude of the observed association? (+1)	0	0		0	
Overall grade of evidence (high, moderate, low, very low)	Low	Low		Low to very low	

High = further research is very unlikely to change our confidence in the estimates; moderate = further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low = further research is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; very low = any estimate of effect is very uncertain.

Grading of the quality of evidence of the efficacy/effectiveness of oral diabetes medications: Second-generation sulfonylureas vs alpha-glucosidase inhibitors

	Key Question 1 Comparative Effectiveness of Short Term Outcomes and Quality of Life				
	HbA1c/2hr PPG	BMI/Weight	SBP/DBP	Lipids	QOL
Quantity of Evidence: Number of studies	11/8; 11, 28, and 7 (indirect)	5/7 (direct); 4 and 16 (placebo-controlled trials)	1/1	4/8/9	0
Total number of patients studied	868	698 (direct)	30	681	
Quality and Consistency of Evidence: Were study designs mostly randomized trials (high quality), non-randomized controlled trials (medium quality), observational studies (low quality), or about a 50:50 mix of experimental and observational (medium quality) ?	High	High	High	High	
Did the studies have serious (-1) or very serious (-2) limitations in quality? (Enter 0 if none)	0	-1	0	0	
Did the studies have important inconsistency? (-1)	-1	-1	0	-1	
Was there some (-1) or major (-2) uncertainty about the directness (i.e. extent to which the people, interventions and outcomes are similar to those of interest? <u>Reminder: we're looking for head to head comparisons of different diabetes meds to get full credit for directness in addressing our question.</u>	-1	0	0	0	
Were data imprecise or sparse? (-1) (i.e. lack of data or very wide confidence intervals that may change conclusions)	0	0	0	0	
Did the studies have high probability of reporting bias? (-1)	-1	-1	0	0	

Appendix F: Evidence Table 4. Grading of the Body of Evidence for Proximal Clinical Outcome Measures

Did the studies show strong evidence of association between intervention and recruitment outcome? ("strong" if significant relative risk or odds ratio > 2 based on consistent evidence from 2 or more studies with no plausible confounders (+1); "very strong" if significant relative risk or odds ratio > 5 based on direct evidence with no major threats to validity (+2))	0	0	0	0	
Did the studies have evidence of a dose-response gradient? (+1)	0	0	0	0	
Did the studies have unmeasured plausible confounders that most likely reduced the magnitude of the observed association? (+1)	0	0	0	0	
Overall grade of evidence (high, moderate, low, very low)	Low	Low	Very Low	Low	

High = further research is very unlikely to change our confidence in the estimates; moderate = further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low = further research is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; very low = any estimate of effect is very uncertain.

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Thiazolidinedione vs. Thiazolidinedione											
Khan, 2002 ⁵¹	%	Rosiglitazone, 60	Pioglitazone, 67	2-8 (fixed)	15-45 (fixed)	7.9 (1.9) 7.6 -0.3*	8.0 (1.7) 7.8 -0.2*	-0.1	NSG vs. GP2		
Goldberg, 2005 ⁵²	%	Rosiglitazone + diet, 356	Pioglitazone + diet, 363	4 (esc) 8	30 (esc) 45	7.5 (SE 0.1) 6.9 -0.6 (SE 0.1)	7.6 (SE 0.1) 6.9 -0.7 (SE 0.1)	0.1	<.05 vs. baseline	<.05 vs. baseline	
Derosa, 2005 ⁵³	%	Rosiglitazone + glimepiride + diet + exercise, 42	Pioglitazone + glimepiride + diet + exercise, 45	4 (fixed) 4 (fixed)	15 (fixed) 4 (fixed)	8 (0.8) 6.7 (0.9) -1.3	8.2 (0.7) 6.8 (0.8) -1.4	0.1	<0.01 vs. baseline	<0.01 vs. baseline	
Thiazolidinedione vs. Metformin											

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Pavo, 2003 ⁵⁹	%	Pioglitazone + placebo, 100	Metformin + placebo, 91	30 (esc) 45	850 (esc) 2550	8.6 7.3 -1.3	8.6 7.1 -1.5	0.2	0.28 vs. GP2 <0.0001 vs. baseline	<0.0001 vs. baseline	
Lawrence, 2004 ⁵⁴	%	Pioglitazone, 20	Metformin, 20	30 (esc) 45	500 bid (esc) 1000 tid	7.43 (0.9) 6.62 (0.5) -0.81 (0.63)	8.04 (0.9) 6.9 (0.5) -1.12 (0.84)	0.31	<0.01 vs. baseline NSG vs. GP2	<0.01 vs. baseline	
Ramachan- dran, 2004 ⁵⁵	%	Pioglitazone + diet, 23	Metformin + diet, 21	15 (esc) 30	250 (esc) 850	9.3 (1.8) 6.7 (1.3) -2.6	9.6 (2.4) 8.2 (2.5) -1.4	-1.2	p<0.01 vs. baseline	p<0.05 vs. baseline	
Schern-thaner, 2004 ⁵⁶	%	Pioglitazone + placebo + diet, 588	Metformin + placebo + diet, 588	30 (esc) 45	850 up to 3 times/day (esc) 2550	8.69 (1.02) 7.28 -1.41	8.68 (0.98) 7.18 -1.5	0.09	NR	NR	
Yamanouchi, 2005 ⁵⁷	%	Pioglitazone + diet + exercise, 38	Metformin + diet + exercise, 39	30 for women and 45 for men (fixed)	750 (fixed)	10.2 (0.8) 7.9 (1.0) -2.3	9.9 (0.7) 7.8 (1.0) -2.1	-0.2	<0.005 vs. baseline	<0.005 vs. baseline	
Hallsten, 2002 ⁵⁸ Virtanen, 2003 ¹⁴³	%	Rosiglitazone + diet, 14	Metformin + diet, 13	2 bid (esc) 4 bid	500 bid (esc) 1000 bid	6.8 (0.2) 6.5 (0.2) -0.3	6.9 (0.2) 6.2 (0.2) -0.7	0.4	<0.05 vs. baseline NSG vs. GP2	<0.0001 vs. baseline	

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year						GP1 BL mean (SD)	GP2 BL mean (SD)				
Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 final mean (SD)	GP2 final mean (SD)	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Hanefeld, 2004 ⁶⁰ QUARTET study group	%	Pioglitazone + unspecified sulfonylurea + placebo, 319	Metformin + unspecified sulfonylurea + placebo, 320	15 (esc) 45 NR	850 (esc) 850 tid NR	8.82 (0.98) 7.61 (0.06) -1.2	8.8 (0.97) 7.45 (0.06) -1.36	0.16		0.065 vs. GP1	
Thiazolidinedione vs. Second Generation Sulfonylurea											
Bakris, 2003 ⁶⁶ St John Sutto, 2002 ⁶⁷	%	Rosiglitazone, 57	Glyburide (no trade drug specified), 64	4 bid (fixed)	NR (esc) 20	9.1 (1.68) 8.2 -0.9 (1.38)	9.5 (1.59) 8.6 -0.9 (1.39)	0	NSG vs. GP2		
Tan, 2004 ⁶⁵	%	Pioglitazone, 91	Glibenclamide, 109	30 (esc) 45	1.75 (esc) 10.5	8.4 (0.7) 7.9 -0.5	8.5 (0.8) 8.1 -0.4	-0.1	<0.005 vs. baseline	<0.005 vs. baseline	
Nakamura, 2000 ⁶⁴	%	Pioglitazone, 15	Glibenclamide, 15	30 (fixed)	5 (fixed)	7.7 (1.2) 6.8 (1.0) -0.9	7.8 (1.1) 6.9 (1.2) -0.9	0.0	<0.05 vs. baseline	<0.05 vs. baseline	
Charbonnel, 2005 ⁶³	%	Pioglitazone	Gliclazide	NR (esc) 45	NR (esc) 320	8.7 7.2 -1.4	8.7 7.3 -1.4	0	NR	NR	
Tan, 2005 ⁶¹ One year extension study for Quartet study group	%	Pioglitazone, 147	Gliclazide, 128	15 (esc) 45	80 (esc) 320	8.55* 7.3* -1.25	8.75* 7.6* -1.15	-0.45 (0.66 - -0.23 [†])	NR	NR	

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year						GP1 BL mean (SD)	GP2 BL mean (SD)				
Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 final mean (SD) Mean diff from BL1	GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Yanagawa, 2004 ⁶²	%	Pioglitazone, 19	Gliclazide, 21	NR	NR	8.3 (0.7) NR NR	8.3 (0.9) NR NR	NR	NR	NSG vs. GP1	
Lawrence, 2004 ⁵⁴	%	Pioglitazone, 20	Gliclazide, 20	30 (esc) 45	80 od (esc) 160 bid	7.43 (0.9) 6.62 (0.5) -0.81 (0.63)	7.85 (0.9) 6.64 (0.5) -1.21 (0.82)	0.4	<0.01 vs. baseline NSG vs. GP2	<0.01 vs. baseline	
Pfutzner, 2005 ⁶⁸ Langenfeld, 2005 ¹⁴⁶ Forst, 2005 ¹⁴⁵	%	Pioglitazone, 89	Glimepiride, 84	45 (fixed)	1 (esc) 6	7.52 (0.85) 6.71 (0.89) -0.81	7.44 (0.89) 6.83 (0.85) -0.61	-0.2	<0.05 vs. baseline	<0.05 vs. baseline	
Ramachandra n, 2004 ⁵⁵	%	Pioglitazone + diet, 23	Glimepiride + diet, 18	15 (esc) 30	1 (esc) 2	9.3 (1.8) 6.7 (1.3) -2.6	10.2 (2.2) 7.7 (1.7) -2.5	-0.1	<0.01 vs. baseline	<0.01 vs. baseline	
Yamanouchi, 2005 ⁵⁷	%	Pioglitazone + diet + exercise, 38	Glimepiride + diet + exercise, 37	30 for women and 45 for men (fixed)	1.0 (esc) 2.0	10.2 (0.8) 7.9 (1.0) -2.3	9.8 (0.7) 7.7 (0.9) -2.1	-0.2	<0.005 vs. baseline	<0.005 vs. baseline	
Tan, 2004 ⁶⁹	%	Pioglitazone + diet + exercise, 109	Glimepiride + diet + exercise, 99	15 (esc) 45	2 (esc) 8	8.54 (0.903) 7.76 -0.78 (0.162)	8.45 (1.02) 7.77 -0.68 (0.169)	-0.1	0.638 vs. GP2 <0.001 vs. baseline	<0.001 vs. baseline	

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2	Other
Matthews, 2005 ⁷⁰	%	Pioglitazone + metformin + diet, 317	Metformin + gliclazide + diet, 313	15 (esc) 45 NR	NR 80 (esc) 320	NR NR -0.99	NR NR -1.01	-0.02	0.837 vs. GP2		
Thiazolidinedione + Metformin vs. Second Generation Sulfonylurea + Metformin											
Derosa, 2005 ⁷²	%	Rosiglitazone + metformin + diet + exercise + behavioral therapy, 48	Metformin + glimepiride + diet + exercise + behavioral therapy, 47	4 (fixed) 1500 (fixed)	1500 (fixed) 2 (fixed)	8 (0.7) 6.8 (0.6) -1.2	7.9 (0.6) 7 (0.7) -0.9	-0.3	<0.01 vs. baseline	<0.05 vs. baseline NSG vs. GP1	
Garber, 2006 ⁷¹	%	Rosiglitazone + metformin + diet, 155	Metformin + glibenclamide + diet, 159	4 (esc) 8 1500-2000 (esc) 2000	1000 (esc) 2000 5 (esc) 10	8.4 (1.1) 7.2 (1.4) -1.1	8.5 (1.2) 6.7 (1.3) -1.5	0.4		<0.001 vs. GP1	
Thiazolidinedione vs. Meglitinide											
Raskin, 2004 ⁷⁴	%	Rosiglitazone, 55	Repaglinide, 59	2 bid (esc) 4 bid	0.5 tid if HbA1c≤8%, 1 tid if HbA1c>8% (esc) 4 tid	9.0 8.5 -0.56 (SE 0.14)	9.3 9.1 -0.17 (SE 0.14)	-0.39	NR	NR	
Jovanovic, 2004 ⁷³	%	Pioglitazone, 57	Repaglinide, 54	30 (fixed)	0.5 tid if HbA1c≤8%, 1 tid if HbA1c>8% (esc) 4 tid	9.1 9.5 0.32 (SE 0.16)	9 8.9 -0.18 (SE 0.17)	0.5	NSG vs. GP2		
Thiazolidinedione vs. Alpha-Glucosidase Inhibitor											
Goke, 2002 ⁷⁵	%	Pioglitazone, 129	Acarbose, 136	45 (fixed)	50 (esc) 100 tid	8.98 (1.2) 7.82 (1.95) -1.2	9.03 (1.32) 8.55 (1.96) -0.5	-0.7	<0.001 vs. GP2		
German Pioglitazone Study Group											

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2	Other
Nakamura, 2000 ⁶⁴	%	Pioglitazone, 15	Voglibose, 15	30 (fixed)	0.6 (fixed)	7.7 (1.2) 6.8 (1.0) -0.9	7.6 (1.1) 6.8 (1.1) -0.8	-0.1	<0.05 vs. baseline	<0.05 vs. baseline	
Other Thiazolidinedione Comparisons											
McCluskey, 2004 ⁷⁶	%	Rosiglitazone + placebo, 15	Rosiglitazone + glimepiride, 24	4 or 8 (fixed)	4 or 8 fixed 2 (esc) 8	8.4 (0.7) 8.1 -0.3 (SE 0.2)	7.9 (0.6) 6.7 -1.2 (SE 0.1)	0.9		<0.05 vs. GP1	
Choi, 2004 ⁷⁷	%	Rosiglitazone + diet, 38	Up-titration of existing medications, 45	8 (other) 4	NR (esc)	7.79 (1.3) 7.17 (0.98) -0.61 (1.15)	7.72 (1.13) 7.23 (0.93) -0.75 (1.07)	0.14	<.05 vs. baseline	<.05 vs. baseline	
Takagi, 2003 ⁷⁸	%	Pioglitazone, 23	Control group (conventional antidiabetic therapy), 21	30 (fixed)	NR (NR)	6.8 (0.6) 6.5 (1.0) -0.3	6.7 (1.2) 6.5 (1.3) -0.2	-0.1	0.8140 vs. GP2		
Metformin vs. Second Generation Sulfonylurea											
Garber, 2002 ⁷⁹	%	Metformin, 161	Glyburide (Micronase), 161	500 (esc) 2000	2.5 (esc) 10	8.26 (1.08) 7.23 -1.03	8.21 (1.09) 6.97 -1.24	0.21	NR	NR	
Garber, 2003 ⁸⁰	%	Metformin, 164	Glyburide (no trade drug specified), 151	500 (esc) 2000	2.5 (esc) 10	8.42 (1.4) 7.01 -1.53	8.67 (1.4) 6.75 -1.9	0.37	NR	NR	

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Blonde, 2002 ⁸¹	%	Metformin, 104	Glyburide (no trade drug specified), 132	500 (esc) 2000	10 bid (fixed)	9.51 (1.34) 9.7 0.39	9.64 (1.44) 9.5 -0.11	0.5	NR	NR	
Goldstein, 2003 ⁸²	%	Metformin, 71	Glipizide, 79	500 (esc) 2000	15 bid (fixed)	8.6 (1.2) 8.4 (0.1) -0.2	8.9 (1.1) 8.5 (0.1) -0.4	0.2	NR	NR	
Campbell, 1994 ⁸³	%	Metformin, 24	Glipizide, 24	500 bid (esc) 3000	5 (esc) 30	11.46 (1.92) 8.64 (1.21) -2.57	11.75 (2.11) 9.72 (1.91) -1.93	-0.64	<0.05 vs. GP2		
Marre, 2002 ⁸⁴	%	Metformin, 104	Glibenclamide, 103	500 (esc) 2000	5 (esc) 20	8.09 (1.84) 7.89 -0.2	7.88 (1.65) 7.58 -0.3	0.1	NSG vs. GP2		
Amador- Licona, 2000 ⁸⁵	%	Metformin, 28	Glibenclamide, 23	850 (esc) NR	5 (esc) NR	8.5 (1.5) 7.6 (0.8) -0.9	8.4 (1.4) 7.6 (0.8) -0.8	0.1	0.003	0.009	
Lawrence, 2004 ⁵⁴	%	Metformin, 20	Gliclazide, 20	500 bid (esc) 1000 tid	80 (esc) 160 bid	8.04 (0.9) 6.9 (0.5) -1.12 (0.84)	7.85 (0.9) 6.64 (0.5) -1.21 (0.82)	0.09	<0.01 vs. baseline NSG vs. GP2	<0.01 vs. baseline	
Noury, 1991 ⁸⁶	%	Metformin, 30	Gliclazide, 27	1700 (fixed)	80 (esc) 240	9.75 (3.67) 8.46 (3.74) -1.29	9.72 (4.14) 8.95 (3.21) -0.77	-0.52	<0.02 vs. baseline NSG vs. GP2	<0.02 vs. baseline	

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Ramachan- dran, 2004 ⁵⁵	%	Metformin + diet, 21	Glimepiride + diet, 18	250 (esc) 850	1 (esc) 2	9.6 (2.4) 8.2 (2.5) -1.4	10.2 (2.2) 7.7 (1.7) -2.5	1.1	<0.05 vs. baseline	<0.01 vs. baseline	
Hermann, 1994 ⁸⁷	%	Metformin + diet, 19	Glyburide + diet, 19	1000 (esc) 3000	3.5 (esc) 10.5	6.9 (SE 0.3) 5.8 (SE 0.2) -0.9 (SE 0.2)	6.7 (SE 0.3) 5.3 (SE 0.1) -1.3 (SE 0.2)	0.4	0.001 vs. baseline	0.001 vs. baseline	>0.1 all group compa rison
DeFronzo, 1995 ⁸⁸	% glyca- ted Hb	Metformin + placebo, 210	Glyburide (no trade drug specified) + placebo, 209	500 (esc) 2500	5 bid (esc) 10 bid	8.9 8.5 -0.4 (SE 0.1)	8.5 8.7 0.2 (SE 0.1)	-0.6	<0.001 vs. GP2		
Charpentier, 2001 ⁸⁹	%	Metformin + placebo, 75	Glimepiride + placebo, 150	850 tid (fixed)	1 (esc) 6	6.79 (1.17) 6.86 (1.45) 0.07 (SE 0.14)	6.52 (1.13) 6.79 (1.43) 0.27 (SE 0.09)	-0.12		0.369 vs. GP1	
Yamanouchi, 2005 ⁵⁷	%	Metformin + diet + exercise, 39	Glimepiride + diet + exercise, 37	750 (fixed)	1 (esc) 2	9.9 (0.7) 7.8 (1.0) -2.1	9.8 (0.7) 7.7 (0.9) -2.1	0	<0.005 vs. baseline	<0.005 vs. baseline	
Derosa, 2004 ⁹⁰	%	Metformin + placebo + diet + exercise, 75	Glimepiride + placebo + diet + exercise, 73	1000 (esc) 1000 tid	1 (esc) 2 bid	8.4 (1.0) 7 (0.9) -1.4 (-5.7, -0.51 [†])	8.5 (1.2) 6.9 (0.7) -1.6 (-6.4, -0.47 [†])	0.2	0.01 vs. baseline	0.01 vs. baseline	

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
1985 ⁹¹ UKPDS, 1 year f/u in obese and non-obese patients	%	Metformin + diet, 16	Unspecified sulfonylurea + diet, 72	NR (esc) 2550	NR (esc) 500 of chlorpropa- mide or 10 bid of glibencla- mide	8.8 (1.8) 8.1 (1) -0.7	NR 7.7* (7.0, 87 [†]) -1.3	0.6	NR	NR	
1995 ⁹² UKPDS, 3 year f/u of obese patients	%	Metformin + diet, 262	Glibenclamide + diet, 212	NR (esc) 850 tid	NR (esc) 500 of chlorpropa- mide or 10 bid of glibencla- mide	7.2* 6.95*; 7.1 (6.9, 7.3 [†]) -0.2* (-0.4, 0.01 ^{**†})	7.1* 7.15* 0.15* (-0.1, 0.4 ^{**†})	-0.35	NR	NR	
Turner, 1998 ⁹³ UKPDS, 6 year f/u of primary diet failure group in obese subjects	%	Metformin + diet, 49	Glyburide (Diabeta) or chlorpropa-mide + diet, 71	NR (esc) 2550	NR (esc) 500 of chlorpropa- mide or 20 of glyburide	NR 8.2 (7.1, 9.4) NR	NR 8.1 (6.8, 9.7) NR	-0.1	NR	NR	
1998 ¹⁵ UKPDS, 10 year f/u of obese patients	%	Metformin, 342	Glibenclamide, 277	850 (esc) 2550	NR	7.3 (1.5); 6.9 ^{*#} 8.2* 1.3	7.2 (1.5); 7 ^{*#} 8* 1	0.3	NR	NR	

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2	Other
Hermann, 1991 ⁹⁴	%	Metformin + diet, 16	Glibenclamide + diet, 17	1000 (esc) 3000	3.5 (esc) 10.5	6.7 (1.3) 5.8 (0.7) -0.9	6.6 (1.3) 5.3 (0.5) -1.3	0.4	<0.01 vs. baseline	<0.001 vs. baseline	
Tosi, 2003 ⁹⁵	%	Metformin, 19	Glibenclamide, 20	500 (esc) 3000	5 (esc) 15	7.7* (1.4) 7.3*§ -0.4§	7.85* (1.4) 7.4*§ -0.45§	0.05§	NR	NR	
Metformin vs. Meglitinide											
Horton, 2000 ⁹⁶	%	Metformin, 133	Nateglinide, 134	500 tid (fixed)	120 tid (fixed)	8.4 (1.2) 7.6 -0.8 (SE 0.1*)	8.3 (1.0) 7.8 -0.5 (SE 0.1*)	-0.3	≤0.0001 vs. baseline	≤0.0001 vs. baseline NSG vs. GP1	
Derosa, 2003 ⁹⁷	%	Metformin + diet + exercise, 56	Repaglinide + diet + exercise, 56	500 bid (esc) 2500	0.5 bid (esc) 4	7.4 (0.9) 6.5 -0.9	7.6 (0.9) 6.8 -0.8	-0.1	<0.01 vs. baseline NSG vs. GP2	<0.01 vs. baseline	
Metformin vs. Alpha-Glucosidase Inhibitor											
Wolever, 2000 ⁹⁸	%	Metformin, 62	Miglitol, 45	500 tid (fixed)	25 tid (esc) 100 tid	8.2 (SE 0.1) 7.4 -0.8 (SE 0.2)	7.9 (SE 0.1) 7.7 -0.2 (SE 0.2)	-0.6	<0.05 vs. GP2		
Willms, 1999 ⁹⁹	%	Metformin, 27	Acarbose, 31	850 bid (fixed)	100 tid (fixed)	10.6 (1.4) 7.7 -2.5 (SEM 0.16)	10.6 (1.3) 7.8 -2.3 (SEM 0.32)	-0.2		0.651 vs. GP1	
Metformin vs. Thiazolidinedione + Metformin											

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Weissman, 2005 ¹⁰⁰	%	Metformin, 277	Rosiglitazone + metformin, 296	1000 (esc) 2000	4 (esc) 8 1000 (fixed)	7.97 (1.2) 7.26 -0.71	8.05 (1.2) 7.12 -0.93	0.2	NR	NR	
Bailey, 2005 ¹⁰¹	%	Metformin, 272	Rosiglitazone + metformin, 279	2500 (esc) 3000	4 (esc) 8 2000 (fixed)	7.5 (1.0) 7.4 (1.1) -0.13	7.4 (1.0) 7.1 (1.1) -0.33	0.22		0.001 vs. GP1	
Gomez-Perez, 2002 ¹⁰²	%	Metformin + placebo, 34	Rosiglitazone + metformin, 36	2500 (fixed)	2500 (fixed) 4 bid (fixed)	9.8* (SE 0.3*) 10.2* (SE 0.3*) 0.3	9.75* (SE 0.2*) 8.6* (SE 0.4*) -1.2	1.5	0.2651 vs. baseline	0.0002 vs. GP1 0.008 vs. baseline	
Gomez-Perez, 2002 ¹⁰²	%	Metformin + placebo, 34	Rosiglitazone + metformin, 35	2500 (fixed)	2500 (fixed) 2 bid (fixed)	9.8* (SE 0.3*) 10.2* (SE 0.3*) 0.3	10.2* (SE 0.2*) 9.5* (SE 0.3*) -0.7	1	0.2651 vs. baseline	0.0132 vs. GP1 0.052 vs. baseline	
Fonseca, 2000 ¹⁰³	%	Metformin + placebo, 113	Rosiglitazone + metformin, 116	2500 (fixed)	4 (fixed) 2500 (fixed)	8.6 (1.3) 9.05 0.45	8.9 (1.3) 8.34 -0.56	-1		<0.001 vs. GP1	
Fonseca, 2000 ¹⁰³	%	Metformin + placebo, 113	Rosiglitazone + metformin, 110	2500 (fixed)	8 (fixed) 2500 (fixed)	8.6 (1.3) 9.05 0.45	8.9 (1.5) 8.12 -0.78	1.2		<0.001 vs. GP1	
Metformin vs. Metformin + Second Generation Sulfonylurea											

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Garber, 2002 ⁷⁹	%	Metformin, 161	Metformin + glyburide (Micronase), 165	500 (esc) 2000	500 (esc) 2000 2.5 (esc) 10	8.26 (1.08) 7.23 -1.03	8.18 (1.14) 6.65 -1.53	0.5		<0.001 vs. GP1	
Garber, 2002 ⁷⁹	%	Metformin, 161	Metformin + glyburide (Micronase), 158	500 (esc) 2000	250 (esc) 1000 1.25 (esc) 5	8.26 (1.08) 7.23 -1.03	8.25 (1.11) 6.77 -1.48	0.45		<0.001 vs. GP1	
Garber, 2003 ⁸⁰	%	Metformin, 164	Metformin + glyburide (no trade drug specified), 171	500 (esc) 2000	250 (esc) 1000 1.25 (esc) 5	8.42 (1.4) 7.01 -1.53	8.78 (1.5) 6.43 -2.27	-0.74		0.0003 vs. GP1	
Blonde, 2002 ⁸¹	%	Metformin, 104	Metformin + glyburide (no trade drug specified), 137	500 (esc) 2000	500 (esc) 2000 5 (esc) 20	9.51 (1.34) 9.7 0.39	9.42 (1.24) 7.9 -1.38	1.77		<0.001 vs. GP1	
Blonde, 2002 ⁸¹	%	Metformin, 104	Metformin + glyburide (no trade drug specified), 135	500 (esc) 2000	500 (esc) 2000 2.5 (esc) 10	9.51 (1.34) 9.7 0.39	9.41 (1.47) 7.9 -1.64	2.03		<0.001 vs. GP1	
Goldstein, 2003 ⁸²	%	Metformin, 71	Metformin + glipizide, 80	500 (esc) 2000	500 (esc) 2000 5 (esc) 20	8.6 (1.2) 8.4 (0.1) -0.2	8.7 (1.2) 7.4 (0.1) -1.3	1.06		<0.001 vs. GP1	
Marre, 2002 ⁸⁴	%	Metformin, 104	Metformin + glibenclamide, 101	500 (esc) 2000	500 (esc) 2000 2.5 (esc) 10	8.09 (1.84) 7.89 -0.2	7.89 (1.62) 6.69 -1.2	1		<0.05 vs. GP1	

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Marre, 2002 ⁸⁴	%	Metformin, 104	Metformin + glibenclamide, 103	500 (esc) 2000	500 (esc) 2000 5 (esc) 20	8.09 (1.84) 7.89 -0.2	7.62 (1.61) 6.72 -0.9	0.7		<0.05 vs. GP1	
Hermann, 1994 ⁸⁷	%	Metformin + diet, 19	Metformin + glyburide + diet, 17	1000 (esc) 3000	2000 (esc) 3000 7.0 (esc) 14.0	6.9 (SE 0.3) 5.8 (SE 0.2) -0.9 (SE 0.2)	8.4 (SE 0.4) 6.2 (SE 0.3) -2.2 (SE 0.4)	1.3	0.001 vs. baseline	0.001 vs. baseline	>0.1 all group com- parison
Hermann, 1994 ⁸⁷	%	Metformin + diet, 19	Metformin + glyburide + diet, 11	1000 (esc) 3000	1000 (esc) 3000 10.5 (esc) 14.0	6.9 (SE 0.3) 5.8 (SE 0.2) -0.9 (SE 0.2)	7.8 (SE 0.3) 5.7 (SE 0.3) -2.0 (SE 0.4)	1.1	0.001 vs. baseline	0.001 vs. baseline	>0.1 all group com- parison
Hermann, 1994 ⁸⁷	%	Metformin + diet, 19	Metformin + glyburide + diet, 12	1000 (esc) 3000	3000 (fixed) 3.5 (esc) 14.0	6.9 (SE 0.3) 5.8 (SE 0.2) -0.9 (SE 0.2)	7.8 (SE 0.3) 5.4 (SE 0.3) -2.3 (SE 0.4)	1.4	0.001 vs. baseline	0.001 vs. baseline	>0.1 all group com- parison
Hermann, 1994 ⁸⁷	%	Metformin + diet, 19	Metformin + glyburide + diet, 46	1000 (esc) 3000	500 (esc) 1500 1.75 (esc) 5.25	6.9 (SE 0.3) 5.8 (SE 0.2) -0.9 (SE 0.2)	6.8 (SE 0.1) 5.6 (SE 0.1) -1.2 (SE 0.1)	0.3	0.001 vs. baseline	0.001 vs. baseline	>0.1 all group com- parison
Hermann, 1991 ⁹⁴	%	Metformin + diet, 16	Metformin + glibenclamide + diet, 11	1000 (esc) 3000	1000 (esc) 3000 10.5 (esc) 14	6.7 (1.3) 5.8 (0.7) -0.9	7.8 (1.4) 5.7 (0.8) -2.2	1.3	<0.01 vs. baseline	<0.001 vs. baseline	
Hermann, 1991 ⁹⁴	%	Metformin + diet, 16	Metformin + glibenclamide + diet, 12	1000 (esc) 3000	3000 (fixed) 3.5 (esc) 14	6.7 (1.3) 5.8 (0.7) -0.9	7.7 (1.1) 5.4 (0.9) -2.3	1.4	<0.01 vs. baseline	<0.001 vs. baseline	

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year						GP1 BL mean (SD)	GP2 BL mean (SD)				
Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 final mean (SD)	GP2 final mean (SD)	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
DeFronzo, 1995 ⁸⁸	% glyca- ted Hb	Metformin + placebo, 210	Metformin + glyburide (no trade drug specified), 213	500 (esc) 2500	500 (esc) 2500 10 (esc) 20	8.9 8.5 -0.4 (SE 0.1)	8.8 7.1 -1.7 (SE 0.1)	1.3	<0.001 vs. GP2		
Charpentier, 2001 ⁸⁹	%	Metformin + placebo, 75	Metformin + glimepiride, 147	850 tid (fixed)	850 tid (fixed) 1 (esc) 6	6.79 (1.17) 6.86 (1.45) 0.07 (SE 0.14)	6.42 (1.08) 5.68 (0.99) -0.74 (SE 0.8)	0.92		<0.001 vs. GP1	
Feinglos, 2005 ¹⁰⁴	%	Metformin + placebo, 56	Metformin + glipizide, 56	at least 1000 (fixed)	at least 1000 (fixed) 2.5 (fixed)	7.64 7.46 (SE 0.1) -0.19	7.45 6.8 (SE 0.1) -0.66	0.47	<0.0002 vs. GP2		
Tosi, 2003 ⁹⁵	%	Metformin, 19	Metformin + glibenclamide, 41	500 (esc) 3000	400 (esc) 2400 2.5 (esc) 15	7.8 (1.4) 7.3§ -0.5§	7.8 (1.0) 5.9§ -1.9§	1.4	NR	NR	
Other Metformin Comparisons											
Fujioka, 2003 ¹⁰⁵	%	Metformin + placebo + diet, 71	Metformin XR + placebo + diet, 75	1000 (esc) 1500	1000 (esc) 1500	7.1 (0.8) 7.25 0.15	7 (0.8) 7.23 0.23	-0.08	NR	NR	
Fujioka, 2003 ¹⁰⁵	%	Metformin + placebo + diet, 71	Metformin XR + placebo + diet, 71	1000 (esc) 1500	1000 (esc) 2000	7.1 (0.8) 7.25 0.15	7 (0.7) 7.04 0.04	0.11	NR	NR	
Second Generation Sulfonylurea vs. Second Generation Sulfonylurea											

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Schern-thaner, 2004 ¹⁰⁶	%	Glimepiride + existing medications, 440	Gliclazide + existing medications, 405	1 (esc) 6	30 (esc) 120	8.2 (1.0) 7.2 (1.1) -1 (1.1)	8.4 (1.1) 7.2 (1.1) -1.1 (1.1)	0.06	<0.001 vs. baseline	<0.001 vs. baseline <0.0001 vs. GP1 (noninferi- ority test)	
Dills, 1996 ¹⁰⁷	%	Glyburide (Micronase), 259	Glimepiride, 261	1.25 (esc) 20	1 (esc) 16	8.5 (1.3) 8.28 (1.48) -0.22	8.5 (1.2) 8.24 (1.51) -0.26	0.04	NSG vs. GP2		
Carlson, 1993 ¹⁰⁸	%	Glyburide (Micronase), 98- 104	Glyburide (Glynase Prestab), 94-99	3 (fixed)	5 (fixed)	7.6 (SE 0.1) 7.4 (SE 0.2) -0.2	7.6 (SE 0.1) 7.5 (SE 0.2) -0.1	-0.1	NSG vs. GP2		
Rosenstock, 1993 ¹⁰⁹	%	Glyburide (no trade drug specified)	Gliclazide	0.5 (esc) 20	5 (esc) 40	5.7 5.3 -0.4	5.8 5.4 -0.4	0.00	NR	NR	
Birkeland, 1994 ¹¹⁰	%	Glyburide (no trade drug specified) + diet, 15	Glipizide + diet, 15	1.75 (esc) 10.5	2.5 (esc) 15	8* 7.4* -0.6	8* 7.5* -0.5	0.1	<0.01 vs. baseline	<0.01 vs. baseline	
Inukai, 2005 ¹¹¹	%	Glimepiride, 120	Glibenclamide or gliclazide, 52	1 or 2 (esc) 6	2.5 (fixed) 40 (fixed)	7.64 (0.8) 7.61 (1.0) -0.03	7.46 (0.83) 7.58 (1.03) 0.12	-0.15	0.73 vs. baseline	0.538 vs. baseline	

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year						GP1 BL mean (SD)	GP2 BL mean (SD)				
Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 final mean (SD)	GP2 final mean (SD)	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Draeger, 1996 ¹¹²	%	Glimepiride, 455	Glibenclamide, 451	1 (esc) 8	2.5 (esc) 20	8.03 8.39 0.38	7.8 8.32 0.31	0.07	0.25 vs. GP2		
Harrower, 1985 ¹¹³	% HbA1	Glipizide, 20	Glibenclamide, 19	2.5 (esc) 20	2.5 (esc) 30	10 (2.0) 11 (3.0) 0.6 (0.81)	11 (6.0) 9 (4.0) -2.8 (0.9)	3.4	NSG vs. baseline and vs. GP2	<0.02 vs. baseline	
Harrower, 1985 ¹¹³	% HbA1	Glipizide, 20	Gliclazide, 20	2.5 (esc) 20	20 (esc) 320	10 (2.0) 11 (3.0) 0.6 (0.81)	13 (5.0) 9 (4.0) -3.7 (0.88)	4.3	NSG vs. baseline <0.01 vs. GP2	<0.01 vs. baseline	
Harrower, 1985 ¹¹³	% HbA1	Glibenclamide, 19	Gliclazide, 20	2.5 (esc) 30	20 (esc) 320	11 (6.0) 9 (4.0) -2.8 (0.9)	13 (5.0) 9 (4.0) -3.7 (0.88)	0.9	<0.02 vs. baseline NSG vs. GP2	<0.01 vs. baseline	
Kardas, 2005 ¹¹⁴ DIACOM	%	Glibenclamide, 48	Gliclazide, 49	10 (esc) 15	60 (esc) 90	7.2 (1.1) 7.6 (1.3) 0.4 (1.2)	6.9 (1.0) 6.4 (1.6) -0.5 (1.3)	0.9	0.0014 vs. baseline 0.001 vs. GP2	0.0006 vs. baseline	
Second Generation Sulfonylurea vs. Meglitinide											
Marbury, 1999 ¹¹⁶	%	Glyburide (no trade drug specified) + placebo, 171	Repaglinide, 338	2.5 (esc) 15	0.5 (esc) 12	8.9 (1.6) 9.0 0.1 (0.11)	8.7 (1.7) 8.78 0.08 (0.07)	0.02	NR	NR	

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Wolffen-buttel, 1999 ¹¹⁷	%	Glyburide (no trade drug specified) + placebo, 109	Repaglinide, 211	1.75 (esc) 10.5	1.5 (esc) 12	7 (1.2) 7.45 0.45 (0.22, 0.69 [†])	7.1 (1.4) 7.68 0.58 (0.41, 0.7 [†])	-0.13	NSG vs. GP2		
Derosa, 2003 ¹¹⁸	%	Glimepiride + placebo, 62	Repaglinide + placebo, 62	1 (esc) 3 mean final dose	1 (esc) 2.5 mean final dose	7.8 (1.2) 6.7 (0.9) -1.1 (-5.6, -0.54 [†])	8 (1.1) 6.8 (0.8) -1.2 (-6.2, -0.48 [†])	0.1	<0.01 vs. baseline NSG vs. GP2	<0.01 vs. baseline	
Madsbad, 2001 ¹¹⁹	%	Glipizide + placebo, 81	Repaglinide, 175	5 (esc) 15	0.5 (esc) 4	7.2 (1.4) 7.7* (SE 0.2) 0.78 (0.46, 1.1 [†])	7.3 (1.2) 7.4* (SE 0.15) 0.19 (-0.02, 0.4 [†])	0.59		<0.05 vs. GP1	
Wolffen-buttel, 1993 ¹²⁰	%	Glibenclamide, 15	Repaglinide, 27	5 (esc) 15	0.5 (esc) 4	8.7 (1.8) 8.5 (2.0) -0.2	9 (1.9) 8.8 (2.0) -0.2	0	NR	NR	
Vakkilainen, 2002 ¹²²	%	Glibenclamide + placebo, 20	Nateglinide + placebo, 23	5 (esc) 10	120 tid (fixed)	7.6 (7.2, 8.1 [†]) 6.9 (6.5, 7.3 [†]) -0.7	7.6 (7.2, 8.0 [†]) 7.4 (7.0, 7.9 [†]) -0.2	-0.5	<0.001 vs. baseline	NSG vs. baseline	
Landgraf, 1999 ¹²¹	%	Glibenclamide + placebo, 98	Repaglinide, 94	1.75, 3.5, 7.0, or 10.5 (esc) 10.5	0.5, 1.0, 2.0, or 4.0 tid (esc) 4 tid	8 7.6 (SE 0.1) -0.4	7.8 7.5 (SE 0.1) -0.3	-0.1	NR	NR	
Second Generation Sulfonylurea vs. Second Generation Sulfonylurea + Thiazolidinedione											

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Pfutzner, 2006 ¹²³	%	Glimepiride + placebo	Rosiglitazone + glimepiride	3 (fixed)	8 (fixed) 3 (fixed)	7.7 (1.4) 7.7 (1.5) 0	8 (1.4) 6.7 (1.0) -1.3	1.3	NSG vs. baseline	<0.001 vs. baseline	
Pfutzner, 2006 ¹²³	%	Glimepiride + placebo	Rosiglitazone + glimepiride	3 (fixed)	4 (fixed) 3 (fixed)	7.7 (1.4) 7.7 (1.5) 0	8.3 (1.4) 7.1 (1.7) -1.2	1.2	NSG vs. baseline	<0.001 vs. baseline	
Rosenstock, 2006 ¹²⁴	%	Glipizide + placebo, 57	Rosiglitazone + glipizide, 90	10 (esc) 20	4 (fixed) 10 (esc) 20	7.65 (0.99) 7.78 0.13	7.72 (1.03) 6.99 -0.65	0.79	0.1871 vs. baseline	<0.0001 vs. baseline <0.0001 vs. GP1	
Kerenyi, 2004 ¹²⁵	%	Glibenclamide + diet, 154	Rosiglitazone + glibenclamide + diet, 160	7.5 (esc) 15	4 bid (fixed) 7.5 (fixed)	8.1 (1.3) 7.96 -0.14	7.9 (1.2) 6.99 -0.91	0.81	0.053 vs. baseline	<0.0001 vs. baseline	
Baksi, 2004 ¹²⁶	%	Gliclazide	Rosiglitazone + gliclazide	160 (esc) 320	160 (fixed) 4 bid (fixed)	8.6 (1.45) NR NR	8.5 (1.51) 7.3 -1.2	1.3		<0.0001 vs. GP1	
Second Generation Sulfonylurea vs. Metformin + Second Generation Sulfonylurea											
Garber, 2002 ⁷⁹	%	Glyburide (Micronase), 161	Metformin + glyburide (Micronase), 165	2.5 (esc) 10	500 (esc) 2000 2.5 (esc) 10	8.21 (1.09) 6.97 -1.24	8.18 (1.14) 6.65 -1.53	0.29		<0.004 vs. GP1	

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Garber, 2002 ⁷⁹	%	Glyburide (Micronase), 161	Metformin + glyburide (Micronase), 158	2.5 (esc) 10	250 (esc) 1000 1.25 (esc) 5	8.21 (1.09) 6.97 -1.24	8.25 (1.11) 6.77 -1.48	0.24		<0.016 vs. GP1	
Garber, 2003 ⁸⁰	%	Glyburide (no trade drug specified), 151	Metformin + glyburide (no trade drug specified), 171	2.5 (esc) 10	250 (esc) 1000 1.25 (esc) 5	8.67 (1.4) 6.75 -1.9	8.78 (1.5) 6.43 -2.27	0.37			0.0003 all group comparison
Blonde, 2002 ⁸¹	%	Glyburide (no trade drug specified), 132	Metformin + glyburide (no trade drug specified), 135	10 bid (fixed)	500 (esc) 2000 2.5 (esc) 10	9.64 (1.44) 9.5 -0.11	9.41 (1.47) 7.9 -1.64	1.53		<0.001 vs. GP1	
Blonde, 2002 ⁸¹	%	Glyburide (no trade drug specified), 132	Metformin + glyburide (no trade drug specified), 137	10 bid (fixed)	500 (esc) 2000 5 (esc) 20	9.64 (1.44) 9.5 -0.11	9.42 (1.24) 7.9 -1.38	1.27		<0.001 vs. GP1	
Erle, 1999 ¹²⁷	%	Glyburide (no trade drug specified), 18	Metformin + glyburide (no trade drug specified), 15	5 (esc) 15	800 (esc) 1600 5 (esc) 10	7.37 (1.48) 7.58 (1.69) 0.21	7.67 (1.75) 6.85 (1.43) -0.82	1.03	NSG vs. baseline	<0.01 vs. baseline and vs. GP1	
DeFronzo, 1995 ⁸⁸	% glyca- ted Hb	Glyburide (no trade drug specified) + placebo, 209	Metformin + glyburide (no trade drug specified), 213	5 bid (esc) 10 bid	500 (esc) 2500 10 (esc) 20	8.5 8.7 0.2 (SE 0.1)	8.8 7.1 -1.7 (SE 0.1)	1.9	<0.001 vs. GP2		

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Charpentier, 2001 ⁸⁹	%	Glimepiride + placebo, 150	Metformin + glimepiride, 147	1 (esc) 6	850 tid (fixed) 1 (esc) 6	6.52 (1.13) 6.79 (1.43) 0.27 (SE 0.09)	6.42 (1.08) 5.68 (0.99) -0.74 (SE 0.08)	1.04		<0.001 vs. GP1	
Goldstein, 2003 ⁸²	%	Glipizide, 79	Metformin + glipizide, 80	30 (fixed)	500 (esc) 2000 5 (esc) 20	8.9 (1.1) 8.5 (0.1) -0.4	8.7 (1.2) 7.4 (0.1) -1.3	1.06		<0.001 vs. GP1	
Marre, 2002 ⁸⁴	%	Glibenclamide, 103	Metformin + glibenclamide, 101	5 (esc) 20	500 (esc) 2000 2.5 (esc) 10	7.88 (1.65) 7.58 -0.3	7.89 (1.62) 6.69 -1.2	0.9		<0.05 vs. GP1	
Marre, 2002 ⁸⁴	%	Glibenclamide, 103	Metformin + glibenclamide, 103	5 (esc) 20	500 (esc) 2000 5 (esc) 20	7.88 (1.65) 7.58 -0.3	7.62 (1.61) 6.72 -0.9	0.6		<0.05 vs. GP1	
Gregorio, 1999 ¹²⁹	%	Glibenclamide or gliclazide, 85	Metformin + glibenclamide or metformin + gliclazide, 89	10 (esc) 15 120 (esc) 240	850 (esc) 1700 NR (fixed) NR (fixed)	10.32 (SE 0.13) 8.58 (SE 0.12) -1.74	10.33 (SE 0.13) 8.54 (SE 0.12) -1.75	0.01	<0.0005 vs. baseline	<0.0005 vs. baseline	
Hermann, 1994 ⁸⁷	%	Glyburide + diet, 19	Metformin + glyburide + diet, 17	3.5 (esc) 10.5	2000 (esc) 3000 7.0 (esc) 14.0	6.7 (SE 0.3) 5.3 (SE 0.1) -1.3 (SE 0.2)	8.4 (SE 0.4) 6.2 (SE 0.3) -2.2 (SE 0.4)	0.9	0.001 vs. baseline	0.001 vs. baseline	>0.1 all group com- parison

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Hermann, 1994 ⁸⁷	%	Glyburide + diet, 19	Metformin + glyburide + diet, 12	3.5 (esc) 10.5	3000 (fixed) 3.5 (esc) 14	6.7 (SE 0.3) 5.3 (SE 0.1) -1.3 (SE 0.2)	7.8 (SE 0.3) 5.4 (SE 0.3) -2.3 (SE 0.4)	1	0.001 vs. baseline	0.001 vs. baseline	>0.1 all group com- parison
Hermann, 1994 ⁸⁷	%	Glyburide + diet, 19	Metformin + glyburide + diet, 11	3.5 (esc) 10.5	1000 (esc) 3000 10.5 (esc) 14	6.7 (SE 0.3) 5.3 (SE 0.1) -1.3 (SE 0.2)	7.8 (SE 0.4) 5.7 (SE 0.3) -2 (SE 0.4)	0.7	0.001 vs. baseline	0.001 vs. baseline	>0.1 all group com- parison
Hermann, 1994 ⁸⁷	%	Glyburide + diet, 19	Metformin + glyburide + diet, 46	3.5 (esc) 10.5	500 (esc) 1500 1.75 (esc) 5.25	6.7 (SE 0.3) 5.3 (SE 0.1) -1.3 (SE 0.2)	6.8 (SE 0.1) 5.6 (SE 0.1) -1.2 (SE 0.1)	-0.1	0.001 vs. baseline	0.001 vs. baseline	>0.1 all group com- parison
Hermann, 1991 ⁹⁴	%	Glibenclamide + diet, 17	Metformin + glibenclamide + diet, 11	3.5 (esc) 10.5	1000 (esc) 3000 10.5 (esc) 14.0	6.6 (1.3) 5.3 (0.5) -1.3	7.8 (1.4) 5.7 (0.8) -2.0	0.7	<0.001 vs. baseline	<0.001 vs. baseline	
Hermann, 1991 ⁹⁴	%	Glibenclamide + diet, 17	Metformin + glibenclamide + diet, 12	3.5 (esc) 10.5	3000 (fixed) 3.5 (esc) 14.0	6.6 (1.3) 5.3 (0.5) -1.3	7.7 (1.1) 5.4 (0.9) -2.2	0.9	<0.001 vs. baseline	<0.001 vs. baseline	
1998 ¹²⁸ UKPDS, 3 year t/u	%	Glibenclamide + diet, 300	Metformin + glibenclamide + diet, 291	10 (fixed)	500 (esc) 2500 10 (fixed)	7.3 [#] (6.2, 8.8 ^{##}) 8 [#] 0.76 (0.52, 0.99 [†])	7.4 [#] (6.4, 8.8 ^{##}) 7.45 ^{*#} 0.47 (0.24, 0.7 [‡])	0.29		0.0208 vs. GP1	

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Tosi, 2003 ⁹⁵	%	Glibenclamide, 20	Metformin + glibenclamide, 41	5 (esc) 15	2400 (max); 15 (max)	7.8 (1.4) 7.4\$ -0.4\$	8.6 (1) 6.4\$ -2.2\$	1.8\$	NR	NR	
Second Generation Sulfonylurea vs. Alpha-Glucosidase Inhibitor											
Feinbock, 2003 ¹³⁰	%	Glimepiride, 93	Acarbose, 59	1 (esc) 6	50 tid (esc) 200 tid	9.1 (1.9) 6.6 (1.3) -2.5	9.4 (2.0) 7.7 (1.9) -1.8	-0.7	0.014 vs. GP2		
Nakamura, 2000 ⁶⁴	%	Glibenclamide, 15	Voglibose, 15	5 (fixed)	0.6 (fixed)	7.8 (1.1) 6.9 (1.2) -0.9	7.6 (1.1) 6.8 (1.1) -0.8	0.1	<0.05 vs. baseline	<0.05 vs. baseline	
Meglitinide vs. Meglitinide											
Rosenstock, 2004 ¹³¹	%	Nateglinide, 69	Repaglinide, 71	60 (esc) 360	5 (esc) 16	8.9 (1.74) 7.9 (1.36) -1.04 (0.14)	8.9 (1.34) 7.3 (1.3) -1.57 (0.15)	0.53		0.002 vs. GP1	
Pioglitazone vs. Placebo											
Saad, 2004 ¹⁶⁴	%	Pioglitazone, 24	Placebo, 27	45 (fixed)	NA	8.5 8.2 -0.3	8.1 8.9 0.8	-1.1	<.05 vs. GP2		
Herz, 2003 ¹⁶³	%	Pioglitazone, 95	Placebo, 96	30 (fixed)	NA	7.5 6.7 -0.8	7.5 7.3 -0.2	-0.6	<0.001 vs. baseline and vs. GP2	0.025 vs. baseline	

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Herz, 2003 ¹⁶³	%	Pioglitazone, 96	Placebo, 96	45 (fixed)	NA	7.6 6.7 -0.9	7.5 7.3 -0.2	-0.7	<0.001 vs. baseline and vs. GP2	0.025 vs. baseline	
Rosenblatt, 2001 ¹⁶²	%	Pioglitazone, 100	Placebo, 93	30 (NR)	NA	10.65 (1.77) 10.05 -0.6	10.4 (1.7) 11.18 0.76	-1.36	< 0.05 vs. baseline <0.0001 vs. GP2	< 0.05 vs. baseline	
Scherbaum, 2002 ¹⁴¹	%	Pioglitazone + diet, 76	Placebo + diet, 76	30 (fixed)	NA	9.06 (1.2) 7.78 (1.18) -1.05 (1.25)	8.75 (1.06) 8.29 (1.05) -0.34 (0.98)	-0.71	0.003 vs. GP2		
Scherbaum, 2002 ¹⁴¹	%	Pioglitazone + diet, 83	Placebo + diet, 76	15 (fixed)	NA	9.33 (1.18) 7.99 (0.95) -0.92 (1.50)	8.75 (1.06) 8.29 (1.05) -0.34 (0.98)	-0.58	NSG vs. GP2		
Nishio, 2006 ¹⁵¹	%	Pioglitazone, 26	Control group (no placebo), 28	30 (fixed)	NA	7.7 (2.2) 6 (0.9) -1.7	6.9 (1.6) 6.5 (1.2) -0.4	-1.3	0.028 vs. baseline	0.356 vs. baseline	
Aronoff, 2000 ¹⁶⁵	%	Pioglitazone, 80	Placebo, 79	7.5 (fixed)	NA	10.0 (SE 0.22) 10.2 (SE 0.25) 0.2 (SE 0.17)	10.4 (SE 0.22) 11.1 (SE 0.26) 0.7 (SE 0.17)	-0.5			

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Aronoff, 2000 165	%	Pioglitazone, 79	Placebo, 79	15 (fixed)	NA	10.2 (SE 0.22) 9.9 (SE 0.27) -0.3 (SE 0.17)	10.4 (SE 0.22) 11.1 (SE 0.26) 0.7 (SE 0.17)	-1	≤0.05 vs. baseline and GP2		
Aronoff, 2000 165	%	Pioglitazone, 85	Placebo, 79	30 (fixed)	NA	10.2 (SE 0.21) 9.9 (SE 0.29) -0.3 (SE 0.17)	10.4 (SE 0.22) 11.1 (SE 0.26) 0.7 (SE 0.17)	-1	≤0.05 vs. baseline and GP2		
Aronoff, 2000 165	%	Pioglitazone, 76	Placebo, 79	45 (fixed)	NA	10.3 (SE 0.22) 9.4 (SE 0.29) -0.9 (SE 0.18)	10.4 (SE 0.22) 11.1 (SE 0.26) 0.7 (SE 0.17)	-1.6	≤0.05 vs. baseline and GP2		
Einhorn, 2000 160	%	Pioglitazone + metformin + diet, 168	Metformin + placebo + diet, 160	30 (fixed) NR (NR)	NR (NR)	9.86 (SE 1.4) NR NR	9.75 (SE 1.3) NR NR	-0.83	<0.05 vs. baseline and vs. GP1	<0.05 vs. baseline	
Smith, 2005 161	%	Pioglitazone + diet, 21	Placebo + diet, 21	30 (esc) 45	NA	6.88 (1.35) -0.96	6.46 (0.72) -0.11	-0.85	0.0054 vs. GP2		
Tseng, 2005 140	%	Pioglitazone + unspecified sulfonylurea, 23	Unspecified sulfonylurea + placebo, 25	30 (fixed) NR (NR)	NR (NR)	NR NR -8.70% [†]	NR NR 2.6% [†]	NR	<0.05 vs. baseline	NSG vs. baseline	
Kipnes, 2001 166	%	Pioglitazone + unspecified sulfonylurea, 176	Unspecified sulfonylurea + placebo, 181	15 (fixed) NR (fixed)	NR (fixed)	10 (9.8, 10.2 [†]) 9.1 (8.9, 9.3 [†]) -0.8 (-1.0, -0.6 [†])	9.9 (9.7, 10.1 [†]) 10 (9.8, 10.2 [†]) 0.1 (-0.1, 0.2 [†])	-0.9 (-1.2, - 0.6 [†])	NR	NR	

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Kipnes, 2001 ¹⁶⁶	%	Pioglitazone + unspecified sulfonylurea, 182	Unspecified sulfonylurea + placebo, 181	30 (fixed) NR (fixed)	NR (fixed)	9.9 (9.7, 10.1 [†]) 8.7 (8.5, 8.9 [†]) -1.2 (-1.4, -1.0 [†])	9.9 (9.7, 10.1 [†]) 10 (9.8, 10.2 [†]) 0.1 (-0.1, 0.2 [†])	-1.3 (-1.6, - 1.0 [†])	NR	NR	
Rosiglitazone vs. Placebo											
Patel, 1999 ¹⁶⁷	%	Rosiglitazone, 70	Placebo, 74	0.05 bid (fixed)	NA	9.1 9.7 0.6 (SE 0.14)	9.1 9.4 0.3 (SE 0.13)	0.3	0.0569 vs. GP2		
Patel, 1999 ¹⁶⁷	%	Rosiglitazone, 72	Placebo, 74	0.25 bid (fixed)	NA	8.9 9.7 0.6 (SE 0.14)	9.1 9.4 0.3 (SE 0.13)	0.3	0.0565 vs. GP2		
Patel, 1999 ¹⁶⁷	%	Rosiglitazone, 79	Placebo, 74	1.0 bid (fixed)	NA	9.0 9.1 0.1 (SE 0.13)	9.1 9.4 0.3 (SE 0.13)	-0.2	0.4716 vs. GP2		
Patel, 1999 ¹⁶⁷	%	Rosiglitazone, 79	Placebo, 74	2.0 bid (fixed)	NA	9.0 8.9 -0.1 (SE 0.13)	9.1 9.4 0.3 (SE 0.13)	-0.4	0.0287 vs. GP2		
Kim, 2005 ¹⁵²	%	Rosiglitazone + diet + exercise, 60	Diet + exercise, 60	4 (fixed)	NA	9.8 (1.8) 8.6 (1.3) -1.2	9.3 (1.3) 9.2 (1.3) -0.1	1.1	<0.001 vs. baseline	NSG vs. baseline	

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Hallsten, 2002 ⁵⁸ Virtanen, 2003 ¹⁴³	%	Rosiglitazone + diet, 14	Placebo + diet, 14	2 bid (esc) 8 bid	NA	6.8 (SE 0.2) 6.5 (SE 0.2) -0.3	6.3 (SE 0.1) 6.1 (SE 0.1) -0.2	0.1	<0.05 vs. baseline		
Lebovitz, 2001 ¹⁶⁹	%	Rosiglitazone, 169	Placebo, 158	4 bid (fixed)	NA	8.8 (1.6) 8.2 -0.6 (SE 0.3*)	9.0 (1.7) 9.9 0.9 (SE 0.3*)	-1.5	<0.0001 vs. baseline and vs. GP2	<0.001 vs. baseline	
Lebovitz, 2001 ¹⁶⁹	%	Rosiglitazone, 166	Placebo, 158	2 bid (fixed)	NA	9.0 (1.5) 8.7 -0.3 (SE 0.2*)	9.0 (1.7) 9.9 0.9 (SE 0.3*)	-1.2	0.0001 vs. baseline	<0.001 vs. baseline	
Phillips, 2001 ¹⁶⁸	%	Rosiglitazone, 186	Placebo, 173	2 bid (fixed)	NA	8.9 (1.5) NR NR	8.9 (1.5) NR NR	-0.9	<0.0001 vs. GP2		
Phillips, 2001 ¹⁶⁸	%	Rosiglitazone, 181	Placebo, 173	8 od (fixed)	NA	8.9 (1.5) NR NR	8.9 (1.5) NR NR	-1.1	<0.0001v s. GP2		
Phillips, 2001 ¹⁶⁸	%	Rosiglitazone, 187	Placebo, 173	4 bid (fixed)	NA	9.0 (1.5) NR NR	8.9 (1.5) NR NR	-1.5	<0.0001v s. GP2		
Phillips, 2001 ¹⁶⁸	%	Rosiglitazone, 181	Placebo, 173	4 od (fixed)	NA	8.9 (1.6) NR NR	8.9 (1.5) NR NR	-0.8	<0.0001v s. GP2		

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Barnett, 2003 ¹⁷²	%	Rosiglitazone + unspecified sulfonylurea, 84	Unspecified sulfonylurea + placebo, 87	4 bid (fixed) NR (NR)	NR (NR)	9.21 (1.27) 8.05 -1.16	9.06 (1.3) 9.32 0.26	-1.42	<0.001 vs. baseline and vs. GP2	<0.001 vs. baseline	
Zhu, 2003 ¹⁸⁸	%	Rosiglitazone + unspecified sulfonylurea, 215	Unspecified sulfonylurea + placebo, 105	2 bid (fixed) NR (fixed)	NR (fixed)	9.8 (1.5) 8.4 (1.4) -1.4 (-1.6, -1.3 [‡])	9.8 (1.3) 9.4 (1.5) -0.4 (-0.6, -0.1 [‡])	-1.04	0.0001 vs. GP2		
Zhu, 2003 ¹⁸⁸	%	Rosiglitazone + unspecified sulfonylurea, 210	Unspecified sulfonylurea + placebo, 105	4 bid (fixed) NR (fixed)	NR (fixed)	9.9 (1.6) 8 (1.27) -1.9 (-2.1, -1.7 [‡])	9.8 (1.3) 9.4 (1.5) -0.4 (-0.6, -0.1 [‡])	-1.44	0.0001 vs. GP2		
Vongthava- ravat, 2002 ¹⁷⁰	%	Rosiglitazone + unspecified sulfonylurea + diet, 164	Unspecified sulfonylurea + diet, 170	2 bid (fixed)	NR (NR)	9.1 7.9 -1.1 (-1.37, - 0.89 [‡])	8.9 9 0.1 (-0.1, 0.2 [‡])	-1.2		0.0001 vs. GP2	
Wolffen-buttel, 2000 ¹⁷¹	%	Rosiglitazone + unspecified sulfonylurea, 199	Unspecified sulfonylurea + placebo, 192	1 bid (fixed) NR (fixed)	NR (fixed)	9.2 (1.19) 8.7 -0.5*	9.21 (1.3) 9.41 0.2*	-0.59	<0.0001 vs. GP2 and vs. baseline	0.0671 vs. baseline	
Wolffen-buttel, 2000 ¹⁷¹	%	Rosiglitazone + unspecified sulfonylurea, 183	Unspecified sulfonylurea + placebo, 192	2 bid (fixed) NR (fixed)	NR (fixed)	9.23 (1.18) 8.33 -0.9*	9.21 (1.3) 9.41 0.2*	-1.03	<0.0001 vs. GP2 and vs. baseline	0.0671 vs. baseline	
Metformin vs. Placebo											

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Garber, 2002 ⁷⁹	%	Metformin, 161	Placebo, 161	500 (esc) 2000	NA	8.26 (1.08) 7.23 -1.03	8.21 (1.0) 8.00 -0.21	-0.82	NR	NR	
Horton, 2000 ⁹⁶	%	Metformin, 133	Placebo, 106	500 tid (fixed)	NA	8.4 (1.2) 7.6 -0.8 (SE 0.1*)	8.3 (1.1) 8.8 0.5 (SE 0.1*)	-1.2	≤0.0001 vs. baseline and vs. GP2		
Willms, 1999 ⁹⁹	%	Metformin, 27	Placebo, 29	850 bid (fixed)	NA	10.6 (1.4) 7.7 -2.5 (SEM 0.16)	10.6 (1.6) 8.7 -1.3 (SEM 0.34)	-1.3	0.004 vs. GP2		
Grant, 1996 ¹⁵⁴	%	Metformin, 27	Placebo, 23	1500 (esc) 3000	NA	NR NR -1.2 (1.3)	NR NR 0.6 (0.8)	-1.8	<0.001 vs. GP2		
Grant, 1996 ¹⁵⁴	%	Metformin, 25	Placebo, 23	1500 (fixed)	NA	NR NR -0.9 (1.0)	NR NR 0.6 (0.8)	-1.5	<0.001 vs. GP2		
DeFronzo, 1995 ⁸⁸	%	Metformin, 143	Placebo, 146	850 (esc) 850 tid	NA	8.4 7.0 -1.4 (SE 0.1)	8.2 7.8 0.4 (SE 0.1)	-1.8	<0.001 vs. GP2		

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Schneider, 1991 ¹⁷³	%	Metformin, 18	Placebo, 16	850 (esc) 1700	NA	6.76 (1.05) 6.08 (0.98) -0.69 (0.87)	6.48 (0.87) 6.34 (1.11) -0.13 (0.69)	-0.56	0.054 vs. GP2		
Doman, 1991 ²⁶⁰	%	Metformin, 30	Placebo, 30	500 (esc) 1000 tid	NA	11.7 (SE 0.4) 10.3 (SE 0.4) -1.4	11.8 (SE 0.4) 13.3 (SE 0.4) 1.5	-3.0	<0.001 vs. GP2		
Wolever, 2000 ⁹⁸	%	Metformin, 62	Placebo, 45	500 tid (fixed)	NA	8.2 (SE 0.1) 7.4 -0.8 (SE 0.2*)	7.8 (SE 0.1) 8.2 0.4 (SE 0.2*)	-1.2	<0.05 vs. GP2		
Teupe, 1991 ¹⁵⁵	%	Metformin + diet, 25	Diet, 29	NR (esc) 1700	NA	9.0 (1.3) 8.1 (1.7) -0.9	8.7 (0.8) 8.0 (1.2) -0.7	-0.2	<0.05 vs. baseline NSG vs. GP2	<0.05 vs. baseline	
Manzella, 2004 ¹⁴⁸	%	Metformin + diet, 60	Placebo + diet, 60	850 bid (fixed)	NA	8.0 (0.2) 7.2 (0.1) -0.8	8.1 (0.2) 7.9 (0.3) -0.2	-0.6	<0.05 vs. GP2		
Hallsten, 2002 ⁵⁸ Virtanen, 2003 ¹⁴³	% glyca- ted Hb	Metformin + diet, 13	Placebo + diet, 14	500 bid (esc) 1000 bid	NA	6.9 (SE 0.2) 6.2 (SE 0.2) -0.7	6.3 (SE 0.1) 6.1 (SE 0.1) -0.2	-0.5	<0.0001 vs. baseline	NSG vs. baseline	
Del Prato, 2003 ¹⁴⁹	%	Metformin + placebo, 250	Placebo, 127	850 (esc) 2550	NA	7.79 (1.61) 6.77 (1.34) -1.02	7.43 (1.48) 7.91 (1.86) 0.48	-1.5	NR	NR	

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Lee, 1998 ²³⁹	%	Metformin + placebo + diet, 24	Placebo + diet, 24	850 (fixed)	NA	8.4 (SE 0.3) 7.4 (SE 0.2) -1	8.4 (SE 0.2) 8.3 (SE 0.2) -0.1	-0.9	<0.05 vs. GP2		
Garber, 1997 ²¹⁷	%	Metformin, 73	Placebo, 79	NR (esc) 500	NA	10.1 (1.7) 10.4 0.3	9.9 (1.9) 11.1 1.2	-0.9	<0.01 vs. GP2		
Garber, 1997 ²¹⁷	%	Metformin, 73	Placebo, 79	NR (esc) 1000	NA	10.0 (2.0) 10.01 0.01	9.9 (1.9) 11.1 1.2	-1.19	<0.001 vs. GP2		
Garber, 1997 ²¹⁷	%	Metformin, 76	Placebo, 79	NR (esc) 1500	NA	9.7 (1.5) 9.2 -0.5	9.9 (1.9) 11.1 1.2	-1.7	<0.001 vs. GP2		
Garber, 1997 ²¹⁷	%	Metformin, 73	Placebo, 79	NR (esc) 2000	NA	10.1 (2.1) 9.3 -0.8	9.9 (1.9) 11.1 1.2	-2	<0.001 vs. GP2		
Garber, 1997 ²¹⁷	%	Metformin, 77	Placebo, 79	NR (esc) 2500	NA	10 (1.8) 9.6 -0.4	9.9 (1.9) 11.1 1.2	-1.6	<0.001 vs. GP2		

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year						GP1 BL mean (SD)	GP2 BL mean (SD)				
Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 final mean (SD) Mean diff from BL1	GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
1985 ⁹¹ UKPDS, 1 year f/u of obese patients	%	Metformin + diet, 16	Diet, 57	NR (esc) 2550	NA	8.8 (1.8) 8.1 (1.0) -0.8	NR 9.0* (7.7, 10.2* [†]) NR	-0.9	NR	NR	
1995 ⁹² UKPDS, 3 year f/u of obese patients	%	Metformin + diet, 262	Diet, 291	NR (esc) 850 tid	NA	7.2* 7.1 (6.9, 7.3* [†]); 6.95* -0.2* (-0.4, 0.01* [†])	7.0* 7.8 (7.6, 8.0* [†]) 0.8* (0.55, 1.1)	-1.0	NR	NR	
1998 ¹⁵ UKPDS, 10 year f/u of obese patients	%	Metformin, 342	Diet, 411	850 (esc) 2550	NA	7.3 (1.5); 6.9* [#] 8* [#] 1.1	7.1 (1.5); 6.9* [#] 9.3* [#] 2.4	-1.3	NR	NR	
Rachmani, 2002 ¹⁵⁰	%	Metformin continued + diet, 195	Metformin stopped + diet, 198	NR (NR)	NA	8.6 (SE 0.4) 8.8 0.2	8.6 (SE 0.5) 9.1 0.5	-0.3	<0.01 vs. baseline NSG vs. GP2	<0.05 vs. baseline	
Second Generation Sulfonylurea vs. Placebo											
Garber, 2002 ⁷⁹	%	Glyburide (Micronase), 161	Placebo, 161	2.5 (esc) 10	NA	8.21 (1.09) 6.97 -1.24	8.21 (1.0) 8.00 -0.21	-1.03	NR	NR	
Birkeland, 1994 ¹¹⁰	%	Glyburide (no trade drug specified) + diet, 15	Placebo + diet, 16	1.75 (esc) 10.5	NA	8* 7.4* -0.6	8.1* 8.5* 0.4	-1	<.05 vs. GP2		

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Birkeland, 1994 ¹¹⁰	%	Glipizide + diet, 15	Placebo + diet, 16	2.5 (esc) 15	NA	8 (1.5*) 7.5 (1.4*) -0.5*	8.1 (1.1*) 8.5 (1.2*) 0.4*	-0.9	<.05 vs. GP2		
Schade, 1998 ¹³⁵	%	Glimepiride, 106	Placebo, 97	1 (esc) 8	NA	9.1 [#] 6.7 [#] -2.1 ^{*#}	8.9 [#] 7.9 [#] -1.0 ^{*#}	-1.4 [#]	0.001 vs. GP2		
Goldberg, 1996 ¹³⁴	%	Glimepiride, 68	Placebo, 59	8 (fixed)	NA	7.8 [#] 7.5 [#] -0.3 [#]	7.8 [#] 9.5 [#] 1.7 [#]	-1.9 [#]	<0.001 vs. GP2		
Goldberg, 1996 ¹³⁴	%	Glimepiride, 65	Placebo, 59	1 (fixed)	NA	7.8 [#] 8 [#] 0.2 [#]	7.8 [#] 9.5 [#] 1.7 [#]	-1.2	<0.001 vs. GP2		
Goldberg, 1996 ¹³⁴	%	Glimepiride, 65	Placebo, 59	4 (fixed)	NA	7.7 [#] 7.7 [#] 0 [#]	7.8 [#] 9.5 [#] 1.7 [#]	-1.8	<0.001 vs. baseline		
Luis Bautista, 2003 ¹⁹³	%	Glimepiride + diet + exercise, 42	Placebo + diet + exercise, 18	1 (esc) 4	NA	10.1 (SE 0.3) 7.8 (SE 0.2) -2.3	10.6 (SE 0.6) 9.9 (SE 0.7) -0.7	-1.8	<0.001 vs. baseline		
Rosenstock, 1996 ¹⁸⁹	%	Glimepiride, 75	Placebo, 66	16 od (fixed)	NA	NR NR -0.4 ^{*#}	7.7 [#] 9.7 [#] 1.3 ^{*#}	-1.7 [#]			<0.01 all group com- parison

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Rosenstock, 1996 ¹⁸⁹	%	Glimepiride, 74	Placebo, 66	4 bid (fixed)	NA	NR NR -0.45* [#]	7.7 [#] 9.7 [#] 1.3* [#]	-1.75 [#]		<0.001 vs. baseline	<0.01 all group com- parison
Rosenstock, 1996 ¹⁸⁹	%	Glimepiride, 76	Placebo, 66	8 od (fixed)	NA	NR NR -0.4* [#]	7.7 [#] 9.7 [#] 1.3* [#]	-1.7 [#]		<0.001 vs. baseline	<0.01 all group com- parison
Rosenstock, 1996 ¹⁸⁹	%	Glimepiride, 80	Placebo, 66	8 bid (fixed)	NA	NR NR -0.6* [#]	7.7 [#] 9.7 [#] 1.3* [#]	-1.75 [#]		<0.001 vs. baseline	<0.01 all group com- parison
Simonson, 1997 ¹³⁶	%	Glipizide GITS, 42	Placebo, 68	10 (fixed)	NA	8.8 (SE 0.2) 7.6 (SE 0.2) -1.2	8.3 (SE 0.2) 9.14 (SE 0.2) 0.84	-2.04	<0.001 vs. GP2		
Simonson, 1997 ¹³⁶	%	Glipizide GITS, 41	Placebo, 68	15 (fixed)	NA	8.6 (SE 0.2) 8.11 (SE 0.2) -0.49	8.3 (SE 0.2) 9.14 (SE 0.2) 0.84	-1.33	<0.0001 vs. GP2		
Simonson, 1997 ¹³⁶	%	Glipizide GITS, 26	Placebo, 68	40 (fixed)	NA	8.4 (SE 0.3) 7.13 (SE 0.3) -1.27	8.3 (SE 0.2) 9.14 (SE 0.2) 0.84	-2.11	<0.0001 vs. GP2		

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Simonson, 1997 ¹³⁶	%	Glipizide GITS, 29	Placebo, 68	60 (fixed)	NA	8.6 (SE 0.3) 7.5 (SE 0.24) -1.1	8.3 (SE 0.2) 9.14 (SE 0.2) 0.84	-1.94	<0.0001 vs. GP2		
Simonson, 1997 ¹³⁶	%	Glipizide GITS, 68	Placebo, 68	20 (fixed)	NA	8.7 (SE 0.2) 7.8 (SE 0.2) -0.9	8.3 (SE 0.2) 9.14 (SE 0.2) 0.84	-1.74	<0.0001 vs. GP2		
Simonson, 1997 ¹³⁶	%	Glipizide GITS, 66	Placebo, 68	5 (fixed)	NA	8.5 (SE 0.2) 7.6 (SE 0.2) -0.9	8.3 (SE 0.2) 9.14 (SE 0.2) 0.84	-1.74	<0.0001 vs. GP2		
Testa, 1998 ¹⁹⁵	%	Glipizide GITS + diet, 377	Placebo + diet, 192	5 (esc) 20	NA	8.5 (1.5) 7.5 (1.94; SE 0.1) -0.9	8.7 (1.4) 9.3 (1.39; SE 0.1) 0.7	-1.6		<.001 vs. GP1	
Vray, 1995 ¹³⁷	% HbA1	Glibenclamide, 46	Traditional Chinese treatment, 46	2.5 tid (fixed)	Admin-istered in 7 capsules (fixed)	NR NR -1.6 (SE 0.3)	NR NR 0.03 (SE 0.4)	-1.63	<0.001 vs. baseline	0.87 vs. baseline	
1998 ¹⁵ UKPDS, 10 year f/u of overweight patients	%	Glibenclamide, 277	Diet, 411	NR	NA	7.2 (1.5); 7* [#] 9.1* [#] 2.1	7.1 (1.5); 6.9* [#] 9.3* [#] 2.4	-0.3 [#]	NR	NR	

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
1998 ¹⁶ UKPDS, 10 year f/u	%	Glibenclamide + diet, 615	Diet, 896	2.5 (esc) 20	NA	6.3 (1.3); 6.9* [#] 8.2* [#] 1.3	6.2 (1.2); 6.9* [#] 8.4* [#] 1.5	0.2 [#]		<0.0001 vs. GP1	
1995 ⁹² UKPDS, 3 year f/u of non- obese patients	%	Glibenclamide + diet, 472	Diet, 373	NR (esc) 10 bid	NA	7.1* 6.9 (6.7, 7.0 [†]) -0.6* (-0.85, - 0.4 [†])	7.1* 7.6 (7.4, 7.7 [†]) 0.3* (0.1, 0.5)	-0.9	<0.05 vs. baseline	<0.05 vs. baseline	
1995 ⁹² UKPDS, 3 year f/u of obese patients	%	Glibenclamide + diet, 212	Diet, 291	NR (esc) 10 bid	NA	7.1* 7.15* 0.15* (-0.15, - 0.4 [†])	7.0* 7.8* (7.6, 8) 0.8* (0.55, 1.1)	-0.65	NSG vs. baseline	<0.05 vs. baseline	
1985 ⁹¹ UKPDS, 1 year f/u	%	Unspecified sulfonylurea + diet, 72	Diet, 57	NR (esc) 500 of chlorpropa- mide or 10 bid of glibencla- mide	NA	9.1 (2.1) 7.8 (1.2) -1.3	8.8 (1.7) 9.1 (1.6) 0.3	-1.6	<0.001 vs. baseline	NSG vs. baseline	
Cefalu, 1998 ²⁶¹	% total glyca- ted Hb	Glipizide GITS, 20	Placebo, 20	5 (esc) 10	NA	10.3 (SE 0.4) 9.6 (SE 0.5) -0.7	9.4 (SE 0.5) 10.6 (SE 0.3) 1.2	1.9	<0.005 vs. baseline		
Repaglinide vs. Placebo											
Bech, 2003 ¹⁹⁷	%	Repaglinide, 164	Placebo, 89	0.5 (esc) 4 per meal	NA	7.8 (1.7) 6.7 (1.2) -1.1	7.6 (1.6) 7.4 (1.5) -0.2	0.9	<0.001 vs. baseline and vs. GP2		

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year						GP1 BL mean (SD)	GP2 BL mean (SD)				
Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 final mean (SD)	GP2 final mean (SD)	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Moses, 2001 ²¹⁸	%	Repaglinide, 260	Placebo, 134	0.5 (esc) 1 per meal	NA	7.8 (SE 1.8) 6.66 -1.14	7.6 (SE 1.5) 7.45 -0.15	-0.99	<0.001 vs. baseline and vs. GP2	0.16 vs. baseline	
Goldberg, 1998 ¹³⁹	%	Repaglinide, 61	Placebo, 28	0.25 tid (esc) 8.0	NA	8.3 7.6* -0.7	8.1 9.2* 1.1	-1.8	≤0.05 vs. GP2		
Jovanovic, 2000 ¹⁹⁴	%	Repaglinide, 146	Placebo, 75	4 tid (fixed)	NA	8.7 (1.7) 8.2 -0.5	8.6 (1.4) 10 1.4	-1.9	<0.001 vs. GP2		
Jovanovic, 2000 ¹⁹⁴	%	Repaglinide, 140	Placebo, 75	1 tid (fixed)	NA	8.9 (1.9) 8.2 -0.7	8.6 (1.4) 10 1.4	-1.8	<0.001 vs. GP2		
Nateglinide vs. Placebo											
Mari, 2005 ²⁶²	%	Nateglinide, 27	Placebo, 30	60 (fixed)	NA	6.6 (0.6) 6.4 -0.2 (0.5)	6.5 (0.6) 6.4 -0.1 (0.5)	-0.1	NR	NR	
Mari, 2005 ²⁶²	%	Nateglinide, 26	Placebo, 30	30 (fixed)	NA	6.5 (0.6) 6.3 -0.2 (0.5)	6.5 (0.6) 6.4 -0.1 (0.5)	-0.1	NR	NR	

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Mari, 2005 ²⁶²	%	Nateglinide, 25	Placebo, 30	120 (fixed)	NA	6.6 (0.7) 6.3 -0.3 (0.4)	6.5 (0.6) 6.4 -0.1 (0.5)	-0.2	NR	NR	
Saloranta, 2002 ²⁴¹	%	Nateglinide, 166	Placebo, 163	30 (fixed)	NA	6.55 (0.63) 6.44 -0.11* (SE 0.5)	6.45 (0.6) 6.61 0.16 (SE 0.5)	-0.26	<0.001 vs. GP2		
Saloranta, 2002 ²⁴¹	%	Nateglinide, 175	Placebo, 163	60 (fixed)	NA	6.53 (0.6) 6.34 -0.19* (SE 0.4)	6.45 (0.6) 6.61 0.16 (SE 0.5)	-0.31	<0.001 vs. GP2		
Saloranta, 2002 ²⁴¹	%	Nateglinide, 171	Placebo, 163	120 (fixed)	NA	6.57 (0.69) 6.29 -0.28* (SE 0.5)	6.45 (0.6) 6.61 0.16 (SE 0.5)	-0.39	<0.001 vs. GP2		
Horton, 2000 ⁹⁶	%	Nateglinide, 134	Placebo, 106	120 (fixed)	NA	8.3 (1.0) 7.8 -0.5 (SE 0.1*)	8.3 (1.1) 8.8 0.5 (SE 0.1*)	-0.9	≤0.0001 vs. baseline and vs. GP2		
Hanefeld, 2000 ¹⁹⁰	%	Nateglinide, 57	Placebo, 60	180 (fixed)	NA	8.5 (1.1) 7.94 -0.56	8.5 (1.0) 8.57 0.07 (-0.18, 0.32 [†])	-0.64	<0.001 vs. GP2		

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year						GP1 BL mean (SD)	GP2 BL mean (SD)				
Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 final mean (SD) Mean diff from BL1	GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Hanefeld, 2000 ¹⁹⁰	%	Nateglinide, 63	Placebo, 60	120 (fixed)	NA	8.3 (0.9) 7.75 -0.55 (-0.97, - 0.27 [†])	8.5 (1.0) 8.57 0.07 (-0.18, 0.32 [†])	-0.62	<0.001 vs. GP2		
Hanefeld, 2000 ¹⁹⁰	%	Nateglinide, 58	Placebo, 60	60 (fixed)	NA	8.3 (1.1) 7.92 -0.38 (-0.8, -0.1 [†])	8.5 (1.0) 8.57 0.07 (-0.18, 0.32 [†])	-0.45	<0.05 vs. GP2		
Hanefeld, 2000 ¹⁹⁰	%	Nateglinide, 51	Placebo, 60	30 (fixed)	NA	8.4 (1.1) 8.2 -0.2 (-0.65, 0.1 [†])	8.5 (1.0) 8.57 0.07 (-0.18, 0.32 [†])	-0.27	NSG vs. GP2		
Alpha-Glucosidase Inhibitor vs. Placebo											
Wolever, 2000 ⁹⁸	%	Acarbose + diet, 28	Placebo, 45	25 tid (esc) 300 tid	NA	7.9 (SE 0.1) 7.8 -0.1* (SE 0.2*)	7.8 (SE 0.1) 8.2 0.4* (SE 0.2*)	-0.5	<0.05 vs. GP2		
Willms, 1999 ⁹⁹	%	Acarbose, 31	Placebo, 29	100 tid (fixed)	NA	10.6 (1.3) 7.8 -2.3 (SEM 0.32)	10.6 (1.6) 8.7 -1.3 (SEM 0.34)	-1	<0.01 vs. GP2		

Appendix F: Evidence Table 5. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: hemoglobin A1c

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2	Other
Hasche, 1999 ¹³⁸	%	Acarbose, 28	Placebo + diet, 32	50 bid (esc) 100 tid	NA	8.6 (0.7) 6.85 (1.7) -1.71 (1.6)	8.2 (0.7) 7.41 (1.0) -0.82 (1.1)	-0.89	0.02 vs. GP2		
Rosenbaum, 2002 ¹⁵³	% total glyca- ted Hb	Acarbose, 20	Placebo, 20	50 bid (esc) 100 tid	NA	6.4 (1.7) 5.6 (1.9) -0.8	6.3 (2.1) 6.3 (2.0) 0	-0.8	0.03 vs. baseline	0.15 vs. baseline	
Metformin + Second Generation Sulfonylurea vs. Placebo											
Garber, 2002 ⁷⁹	%	Metformin + glyburide (Micronase), 158	Placebo, 161	250 (esc) 1000 1.25 (esc) 5	NA	8.25 (1.11) 6.77 -1.48	8.21 (1.0) 8.00 -0.21	-1.27	<0.001 vs. GP2		
Garber, 2002 ⁷⁹	%	Metformin + glyburide (Micronase), 165	Placebo, 161	500 (esc) 2000 2.5 (esc) 10	NA	8.18 (1.14) 6.65 -1.53	8.21 (1.0) 8.00 -0.21	-1.32	<0.001 vs. GP2		

Comp = comparison; BL = baseline; GP = group; mg = milligrams; esc = escalated; max = maximum; diff = difference; NR = not reported; NSG = not significant; NA = not applicable; SD = standard deviation; SE = standard error; SEM = standard error of the mean; od = once daily; bid = twice daily; tid = three times daily; HbA1c = hemoglobin A1c; HbA1 = hemoglobin A1; Hb = hemoglobin; UKPDS = United Kingdom Prospective Diabetes Study; f/u = follow-up; DIACOM = effect of Dosing frequency of oral Antidiabetic agents on the COMpliance and biochemical control of type 2 diabetes; XR = extended release; GITS = gastrointestinal therapeutic system; vs = versus

* Number obtained from a figure

† Percent change from baseline

‡ 95% confidence interval

Median

Interquartile range

§ Data from after first cross-over

Appendix F: Evidence Table 6. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: two hour postprandial glucose

Author, year						GP1 BL mean (SD)	GP2 BL mean (SD)				
Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 final mean (SD)	GP2 final mean (SD)	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Thiazolidinedione vs. Other Diabetic Medications											
Rama- chandran, 2004 ⁵⁵	mg	Pioglitazone + diet, 23	Glimepiride + diet, 18	15 (esc) 30	1 (esc) 2	286.2 (84.6) 178.2 (61.2) -108	334.8 (75.6) 207 (79.2) -127.8	19.8	<0.01 vs. baseline	<0.01 vs. baseline	
Rama- chandran, 2004 ⁵⁵	mg	Pioglitazone + diet, 23	Metformin + diet, 21	15 (esc) 30	250 (esc) 850	286.2 (84.6) 178.2 (61.2) -108	313.2 (75.6) 223.2 (86.4) -90	-18	<0.01 vs. baseline	<0.01 vs. baseline	
Derosa, 2005 ⁵³	mg	Rosiglitazone + glimepiride + diet + exercise, 42	Pioglitazone + glimepiride + diet + exercise, 45	4 (fixed) 4 (fixed)	15 (fixed) 4 (fixed)	192.78 (27.9) 163.8 (25.02) -28.98	194.76 (25.02) 159.84 (21.96) -34.92	5.94	<0.01 vs. baseline	<0.01 vs. baseline	

Appendix F: Evidence Table 6. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: two hour postprandial glucose

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2	Other
Derosa, 2005 ⁷²	mg	Rosiglitazone + metformin + diet + exercise + behavioral therapy, 48	Glimepiride + metformin diet + exercise + behavioral therapy, 47	4 (fixed) 1500 (fixed)	1500 (fixed) 2 (fixed)	199 (21) 170 (18) -29	194 (19) 171 (21) -23	-6	<0.01 vs. baseline	<0.05 vs. baseline	
Metformin vs. Second Generation Sulfonylurea											
Garber, 2002 ⁷⁹	mg	Metformin, 161	Glyburide (Micronase), 161	500 (esc) 2000	2.5 (esc) 10	NR NR -41.4	NR NR -39.6	-1.8	NR	NR	
Garber, 2003 ⁸⁰	mg	Metformin, 164	Glyburide (no trade drug specified), 151	500 (esc) 2000	2.5 (esc) 10	232.2 169 -70	251 184 -62.6	-7.4	NR	NR	
Blonde, 2002 ⁸¹	mg	Metformin, 153	Glyburide (no trade drug specified), 164	500 (esc) 2000	10 (fixed)	280.8 (72) 286.2 5.4	289.8 (72) 289.8 0	5.4	NR	NR	
Noury, 1991 ⁸⁶	mg	Metformin, 30	Gliclazide, 27	1700 (fixed)	80 (esc) 240	211 (96) 174 (82) -37	221 (91) 181 (99) 40	3	<0.05 vs. baseline	<0.05 vs. baseline	
Rama-chandran, 2004 ⁵⁵	mg	Metformin + diet, 21	Glimepiride + diet, 18	250 (esc) 850	1 (esc) 2	313.2 (75.6) 223.2 (86.4) -90	334.8 (75.6) 207 (79.2) -127.8	37.8	<0.01 vs. baseline	<0.01 vs. baseline	

Appendix F: Evidence Table 6. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: two hour postprandial glucose

Author, year						GP1 BL mean (SD)	GP2 BL mean (SD)				
Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 final mean (SD) Mean diff from BL1	GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Charpentier, 2001 ⁸⁹	mg	Metformin + placebo, 75	Glimepiride + placebo, 150	850 tid (fixed)	1 (esc) 6	273.6 (100.8) 304.2 (108) 30.6	268.2 (93.6) 264.6 (106.2) -3.6	34.2		<0.001 vs. GP2	
Derosa, 2004 ⁹⁰	mg	Metformin + placebo + diet + exercise, 75	Glimepiride + placebo + diet + exercise, 73	1000 (esc) 1000 tid	1 (esc) 2 bid	192 (28) 166 (28) -26	189 (33) 162 (26) -27	1	<0.01 vs. baseline	<0.01 vs. baseline	
Metformin vs. Metformin + Second Generation Sulfonylurea											
Garber, 2002 ⁷⁹	mg	Metformin, 161	Metformin + glyburide (Micronase), 165	500 (esc) 2000	500 (esc) 2000 2.5 (esc) 10	NR NR -41.4	NR NR -59.4	18	NR	NR	
Garber, 2002 ⁷⁹	mg	Metformin, 161	Metformin + glyburide (Micronase), 158	500 (esc) 2000	250 (esc) 1000 1.25 (esc) 5	NR NR -41.4	NR NR -61.2	19.8	NR	NR	
Garber, 2003 ⁸⁰	mg	Metformin, 164	Metformin + glyburide (no trade drug specified), 171	500 (esc) 2000	250 (esc) 1000 1.25 (esc) 5	232.2 169 -70	245.8 161 -82.5	12.5		0.016 vs. GP1	
Blonde, 2002 ⁸¹	mg	Metformin, 153	Metformin + glyburide (no trade drug specified), 162	500 (esc) 2000	500 (esc) 2000 5 (esc) 20	280.8 (72) 286.2 5.4	279 (63) 216 -63	68.4		<0.001 vs. GP1	

Appendix F: Evidence Table 6. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: two hour postprandial glucose

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Blonde, 2002 ⁸¹	mg	Metformin, 153	Metformin + glyburide (no trade drug specified), 160	500 (esc) 2000	500 (esc) 2000 2.5 (esc) 10	280.8 (72) 286.2 5.4	280.8 (64.8) 223.2 -57.6	63		<0.001 vs. GP1	
Charpentier, 2001 ⁸⁹	mg	Metformin + placebo, 75	Metformin + glimepiride, 147	850 tid (fixed)	850 tid (fixed) 1 (esc) 6	273.6 (100.8) 304.2 (108) 30.6	266.4 (91.8) 221.4 (66.6) -45	75.6	NR	<0.001 vs. baseline	
Second Generation Sulfonylurea vs. Metformin + Second Generation Sulfonylurea											
Garber, 2002 ⁷⁹	mg	Glyburide (Micronase), 161	Metformin + glyburide (Micronase), 158	2.5 (esc) 10	250 (esc) 1000 1.25 (esc) 5	NR NR -39.6	NR NR -61.2	21.6	NR	NR	
Garber, 2002 ⁷⁹	mg	Glyburide (Micronase), 161	Metformin + glyburide (Micronase), 165	2.5 (esc) 10	500 (esc) 2000 2.5 (esc) 10	NR NR -39.6	NR NR -59.4	19.8	NR	NR	
Garber, 2003 ⁸⁰	mg	Glyburide (no trade drug specified), 151	Metformin + glyburide (no trade drug specified), 171	2.5 (esc) 10	250 (esc) 1000 1.25 (esc) 5	251 184 -62.6	245.8 161 -82.5	20		<0.001 vs. GP1	
Erle, 1999 ¹²⁷	mg	Glyburide (no trade drug specified), 18	Metformin + glyburide (no trade drug specified), 15	5 (esc) 15	800 (esc) 1600 5 (esc) 10	285 (103) 258 (63) -27	272 (85) 230 (77) -42	15	NSG vs. baseline	<0.05 vs. baseline <0.01 vs. GP1	

Appendix F: Evidence Table 6. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: two hour postprandial glucose

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Blonde, 2002 ⁸¹	mg	Glyburide (no trade drug specified), 164	Metformin + glyburide (no trade drug specified), 162	10 bid (fixed)	500 (esc) 2000 5 (esc) 20	289.8 (72) 289.8 0	279 (63) 216 -63	63		<0.001 vs. GP1	
Blonde, 2002 ⁸¹	mg	Glyburide (no trade drug specified), 164	Metformin + glyburide (no trade drug specified), 160	10 bid (fixed)	500 (esc) 2000 2.5 (esc) 10	289.8 (72) 289.8 0	280.8 (64.8) 223.2 -57.6	57.6		<0.001 vs. GP1	
Charpentier, 2001 ⁸⁹	mg	Glimepiride + placebo, 150	Metformin + glimepiride, 147	1 (esc) 6	850 tid (fixed) 1 (esc) 6	268.2 (93.6) 264.6 (106.2) -3.6	266.4 (91.8) 221.4 (66.6) -45	41.4		<0.001 vs. GP1	
Second Generation Sulfonylurea vs. Second Generation Sulfonylurea											
Carlson, 1993 ¹⁰⁸	mg	Glyburide (Micronase), 102	Glyburide (Glynase Prestab), 100	3 (fixed)	5 (fixed)	213.7 226.5 (SE 8.2) 12.8	224.7 226.1 (SE 6.6) 1.4	11.4	<0.01 vs. baseline	NR	
Dills, 1996 ¹⁰⁷	mg	Glyburide (Micronase), 288	Glimepiride, 289	1.25 (esc) 20	1 (esc) 16	NR NR 51	NR NR 53	-2	≤0.001 vs. baseline	≤0.001 vs. baseline	
Baba, 1983 ¹³³	mg	Glibendamide, 131	Gliclazide, 146	2.5 (esc) 10	40 (esc) 160	275 200 -75	295 207.5 -87.5	12.5	<0.05 vs. baseline NSG vs. GP2	<0.05 vs. baseline	
Repaglinide vs. Other Diabetes Medications											

Appendix F: Evidence Table 6. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: two hour postprandial glucose

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2	Other
Derosa, 2003 ¹¹⁸	mg	Repaglinide + diet + exercise, 56	Metformin + diet + exercise, 56	0.5 bid (esc) 4	500 bid (esc) 2500	183.6 (34.92) 154.8 (30.06) -28.8	194.4 (30.06) 172.8 (27.9) -21.6	-7	<0.05 vs. baseline and vs. GP2	<0.05 vs. baseline	
Derosa, 2003 ¹¹⁸	mg	Repaglinide + placebo	Glimepiride + placebo	1 (esc) 2.5 mean final dose	1 (esc) 3 mean final dose	194 (30) 148 (27) -46	188 (32) 167 (28) -21	-25	<0.01 vs. baseline	<0.05 vs. baseline	
Wolffen-buttel, 1993 ¹²⁰	mg	Repaglinide, 27	Glibenclamide, 15	0.5 (esc) 4	5 (esc) 15	248.4 (70.2) 219.6 (75.6) -28.8	212.4 (57.6) 210.6 (39.6) -1.8	-27	<0.05 vs. baseline	NR	
Landgraf, 1999 ¹²¹	mg	Repaglinide, 94	Glibenclamide + placebo, 98	0.5 (esc) 4	1.75 (esc) 10.5	273.6 (61.2) 145.8 (SE 10.8) -127.8	280.8 (64.8) 163.8 (SE 10.8) -117	-18	0.07 vs. GP2		
Metformin vs. Placebo											
Garber, 2002 ⁷⁹	mg	Metformin, 161	Placebo, 161	500 (esc) 2000	NA	NR NR -41.4	NR NR 5.4	-46.8	NR	NR	
Second Generation Sulfonylurea vs. Placebo											
Garber, 2002 ⁷⁹	mg	Glyburide (Micronase), 161	Placebo, 161	2.5 (esc) 10	NA	NR NR -39.6	NR NR 5.4	-45	NR	NR	

Appendix F: Evidence Table 6. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: two hour postprandial glucose

Author, year						GP1 BL mean (SD)	GP2 BL mean (SD)				
Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 final mean (SD) Mean diff from BL1	GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Goldberg, 1996 ¹³⁴	mg	Glimepiride, 69	Placebo, 55	4 (fixed)	NA	284.4 203.4 -81	286.2 313.2 27	-108	<0.001 vs. GP2		
Goldberg, 1996 ¹³⁴	mg	Glimepiride, 65	Placebo, 55	1 (fixed)	NA	280.8 216 -64.8	286.2 313.2 27	-91.8	<0.001 vs. GP2		
Goldberg, 1996 ¹³⁴	mg	Glimepiride, 64	Placebo, 55	8 (fixed)	NA	295.2 212.4 -82.8	286.2 313.2 27	-109.8	<0.001 vs. GP2		
Schade, 1998 ¹³⁵	mg	Glimepiride, 108	Placebo, 101	1 (esc) 8	NA	291 [#] 174 [#] -117	268 [#] 237 [#] -31	-86	<0.001 vs. GP2		
Simonson, 1997 ¹³⁶	mg	Glipizide GITS, 68	Placebo, 69	5 (fixed)	NA	NR NR -60 (10)* -52 (10) [†]	NR NR NR	NR	<0.01 vs. GP2		NSG all glipi- zide doses
Simonson, 1997 ¹³⁶	mg	Glipizide GITS, 42	Placebo, 69	10 (fixed)	NA	NR NR -57 (10)	NR NR NR	NR	<0.01 vs. GP2		NSG all glipi- zide doses

Appendix F: Evidence Table 6. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: two hour postprandial glucose

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Simonson, 1997 ¹³⁶	mg	Glipizide GITS, 42	Placebo, 69	15 (fixed)	NA	NR NR -38 (10)	NR NR NR	NR	<0.01 vs. GP2		NSG all glipi- zide doses
Simonson, 1997 ¹³⁶	mg	Glipizide GITS, 69	Placebo, 69	20 (fixed)	NA	NR NR -58 (10)* -57 (10) [†]	NR NR NR	NR	<0.01 vs. GP2		NSG all glipi- zide doses
Simonson, 1997 ¹³⁶	mg	Glipizide GITS, 28	Placebo, 69	40 (fixed)	NA	NR NR -83 (11)	NR NR NR	NR	<0.01 vs. GP2		NSG all glipi- zide doses
Simonson, 1997 ¹³⁶	mg	Glipizide GITS, 29	Placebo, 69	60 (fixed)	NA	NR NR -49 (10)	NR NR NR	NR	<0.01 vs. GP2		NSG all glipi- zide doses
Vray, 1995 ¹³⁷	mg	Glibenclamide, 46	Placebo, 51	2.5 tid (fixed)	NA	NR NR -35.1	NR NR -5.94	-29.2	<0.001 vs. GP2		
Metformin + Second Generation Sulfonylurea vs. Placebo											
Garber, 2002 ⁷⁹	mg	Metformin + glyburide (Micronase), 165	Placebo, 161	500 (esc) 2000 2.5 (esc) 10	NA	NR NR -59.4	NR NR 5.4	-64.8	NR	NR	

Appendix F: Evidence Table 6. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: two hour postprandial glucose

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Garber, 2002 ⁷⁹	mg	Metformin + glyburide (Micronase), 158	Placebo, 161	250 (esc) 1000 1.25 (esc) 5	NA	NR NR -61.2	NR NR 5.4	-66.6	NR	NR	
Acarbose vs. Placebo											
Hasche, 1999 ¹³⁸	mg	Acarbose + diet, 28	Placebo + diet, 32	50 bid (esc) 100 tid	NA	219.4 (40.7) 139.4 -80	228.9 (36) 164 -64.9	-15	0.11 vs. GP2		
Repaglinide vs. Placebo											
Goldberg, 1998 ¹³⁹	mg	Repaglinide, 59	Placebo, 27	0.25 (esc) 8	NA	NR 214.2 -46.8	NR 300.6 55.8	-104	0.000 vs. GP2		
Pioglitazone vs. Placebo											
Tseng, 2005 ¹⁴⁰	%	Pioglitazone + unspecified sulfonylurea, 23	Unspecified sulfonylurea + placebo, 25	30 (fixed) NR (NR)	NR (NR)	NR NR -12.5 [†]	NR NR 0.3 [†]	-12.8 [†]	<0.05 vs. baseline	NSG vs. baseline	
Scherbaum, 2002 ¹⁴¹	mg	Pioglitazone + diet, 83	Placebo + diet, 76	15 (fixed)	NA	NR NR NR	NR NR NR	NR	0.014 vs. GP2		
Scherbaum, 2002 ¹⁴¹	mg	Pioglitazone + diet, 76	Placebo + diet, 76	30 (fixed)	NA	NR NR NR	NR NR NR	NR	0.014 vs. GP2		

Appendix F: Evidence Table 6. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: two hour postprandial glucose

Comp = comparison; BL = baseline; GP = group; mg = milligrams; max = maximum; esc = escalated; diff = difference; SD = standard deviation; SE = standard error; NR = not reported; NSG = not significant; NA = not applicable; bid = twice daily; tid = three times daily; GITS = gastrointestinal therapeutic system; vs = versus

* Data from Trial 1

† Data from Trial 2

‡ Percent change from baseline

Median

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Thiazolidinedione vs. Thiazolidinedione											
Khan, 2002 ⁵¹	kg	Rosiglitazone, 60	Pioglitazone, 67	2-8 (fixed)	15-45 (fixed)	103.2 (24.8) NR 2*	101.4 (24.2) NR 2*	0	<0.01 vs. baseline	<0.01 vs. baseline	
Goldberg, 2005 ⁵²	kg	Rosiglitazone + diet, 356	Pioglitazone + diet, 363	4 (esc) 8	30 (esc) 45	92.5 (21) 94.1 1.6 (SE 0.2)	93.7 (20.6) 95.7 2.0 (SE 0.2)	-0.4	0.164 vs. GP2		
Thiazolidinedione vs. Metformin											

Appendix F: Evidence Table 7. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: weight

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Hallsten, 2002 ⁵⁸ Virtanen, 2003 ¹⁴³	kg	Rosiglitazone + diet, 14	Metformin + diet, 13	2 bid (esc) 4 bid	500 bid (esc) 1000 bid	83.7 (7.9) 84.3 (3.5) 0.6	88.8 (10.8) 86.8 -2	2.6	NSG vs. baseline	<0.05 vs. baseline	
Pavo, 2003 ⁵⁹	kg	Pioglitazone + placebo, 100	Metformin + placebo, 91	30 (esc) 45	850 (esc) 2550	86.1 (15.6) 86.8 0.7 (0.4)	88.9 (15.9) 90.2 -2.4	3.1	<0.0001 vs. GP2		
Rama- chandran, 2004 ⁵⁵	kg	Pioglitazone + diet, 23	Metformin + diet, 21	15 (esc) 30	250 (esc) 850	68.9 (9.1) 67.8 (7.9) -1.1	67.7 (11.5) 67 (11.4) -0.7	-0.4	NR	NR	
Natali, 2004 ¹⁴⁴	kg	Rosiglitazone, 44	Metformin, 22	4 bid (fixed)	500 tid (fixed)	80.4 (SEM 10.1) 80.9 0.5 (0.5)	77.3 (SEM 12.5) 76.7 -0.6 (0.4)	1.2	NSG vs. baseline and vs. GP2	NSG vs. baseline	
Schern-thaner, 2004 ⁵⁶	kg	Pioglitazone + placebo + diet, 597	Metformin + placebo + diet, 597	30 (esc) 45	850 up to 3 times/day (esc) 2550	NR NR 1.9	NR NR -2.5	4.4	NR	NR	
Hanefeld, 2004 ⁶⁰ QUARTET study group	kg	Pioglitazone + unspecified sulfonylurea + placebo, 319	Metformin + unspecified sulfonylurea + placebo, 320	15 (esc) 45 NR	850 (esc) 850 tid NR	85.3 (15.1) 88.1 2.8	84.9 (14.5) 83.9 -1	3.8	NR	NR	
Thiazolidinedione vs. Second Generation Sulfonylurea											

Appendix F: Evidence Table 7. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: weight

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2	Other
St John Sutton, 2002 ⁶⁷	kg	Rosiglitazone, 104	Glyburide (no trade drug specified), 99	4 bid (fixed)	NR (esc) 20	86.2 (15.6) 91.2 5 (3.7-6.2 [†])	85.1 (13.6) 88.5 3.4 (2.7-4.1 [†])	1.6	<0.05 vs. baseline	<0.05 vs. baseline	
Tan, 2004 ⁶⁵	kg	Pioglitazone, 90	Glibenclamide, 108	30 (esc) 45	1.75 (esc) 10.5	88.7 (17.4) 91.7 3	89.1 (16) 90.2 1.1	1.9	<0.001 vs. baseline 0.002 vs. GP2	0.008 vs. baseline	
Tan, 2005 ⁶¹ One year extension study for Quartet study group	kg	Pioglitazone, 146	Gliclazide, 127	15 (esc) 45	80 (esc) 320	91.7 95.6 3.9	89.2 93.4 4.2	-0.3	<0.001 vs. GP2		
Rama-chandran, 2004 ⁶⁵	kg	Pioglitazone + diet, 23	Glimepiride + diet, 18	15 (esc) 30	1 (esc) 2	68.9 (9.1) 67.8 (7.9) -1.1	65.7 (9.1) 67.5 (9.2) 1.8	-2.9	NR	<0.05 vs. baseline	
Charbonnel, 2005 ⁶³	kg	Pioglitazone	Gliclazide	NR (esc) 45	NR (esc) 320	NR NR 2.8	NR NR 1.9	0.9	NR	NR	
Thiazolidinedione + Metformin vs. Second Generation Sulfonylurea + Metformin											
Derosa, 2005 ⁷²	kg	Rosiglitazone + metformin + diet + exercise + behavioral therapy, 48	Metformin + glimepiride + diet + exercise + behavioral therapy, 47	4 (fixed) 1500 (fixed)	1500 (fixed) 2 (fixed)	74.2 (3.6) 68.3 (3) -5.9	75.6 (4.2) 71.1 (3.2) -4.5	-1.4	<0.01 vs. baseline	<0.05 vs. baseline	

Appendix F: Evidence Table 7. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: weight

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Garber, 2006 ⁷¹	kg	Rosiglitazone + metformin + diet, 155	Metformin + glibenclamide + diet, 159	4 (esc) 8 1500-2000 (esc) 2000	1000 (esc) 2000 5 (esc) 10	94 95.4 1.4	92 95 3	-1.5		<0.001 vs. GP1	
Thiazolidinedione vs. Meglitinide											
Raskin, 2004 ⁷⁴	kg	Rosiglitazone, 37	Repaglinide, 38	2 bid (esc) 4 bid	0.5 tid if HbA1c≤8%, 1 tid if HbA1c>8% (esc) 4 tid	NR NR 2.3	NR NR 1.6	0.7	NR	NR	
Jovanovic, 2004 ⁷³	kg	Pioglitazone	Repaglinide	30 (fixed)	0.5 tid if HbA1c≤8%, 1 tid if HbA1c>8% (esc) 4 tid	NR NR 2	NR NR 0.3	1.7	<0.05 vs. baseline	NR	
Other Thiazolidinedione Comparisons											
Goke, 2002 ⁷⁵	kg	Pioglitazone, 129	Acarbose, 136	45 (fixed)	50 (esc) 100 tid	NR NR 1.23 (5.42)	NR NR -2.09 (3.58)	3.3		<0.001 vs. GP1	
German Pioglitazone Study Group											
McCluskey, 2004 ⁷⁶	kg	Rosiglitazone + placebo, 15	Rosiglitazone + glimepiride, 24	4 or 8 (fixed)	4 or 8 fixed; 2 (esc) 8	99.4 (SE 5.1) 101.8 2.4	100.5 (SE 4) 105.6 5.1	-2.7	NSG vs. GP2		
Metformin vs. Second Generation Sulfonylurea											
Garber, 2002 ⁷⁹	kg	Metformin, 161	Glyburide (Micronase), 161	500 (esc) 2000	2.5 (esc) 10	NR NR -0.6	NR NR 1.7	-2.3	<0.05 vs. baseline		

Appendix F: Evidence Table 7. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: weight

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Garber, 2003 ⁸⁰	kg	Metformin, 164	Glyburide (no trade drug specified), 151	500 (esc) 2000	2.5 (esc) 10	92.8 (15.6) 91.7 -1.1	91 (16.0) 93 2	-3.1	<0.001 vs. baseline	NSG vs. baseline	
Blonde, 2002 ⁸¹	kg	Metformin, 153	Glyburide (no trade drug specified), 164	500 (esc) 2000	10 bid (fixed)	89.5 (16.9) 87.5 -2	88 (15.9) 88.5 0.5	-2.5	NR	NR	
Campbell, 1994 ⁸³	kg	Metformin, 24	Glipizide, 24	500 bid (esc) 3000	5 (esc) 30	78.2 (15.7) 76.23 -1.97	82.2 (16.8) 84.8 2.67	-4.57	<0.001 vs. GP2		
Goldstein, 2003 ⁸²	kg	Metformin, 75	Glipizide, 83	500 (esc) 2000	15 bid (fixed)	94.2 (16.7) 91.5 -2.7 (SE 0.3)	90 (17.4) 89.6 -0.4 (SE 0.3)	-2.3	NR	NR	
Marre, 2002 ⁸⁴	kg	Metformin, 104	Glibenclamide, 103	500 (esc) 2000	5 (esc) 20	84.9 (17.6) 84.1 -0.8	82.5 (15.4) 83.4 0.9	-1.7	NR	NR	
Amador- Licona, 2000 ⁸⁵	kg	Metformin, 28	Glibenclamide, 23	850 (esc) NR	5 (esc) NR	70.7 (14.8) 69.6 (14.3) -0.9	73.2 (11.8) 74.1 (12.6) 0.9	-1.7	0.07 vs. baseline	0.1 vs. baseline	
Noury, 1991 ⁸⁶	kg	Metformin, 30	Gliclazide, 27	1700 (fixed)	80 (esc) 240	80.4 (14.4) 79.5 (14.5) -0.9	79 (16.2) 79 (15.4) 0	-0.9	<0.03 vs. baseline NSG vs. GP2	NSG vs. baseline	

Appendix F: Evidence Table 7. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: weight

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Rama- chandran, 2004 ⁵⁵	kg	Metformin + diet, 21	Glimepiride + diet, 18	250 (esc) 850	1 (esc) 2	67.7 (11.5) 67 (11.4) -0.7	65.7 (9.1) 67.5 (9.2) 1.8	-2.5	NR	<0.05 vs. baseline	
Hermann, 1994 ⁸⁷	kg	Metformin + diet, 19	Glyburide + diet, 19	1000 (esc) 3000	3.5 (esc) 10.5	78.6 (SE 2.9) 78.8 (SE 2.9) -0.8 (SE 0.5)	82.6 (SE 2.7) 86.2 (SE 3.3) 2.8 (SE 0.7)	-3.6	>0.1 vs. baseline	0.001 vs. baseline	
Hermann, 1991 ⁹⁴	kg	Metformin + diet, 16	Glibenclamide + diet, 17	1000 (esc) 3000	3.5 (esc) 10.5	76.5 (11.5) 76.1 (11.1) -0.4	84.1 (13.2) 87.4 (14.8) 3.3	3.7	NSG vs. baseline	<0.01 vs. baseline	
1995 ⁹² UKPDS, 3 year f/u of obese patients	kg	Metformin + diet, 262	Glibenclamide + diet, 472	NR (esc) 850 tid	NR (esc) 500 of chlorpropa- mide or 10 bid of glibencla- mide	88 (14.7) 87 -1	86 (14.7) 87 1	-2	NR	NR	
Turner, 1998 ⁹³ UKPDS, 6 year f/u of primary diet failure group	kg	Metformin + diet, 49	Glyburide (Diabeta) or chlorpropa-mide + diet, 231	NR (esc) 2550	NR (esc) 500 of chlorpropa- mide or 20 of glyburide	NR NR -1.3 (SE 0.2)	NR NR 3.7 (-0.5)	-5	NSG vs. baseline	NSG vs. baseline	

Appendix F: Evidence Table 7. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: weight

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2	Other
1998 ¹⁵ UKPDS, 10 year f/u of obese patients for metformin and obese and non-obese patients for glibenclamide	kg	Metformin, 181	Glibenclamide, 148	850 (esc) 2550	NR	87 (SE 17) 88.25 1.25*	NR NR 3.4*	-2	NR	NR	
DeFronzo, 1995 ⁸⁸	kg	Metformin + placebo, 210	Glyburide (no trade drug specified) + placebo, 209	500 (esc) 2500	5 bid (esc) 10 bid	92.6 (14.5) 87.8 -3.8 (SE 0.2)	NR NR -0.3 (SE 0.2)	-3.5	<0.001 vs. baseline	NSG vs. baseline	
Charpentier, 2001 ⁸⁹	kg	Metformin + placebo, 75	Glimepiride + placebo, 150	850 tid (fixed)	1 (esc) 6	82.2 (range 53-115) 81.46 -0.74 (2.58)	81 (range 48-135) 81.78 0.78 (2.98)	-1.52	NR	NR	
Metformin vs. Meglitinide											
Derosa, 2003 ⁹⁷	kg	Metformin + diet + exercise, 56	Repaglinide + diet + exercise, 56	500 bid (esc) 2500	0.5 bid (esc) 4	72.3 (7.1) 70.3 -2 (-6, 4 [†])	70.0 (6.5) 69.6 -0.4 (-0.8, 0.28 [†])	-1.6	0.14 vs. baseline NSG vs. GP2	>0.2 vs. baseline	
Metformin vs. Alpha-Glucosidase Inhibitor											
Willms, 1999 ⁹⁹	kg	Metformin, 27	Acarbose, 31	850 bid (fixed)	100 tid (fixed)	88.6 (17.7) 87.0 -1.6 (SE 0.89)	86.1 (15.4) 83.2 -2.9 (SE 0.72)	1.3	NSG vs. GP2		

Appendix F: Evidence Table 7. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: weight

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2	Other
Metformin vs. Metformin + Thiazolidinedione											
Bailey, 2005 ¹⁰¹	kg	Metformin, 272	Rosiglitazone + metformin, 279	2500 (esc) 3000	4 (esc) 8 2000 (fixed)	89.5 (14.4) 88.6 -0.9 (SE 0.26)	90.9 (15.6) 92.2 1.3 (SE 0.22)	-2.2	NR	NR	
Fonseca, 2000 ¹⁰³	kg	Metformin + placebo, 113	Rosiglitazone + metformin, 116	2500 (fixed)	4 (fixed) 2500 (fixed)	NR NR -1.2	NR NR 0.7	-1.9		0.0001 vs. GP1	
Fonseca, 2000 ¹⁰³	kg	Metformin + placebo, 113	Rosiglitazone + metformin, 110	2500 (fixed)	8 (fixed) 2500 (fixed)	NR NR -1.2	NR NR 1.9	-3.1		0.0001 vs. GP1	
Metformin vs. Metformin + Second Generation Sulfonylurea											
Garber, 2002 ⁷⁹	kg	Metformin, 161	Metformin + glyburide (Micronase), 165	500 (esc) 2000	500 (esc) 2000 2.5 (esc) 10	88.6 (14.9) 88 -0.6	NR NR 1.9	2.5		<0.05 vs. baseline	
Garber, 2002 ⁷⁹	kg	Metformin, 161	Metformin + glyburide (Micronase), 158	500 (esc) 2000	250 (esc) 1000 1.25 (esc) 5	NR NR -0.6	NR NR 1.4	-2		<0.05 vs. baseline	
Garber, 2003 ⁸⁰	kg	Metformin, 164	Metformin + glyburide (no trade drug specified), 171	500 (esc) 2000	250 (esc) 1000 1.25 (esc) 5	92.8 (15.6) 91.7 -1.1	91.9 (17.4) 93.5 1.6	-2.7	<0.001 vs. baseline	NSG vs. baseline	

Appendix F: Evidence Table 7. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: weight

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Goldstein, 2003 ⁸²	kg	Metformin, 75	Metformin + glipizide, 81	500 (esc) 2000	500 (esc) 2000 5 (esc) 20	94.2 (16.7) 91.5 -2.7 (SE 0.3)	95.1 (17.8) 94.8 -0.3 (SE 0.3)	-2.4	<0.001 vs. GP2		
Marre, 2002 ⁸⁴	kg	Metformin, 104	Metformin + glibenclamide, 101	500 (esc) 2000	500 (esc) 2000 2.5 (esc) 10	84.9 (17.6) 84.1 -0.8	84.7 (15.1) 85.3 0.6	-1.4	NR	NR	
Marre, 2002 ⁸⁴	kg	Metformin, 104	Metformin + glibenclamide, 103	500 (esc) 2000	500 (esc) 2000 5 (esc) 20	84.9 (17.6) 84.1 -0.8	83.1 (13.3) 84.1 1	-1.8	NR	NR	
Hermann, 1994 ⁸⁷	kg	Metformin + diet, 19	Metformin + glyburide + diet, 46	1000 (esc) 3000	2000 (esc) 3000 7 (esc) 14.0	78.6 (SE 2.9) 78.8 (SE 2.9) -0.2 (SE 0.5)	80.2 (SE 2.4) 81 (SE 2.5) 0.7 (SE 0.4)	-0.9	>0.1 vs. baseline	>0.1 vs. baseline	
DeFronzo, 1995 ⁸⁸	kg	Metformin + placebo, 210	Metformin + glyburide (no trade drug specified), 213	500 (esc) 2500	500 (esc) 2500 10 (esc) 20	NR NR -3.8 (SE 0.2)	NR NR 0.4 (SE 0.2)	-4.2	<0.001 vs. baseline	NSG vs. baseline	
Charpentier, 2001 ⁸⁹	kg	Metformin + placebo, 75	Metformin + glimepiride, 147	850 tid (fixed)	850 tid (fixed) 1 (esc) 6	82.2 (range 53-115) 81.46 -0.74 (2.58)	81.2 (range 52.6-116) 81.8 0.6 (2.86)	-1.34	NR	NR	

Appendix F: Evidence Table 7. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: weight

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Feinglos, 2005 ¹⁰⁴	kg	Metformin + placebo, 56	Metformin + glipizide, 56	at least 1000 (fixed)	at least 1000 (fixed) 2.5 (fixed)	90.8 (18.4) 89.1 -1.7	90 (18.7) 90.4 0.4	-2.1	< 0.0001 vs. GP2		
Hermann, 1991 ⁹⁴	kg	Metformin + diet, 16	Metformin + glibenclamide + diet, 12	1000 (esc) 3000	3000 (fixed) 3.5 (esc) 14	76.5 (11.5) 76.1 (11.1) -0.4	87.3 (15.6) 87.3 (15.9) 0	-0.4	NSG vs. baseline	NSG vs. baseline	
Hermann, 1991 ⁹⁴	kg	Metformin + diet, 16	Metformin + glibenclamide + diet, 11	1000 (esc) 3000	1000 (esc) 3000 10.5 (esc) 14	76.5 (11.5) 76.1 (11.1) -0.4	74.4 (11.4) 76 (11.8) +1.6	-2	NSG vs. baseline	<0.001 vs. baseline	
Second Generation Sulfonylurea vs. Second Generation Sulfonylurea											
Kilo, 1988 ¹⁴⁷	kg	Glyburide (no trade drug specified), 47	Glipizide, 52	1.25, 2.5, or 5 (esc) 20	5 or 10 (esc) 40	NR NR NR	NR NR NR	NR	NSG vs. GP2		
Inukai, 2005 ¹¹¹	kg	Glimepiride, 120	Glibenclamide + gliclazide, 52	1 or 2 (esc) 6	2.5 (fixed) 40 (fixed)	62.2 (12.6) 62.2 (12.3) 0	62.9 (13.4) 63.4 (13.1) 0.5	-1.17	NR	NR	
Harrower, 1985 ¹¹³	kg	Glipizide, 20	Glibenclamide, 19	2.5 (esc) 20	2.5 (esc) 30	64 (15) 64 (15) 0.86 (0.91)	57 (26) 59 (26) 2.03 (0.85)	-1.17	NSG vs. baseline	<0.05 vs. baseline	

Appendix F: Evidence Table 7. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: weight

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Harrower, 1985 ¹¹³	kg	Glipizide, 2	Gliclazide, 20	2.5 (esc) 20	20 (esc) 320	64 (15) 64 (15) 0.86 (0.91)	65 (13) 65 (13) 0.18 (1.04)	0.68	NSG vs. baseline	NSG vs. baseline	
Harrower, 1985 ¹¹³	kg	Glibenclamide, 19	Gliclazide, 20	2.5 (esc) 30	20 (esc) 320	57 (26) 59 (26) 2.03 (0.85)	65 (13) 65 (13) 0.18 (1.04)	1.85	<0.05 vs. baseline	NSG vs. baseline	
Schern-thaner, 2004 ¹⁰⁶	kg	Glimepiride + existing medications + diet, 440	Gliclazide + existing medications + diet, 405	1 (esc) 6	30 (esc) 120	83.7 84.3 0.6	83.1 83.6 0.5	0.1	NSG vs. baseline	NSG vs. baseline	
Second Generation Sulfonylurea vs. Meglitinide											
Wolffen-buttel, 1999 ¹¹⁷	kg	Glyburide (no trade drug specified) + placebo, 109	Repaglinide, 211	1.75 (esc) 10.5	1.5 (esc) 12	81.3 (12.2) 82 (11.9) 0.7	81.5 (13.4) 81.5 (13.5) 0	0.7	NSG vs. baseline	NSG vs. baseline	
Marbury, 1999 ¹¹⁶	kg	Glyburide (no trade drug specified) + placebo, 216	Repaglinide, 115	2.5 (esc) 15	0.5 (esc) 12	NR NR 0.05 (SE 0.5)	NR NR -0.22 (SE 0.5)	0.27	NSG vs. GP2		
Derosa, 2003 ¹¹⁸	kg	Glimepiride + placebo, 62	Repaglinide + placebo, 62	1 (esc) 3 mean final dose	1 (esc) 2.5 mean final dose	77.1 (5.9) 76.6 (5.3) -0.5	76.4 (5.2) 76.5 (5.3) 0.1	-0.6	NSG vs. GP2		

Appendix F: Evidence Table 7. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: weight

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2	Other
Wolffen-buttel, 1993 ¹²⁰	kg	Glibenclamide, 15	Repaglinide, 27	5 (esc) 15	0.5 (esc) 4	70.9 (10.8) 70.5 (10.2) -0.4	74 (9.6) 72.3 (9.4) -1.7	1.3	NSG vs. baseline	<0.05 vs. baseline	
Landgraf, 1999 ¹²¹	kg	Glibenclamide + placebo, 100	Repaglinide, 94	1.75, 3.5, 7.0, or 10.5 (esc) 10.5	0.5, 1.0, 2.0, or 4.0 tid (esc) 4 tid	78.9 (12.8) 77.5 -1.4	79.6 (10.3) 78.9 -0.7	-0.7	NSG vs. baseline and GP2	NSG vs. baseline	
Second Generation Sulfonylurea vs. Second Generation Sulfonylurea + Thiazolidinedione											
Rosenstock, 2006 ¹²⁴	kg	Glipizide + placebo, 57	Rosiglitazone + glipizide, 90	10 (esc) 20	4 (fixed) 10 (esc) 20	NR NR -1.2	NR NR 4.3	-5.5	NR	NR	
Baksi, 2004 ¹²⁶	kg	Gliclazide	Rosiglitazone + gliclazide	160 (esc) 320	160 (fixed) 4 bid (fixed)	NR NR NR	NR NR NR	-3.4		0.0001 vs. GP1	
Second Generation Sulfonylurea vs. Metformin + Second Generation Sulfonylurea											
Garber, 2003 ⁸⁰	kg	Glyburide (no trade drug specified), 151	Metformin + glyburide (no trade drug specified), 171	2.5 (esc) 10	250 (esc) 1000 1.25 (esc) 5	91 (16) 93 2	91.1 (17.4) 92.7 1.6	0.4	NSG vs. baseline	NSG vs. baseline	
Erle, 1999 ¹²⁷	kg	Glyburide (no trade drug specified), 18	Metformin + glyburide (no trade drug specified), 15	5 (esc) 15	800 (esc) 1600 5 (esc) 10	85.2 (12.5) 85.2 (13.3) 0	85.5 (13.2) 85.3 (13.3) -0.2	0.2	NSG vs. baseline	NSG vs. baseline	

Appendix F: Evidence Table 7. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: weight

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Blonde, 2002 ⁸¹	kg	Glyburide (no trade drug specified), 164	Metformin + glyburide (no trade drug specified), 160	10 bid (fixed)	500 (esc) 2000 2.5 (esc) 10	88 (15.9) NR <1	89.4 (17.5) NR <1	NR	NR	NR	
Blonde, 2002 ⁸¹	kg	Glyburide (no trade drug specified), 164	Metformin + glyburide (no trade drug specified), 162	10 bid (fixed)	500 (esc) 2000 5 (esc) 20	88 (15.9) NR <1	89.6 (16.8) NR <1	NR	NR	NR	
Garber, 2002 ⁷⁹	kg	Glyburide (Micronase), 161	Metformin + glyburide (Micronase), 158	2.5 (esc) 10	250 (esc) 1000 1.25 (esc) 5	NR NR 1.7	NR NR 1.4	0.3	<0.05 vs. baseline	<0.05 vs. baseline	
Garber, 2002 ⁷⁹	kg	Glyburide (Micronase), 161	Metformin + glyburide (Micronase), 165	2.5 (esc) 10	500 (esc) 2000 2.5 (esc) 10	NR NR 1.7	NR NR 1.9	-0.2	<0.05 vs. baseline	<0.05 vs. baseline	
DeFronzo, 1995 ⁸⁸	kg	Glyburide (no trade drug specified) + placebo, 209	Metformin + glyburide (no trade drug specified), 213	5 bid (esc) 10 bid	500 (esc) 2500 10 (esc) 20	92.6 92.3 -0.3 (SE 0.2)	92.1 91.7 -0.4 (SE 0.2)	-0.7	NSG vs. baseline	<0.001 vs. baseline	
Charpentier, 2001 ⁸⁹	kg	Glimepiride + placebo, 150	Metformin + glimepiride, 147	1 (esc) 6	850 tid (fixed) 1 (esc) 6	81 (range 48- 135) 81.78 0.78 (2.98)	81.2 (range 52.6-116) 81.8 0.6 (2.86)	0.18	NR	NR	

Appendix F: Evidence Table 7. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: weight

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Goldstein, 2003 ⁸²	kg	Glipizide, 83	Metformin + glipizide, 81	30 (fixed)	500 (esc) 2000 5 (esc) 20	90 (17.8) 89.6 -0.4 (SE 0.3)	95.1 (17.8) 94.8 -0.3 (SE 0.3)	-0.1	NR	NR	
Marre, 2002 ⁸⁴	kg	Glibenclamide, 103	Metformin + glibenclamide, 103	5 (esc) 20	500 (esc) 2000 5 (esc) 20	82.5 (15.4) 83.4 0.9	83.1 (13.3) 84.1 1	-0.1	NR	NR	
Marre, 2002 ⁸⁴	kg	Glibenclamide, 103	Metformin + glibenclamide, 101	5 (esc) 20	500 (esc) 2000 2.5 (esc) 10	82.5 (15.4) 83.4 0.9	84.7 (15.1) 85.3 0.6	0.3	NR	NR	
Hermann, 1994 ⁸⁷	kg	Glyburide + diet, 19	Metformin + glyburide + diet, 46	3.5 (esc) 10.5	500 (esc) 1500 1.75 (esc) 5.25	82.6 (SE 2.7) 86.2 (SE 3.3) 2.8 (SE 0.7)	80.2 (SE 2.4) 81 (SE 2.5) 0.7 (SE 0.4)	2.1	0.001 vs. baseline 0.008 vs. GP2	NSG vs. baseline	
Hermann, 1991 ⁹⁴	kg	Glibenclamide + diet, 17	Metformin + glibenclamide + diet, 12	3.5 (esc) 10.5	3000 (fixed) 3.5 (esc) 14.0	84.1 (13.2) 87.4 (14.8) 3.3	87.3 (15.6) 87.3 (15.9) 0	3.3	<0.01 vs. baseline		
Hermann, 1991 ⁹⁴	kg	Glibenclamide + diet, 17	Metformin + glibenclamide + diet, 11	3.5 (esc) 10.5	1000 (esc) 3000 10.5 (esc) 14.0	84.1 (13.2) 87.4 (14.8) 3.3	74.4 (11.4) 76 (11.8) 1.6	1.9	<0.01 vs. baseline	<0.001 vs. baseline	

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Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2	Other
1998 ¹²⁸ UKPDS, 3 year f/u	kg	Glibenclamide + diet, 300	Metformin + glibenclamide + diet, 291	10 (fixed)	500 (esc) 2500 10 (fixed)	NR NR -0.78 (-1.26)	NR NR -1.08 (-1.55)	0.3	0.0015 vs. baseline NSG vs. GP2	<0.00001 vs. baseline	
Gregorio, 1999 ¹²⁹	kg	Metformin + glibenclamide + gliclazide, 89	Glibenclamide + gliclazide, 85	10 (esc) 15 120 (esc) 240	850 (esc) 1700 NR (fixed) NR (fixed)	76.4 (SE 1.41) 76 (SE 1.51) -0.4	76.6 (SE 1.73) 76.7 (SE 1.69) 0.1	-0.5	NR	NR	
Second Generation Sulfonylurea vs. Alpha-Glucosidase Inhibitor											
Feinbock, 2003 ¹³⁰	kg	Glimepiride, 108	Acarbose, 103	1 (esc) 6	50 tid (esc) 200 tid	85 (12.8) 84.6 -0.4 (5.2)	83 (12.5) 81.1 -1.9 (3.9)	1.5	NSG vs. baseline	0.001 vs. baseline	
Repaglinide vs. Nateglinide											
Rosenstock, 2004 ¹³¹	kg	Repaglinide	Nateglinide	5 (esc) 16	60 (esc) 360	NR NR 1.8	NR NR 0.7	1.1	0.04 vs. GP2		
Pioglitazone vs. Placebo											
Rosenblatt, 2001 ¹⁶²	kg	Pioglitazone, 101	Placebo, 96	30 (NR)	NA	89.8 (18) 91.15 1.35	87.2 (18.4) 86.33 -1.87	3.22	<0.0001 vs. baseline and vs. placebo	<0.0001 vs. baseline	
Herz, 2003 ¹⁶³	kg	Pioglitazone, 95	Placebo, 97	30 (fixed)	NA	86.6 (15.9) 86.95 0.35	86.3 (17.4) 84.72 -1.58	1.93	<0.001 vs. GP2		

Appendix F: Evidence Table 7. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: weight

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Herz, 2003 ¹⁶³	kg	Pioglitazone, 96	Placebo, 97	45 (fixed)	NA	84.1 (16.8) 84.92 0.82	86.3 (17.4) 84.72 -1.58	2.4	<0.001 vs. GP2		
Aronoff, 2000 ¹⁶⁵	kg	Pioglitazone, 81	Placebo, 79	7.5 (fixed)	NA	93.5 (SE 1.59) 92.9 -0.6 (SE 0.9)	90.4 (SE 1.47) 89.1 -1.3 (SE 0.36)	0.7	NSG vs. GP2		
Aronoff, 2000 ¹⁶⁵	kg	Pioglitazone, 79	Placebo, 79	15 (fixed)	NA	91.2 (SE 1.8) 92.5 1.3 (SE 0.33)	90.4 (SE 1.47) 89.1 -1.3 (SE 0.36)	2.6	NSG vs. GP2		
Aronoff, 2000 ¹⁶⁵	kg	Pioglitazone, 87	Placebo, 79	30 (fixed)	NA	90.3 (SE 0.38) 91.6 1.3 (SE 0.38)	90.4 (SE 1.47) 89.1 -1.3 (SE 0.36)	2.6	NSG vs. GP2		
Aronoff, 2000 ¹⁶⁵	kg	Pioglitazone, 79	Placebo, 79	45 (fixed)	NA	90.8 (SE 0.39) 93.6 2.8 (SE 0.39)	90.4 (SE 1.47) 89.1 -1.3 (SE 0.36)	4.1	NSG vs. GP2		
Smith, 2005 ¹⁶¹	kg	Pioglitazone + diet, 21	Placebo + diet, 21	30 (esc) 45	NA	93.48 (18.48) 97.36 3.88 (3.11)	92.13 (14.65) 91.34 -0.79 (3.36)	4.67	0.0004 vs. GP2		
Tseng, 2005 ¹⁴⁰	kg	Pioglitazone + unspecified sulfonylurea, 23	Unspecified sulfonylurea + placebo, 25	30 (fixed) NR (NR)	NR (NR)	61.3 (10.9) 62.3 (11.4) 1	NR NR NR	NR	<0.001 v s. baseline	NSG vs. baseline	

Appendix F: Evidence Table 7. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: weight

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Kipnes, 2001 ¹⁶⁶	kg	Pioglitazone + existing unspecified sulfonylurea, 189	Existing unspecified sulfonylurea + placebo, 187	30 (fixed) NR (fixed)	NR (fixed)	NR NR 2.9	NR NR -0.8	3.7	<0.05 vs. GP1		
Kipnes, 2001 ¹⁶⁶	kg	Pioglitazone + existing unspecified sulfonylurea, 184	Existing unspecified sulfonylurea + placebo, 187	15 (fixed) NR (fixed)	NR (fixed)	NR NR 1.9	NR NR -0.8	2.7	<0.05 vs. GP1		
Einhorn, 2000 ¹⁶⁰	kg	Pioglitazone + existing metformin + diet, 168	Placebo + existing metformin + diet, 160	30 (fixed) NR (NR)	NR (NR)	NR NR 0.95	NR NR -1.36	2.31	NR	NR	
Rosiglitazone vs. Placebo											
Virtanen, 2003 ¹⁴³	kg	Rosiglitazone + diet, 14	Placebo + diet, 14	2 bid (esc) 8 bid	NA	83.7 (7.9) 84.3 (3.5) 0.6	88.3 (9.7) 88.4 (9.7) 0.1	0.5	NSG vs. GP2		
Lebovitz, 2001 ¹⁶⁹	kg	Rosiglitazone, 166	Placebo, 158	2 bid (fixed)	NA	NR NR 1.6 (3.1)	NR NR -1 (2.9)	2.6	<0.05 vs. baseline and vs. GP2		
Lebovitz, 2001 ¹⁶⁹	kg	Rosiglitazone, 169	Placebo, 158	4 bid (fixed)	NA	NR NR 3.5 (3.6)	NR NR -1 (2.9)	4.5	<0.05 vs. baseline and vs. GP2		

Appendix F: Evidence Table 7. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: weight

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Natali, 2004 ¹⁴⁴	kg	Rosiglitazone, 24	Placebo, 22	8 (fixed)	NA	80.4 (SEM 10.1) 80.9 0.5 (0.5)	86.9 (SEM 10.5) 86.6 -0.3 (0.8)	1	NSG vs. GP2		
Barnett, 2003 ¹⁷²	kg	Rosiglitazone + unspecified sulfonylurea, 84	Unspecified sulfonylurea + placebo, 87	4 bid (fixed) NR (NR)	NR (NR)	NR NR 3.9 (3.16)	NR NR -0.1	4	<0.001 vs. GP2		
Metformin vs. Placebo											
DeFronzo, 1995 ⁸⁸	kg	Metformin, 143	Placebo, 146	850 (esc) 850 tid	NA	92.6 92 -0.6 (SE 0.3)	NR NR -1.1 (SE 0.2)	-0.5	NSG vs. GP2		
Garber, 2002 ⁷⁹	kg	Metformin, 161	Placebo, 161	500 (esc) 2000	NA	87 (14.9) 86.4 -0.6	NR NR -0.7	0.1	NSG vs. GP2		
Willms, 1999 ⁹⁹	kg	Metformin, 27	Placebo, 29	850 bid (fixed)	NA	88.6 (17.7) 87 -1.6 (SE 0.89)	90.2 (15.4) 87.85 -2.4 (SE 0.99)	0.8	NR	NR	
Natali, 2004 ¹⁴⁴	kg	Metformin	Placebo	1500 (fixed)	NA	77.3 (SEM 12.5) 76.7 -0.6 (0.4)	86.9 (SEM 10.5) 86.6 -0.3 (0.8)	-0.3	NSG vs. baseline	NSG vs. baseline	

Appendix F: Evidence Table 7. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: weight

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Dornan, 1991 ²⁶⁰	kg	Metformin, 30	Placebo, 30	500 (esc) 1000 tid	NA	84.6 (14.8) 84.6 (SE 2.6) 0	79.5 (13.7) 78.6 (SE 2.4) -0.9	0.9	NSG vs. GP2		
Teupe, 1991 ¹⁵⁵	kg	Metformin + diet, 25	Diet, 29	NR (esc) 1700	NA	87.7 (11.9) 85.1 (10) -2.6	83.1 (11.7) 81 (11.7) -2.1	-0.5	NR	NR	
1995 ⁹² UKPDS, 3 year f/u of obese patients in primary diet failure and main random- ization groups	kg	Metformin + diet, 262	Diet, 291	NR (esc) 850 tid	NA	88* 87.4 (85.3, 89.5 [‡]) -0.6*	87* 86.2 (84.4, 88 [‡]) -0.8*	0.2	NR	NR	
1998 ¹⁵ UKPDS, 10 year f/u of obese patients for metformin and obese and non- obese patients for glibencla- mide	kg	Metformin, 181	Diet, 200	850 (esc) 2550	NA	87 (17) 88.25 1.25*	NR NR 1.25*	0	NR	NR	

Appendix F: Evidence Table 7. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: weight

Author, year						GP1 BL mean (SD)	GP2 BL mean (SD)				
Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 final mean (SD) Mean diff from BL1	GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Hallsten, 2002 ³²⁴ Virtanen, 2003 ¹⁴³	kg	Metformin + diet, 13	Placebo + diet, 14	500 bid (esc) 1000 bid	NA	88.8 (SE 3.1) 86.8 (SE 3) -2	88.3 (SE 2.6) 88.4 (SE 2.6) 0.1	-2.1	<0.05 vs. GP2		
Del Prato, 2003 ¹⁴⁹	kg	Metformin + placebo, 284	Placebo, 138	850 (esc) 2550	NA	82.6 (14.6) 81.9 (15) -0.7	84.5 (14.8) 83.5 (14.5) -1	0.3	NR	NR	
Lee, 1998 ²⁵⁹	kg	Metformin + placebo + diet, 24	Placebo + diet, 24	850 (fixed)	NA	112.3 (SE 6.9) 103.5 (SE 6.6) -8.8	109.8 (SE 3.4) 108.8 (SE 3.4) -1	-7.8	<0.001 vs. GP2		
Second Generation Sulfonylurea vs. Placebo											
Simonson, 1997 ¹³⁶ Trial 1	kg	Glipizide GITS	Placebo	5, 20, 40 or 60 (fixed)	NA	NR NR -0.32 (0.27)	NR NR -3.58 (0.59)	3.27	NSG vs. baseline <0.001 vs. GP2		
Simonson, 1997 ¹³⁶ Trial 2	kg	Glipizide GITS	Placebo	5, 10, 15, or 20 (fixed)	NA	NR NR 0.14 (0.18)	NR NR -3.13 (0.36)	2.99	NSG vs. baseline <0.001 vs. GP2		
Cefalu, 1998 ²⁶¹	kg	Glipizide GITS, 20	Placebo, 20	5 (esc) 10	NA	82.7 (16.2) 82.7 0	89.5 (14.2) 88.6 -0.9	0.9	NSG vs. baseline	NSG vs. baseline	

Appendix F: Evidence Table 7. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: weight

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Garber, 2002 ⁷⁹	kg	Glyburide (Micronase), 161	Placebo, 161	2.5 (esc) 10	NA	87.2 (15.3) 88.9 1.7	86.2 (16.6) 85.5 -0.7	2.4	<0.05 vs. baseline		
Luis Bautista, 2003 ¹⁹³	kg	Glimepiride + diet + exercise, 48	Placebo + diet + exercise, 22	1 (esc) 4	NA	83.3 (SE 17) 85.5 2.3 (2.6)	76.3 (SE 18.5) 74.2 -2.1	4.4 (SE 1.1)	<0.001 vs. GP2		
Vray, 1995 ¹³⁷	kg	Glibenclamide, 51	Traditional Chinese treatment, 46	2.5 tid (fixed)	Admin-istered in 7 capsules (fixed)	NR NR 0.67 (SE 0.4)	NR NR -0.54 (SE 0.3)	1.21	<0.001 vs. baseline	0.89 vs. baseline	
1998 ¹⁶ UKPDS, 10 year f/u	kg	Glibenclamide + diet, 615	Diet, 896	2.5 (esc) 20	NA	NR NR 4* (0.7)	NR NR 2.2*	1.8	<0.001 vs. GP2		
1995 ⁹² UKPDS, 3 year f/u of obese patients	kg	Glibenclamide + diet, 212	Diet, 291	NR (esc) 10 bid	NA	86 (14.7) 87 1	87* 86.2 (84.4, 88) -0.8	1.8			
1995 ⁹² UKPDS, 3 year f/u of non- obese patients	kg	Glibenclamide + diet, 472	Diet, 373	NR (esc) 10 bid	NA	69* 73* 4	68* 69* 1	3			

Appendix F: Evidence Table 7. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: weight

Author, year						GP1 BL mean (SD)	GP2 BL mean (SD)				
Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 final mean (SD) Mean diff from BL1	GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
1998 ¹⁵ UKPDS, 10 year f/u of obese	kg	Glibenclamide, 148	Diet, 200	NR	NA	86 (range 14- 16) 89.4 3.4*	87 (range 14- 16) 88.25 1.25*	2.15	NR	NR	
Meglitinide vs. Placebo											
Saloranta, 2002 ²⁴¹	kg	Nateglinide, 166	Placebo, 163	30 (fixed)	NA	NR NR 0.65	NR NR .31	0.34	NR	NR	
Moses, 2001 ²¹⁸	kg	Repaglinide, 260	Placebo, 134	0.5 (esc) 1 per meal	NA	84 (16.1) 84.35 0.35	86.6 (16.7) 87* 0.4	-0.05	NSG vs. baseline and vs. GP2		
Alpha-Glucosidase Inhibitor vs. Placebo											
Willms, 1999 ⁹⁹	kg	Acarbose, 31	Placebo, 29	100 tid (fixed)	NA	86.1 (15.4) 83.2 -2.9 (SE 0.72)	90.2 (15.4) 87.8 -2.4 (SE 0.99)	-0.5	NR	NR	
Rosen-baum, 2002 ¹⁵³	kg	Acarbose, 20	Placebo, 20	50 bid (esc) 100 tid	NA	75.1 (11.6) 73.1 (11.6) -2	80.2 (9.8) 79.3 (9.7) -0.9	-1.1	<0.01 vs. baseline	0.1 vs. baseline	
Hasche, 1999 ¹³⁸	kg	Acarbose + diet, 28	Placebo + diet, 32	50 bid (esc) 100 tid	NA	74.9 (8.7) 73.5 -1.4	74.5 (8.6) 73.2 -1.3	-0.1	NR	NR	
Metformin + Second Generation Sulfonylurea vs. Placebo											

Appendix F: Evidence Table 7. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: weight

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Garber, 2002 ^{†‡}	kg	Metformin + glyburide (Micronase), 165	Placebo, 161	500 (esc) 2000 2.5 (esc) 10	NA	NR NR 1.9	NR NR -0.7	2.6	<0.05 vs. GP2		
Garber, 2002 ^{†‡}	kg	Metformin + glyburide (Micronase), 158	Placebo, 161	250 (esc) 1000 1.25 (esc) 5	NA	NR NR 1.4	NR NR -0.7	2.1	<0.05 vs. GP2		

Comp = comparison; BL = baseline; GP = group; mg = milligrams; max = maximum; esc = escalated; diff = difference; kg = kilograms; NR = not reported; NSG = not significant; NA = not applicable; SD = standard deviation; SE = standard error; SEM = standard error of the mean; od = once daily; bid = twice daily; tid = three times daily; HbA1c = hemoglobin A1c; UKPDS = United Kingdom Prospective Diabetes Study; f/u = follow-up; GITS = gastrointestinal therapeutic system; vs = versus

* Number obtained from a figure

† 95% confidence interval

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Thiazolidinedione vs. Thiazolidinedione											

Appendix F: Evidence Table 8. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: body mass index

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2	Other
Derosa, 2005 ⁵³	kg/m ²	Rosiglitazone + glimepiride + diet + exercise, 42	Pioglitazone + glimepiride + diet + exercise, 45	4 (fixed) 4 (fixed)	15 (fixed) 4 (fixed)	24.3 (0.7) 25.8 (0.9) 1.5	24.4 (0.8) 25.6 (0.9) 1.2	0.3	<0.05 vs. baseline NSG vs. GP2	<0.05 vs. baseline	
Thiazolidinedione vs. Metformin											
Virtanen, 2003 ¹⁴³	kg/m ²	Rosiglitazone + diet, 14	Metformin + diet, 13	2 bid (esc) 4 bid	500 bid (esc) 1000 bid	29.1 (SE 1) 29.3 (SE 1.1) 0.2	29.9 (SE 1.1) 29.2 (SE 1.1) -0.7	0.9	NSG vs. baseline	NSG vs. baseline	
Lawrence, 2004 ⁵⁴	kg/m ²	Pioglitazone, 20	Metformin, 20	30 (esc) 45	500 bid (esc) 1000 tid	30.6 [#] (29.4-35.2) ^{##} 32.1 [#] (29.8-NR) ^{##} 1.5	29.2 [#] (28.1-31.6) ^{##} 28.6 [#] (27.3-NR) ^{##} -0.6	2.1	<0.05 vs. baseline	<0.05 vs. baseline	
Rama-chandran, 2004 ⁵⁵	kg/m ²	Pioglitazone + diet, 23	Metformin + diet, 21	15 (esc) 30	250 (esc) 850	25.5 (2.2) 25.1 (2) -0.4	25.7 (2.6) 25.5 (3) -0.2	-0.2	NR	NR	
Yama-nouchi, 2005 ⁵⁷	kg/m ²	Pioglitazone + diet + exercise, 38	Metformin + diet + exercise, 39	30 for women and 45 for men (fixed)	750 (fixed)	25.8 (4.2) 26.7 (3.9) 0.9	26.2 (3.8) 25.5 (4.2) -0.7	1.6	NSG vs. baseline	NSG vs. baseline	

Appendix F: Evidence Table 8. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: body mass index

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Thiazolidinedione vs. Second Generation Sulfonylurea											
Pfutzner, 2005 ⁶⁸ Langenfeld, 2005 ¹⁴⁶ Forst, 2005 ¹⁴⁵	kg/m ²	Pioglitazone, 89	Glimepiride, 84	45 (fixed)	1 (esc) 6	31.7 (5) 33.1 (5.1) 1.4	31.8 (4.3) 31.8 (4.1) 0	1.4		0.001 vs. GP1	
Lawrence, 2004 ⁵⁴	kg/m ²	Pioglitazone, 20	Gliclazide, 20	30 (esc) 45	80 od (esc) 160 bid	30.6 [#] (29.4- 35.2) ^{###} 32.1 [#] (29.8- NR) ^{###} 1.5	28.7 [#] (28.3- 34.4) ^{###} 30.6 [#] (28.0- NR) ^{###} 1.9	-0.4	<0.05 vs. baseline	<0.05 vs. baseline	
Yanagawa, 2004 ⁶²	kg/m ²	Pioglitazone, 19	Gliclazide, 21	NR	NR	24.6 (2) NR NR	24 (3.5) NR NR	NR		NSG vs. GP2	
Rama- chandran, 2004 ⁵⁵	kg/m ²	Pioglitazone + diet, 23	Glimepiride + diet, 18	15 (esc) 30	1 (esc) 2	25.5 (2.2) 25.1 (2) -0.4	24.6 (2.5) 25.3 (2.5) 0.7	-1.1	NR	NR	
Yama-nouchi, 2005 ⁵⁷	kg/m ²	Pioglitazone + diet + exercise, 38	Glimepiride + diet + exercise, 37	30 for women and 45 for men (fixed)	1.0 (esc) 2.0	25.8 (4.2) 26.7 (3.9) 0.9	25.6 (3.5) 25.4 (4) -0.2	1.1	NSG vs. baseline	NSG vs. baseline	

Appendix F: Evidence Table 8. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: body mass index

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2	Other
Thiazolidinedione + Metformin vs. Second Generation Sulfonylurea + Metformin											
Derosa, 2005 ⁷²	kg/m ²	Rosiglitazone + metformin + diet + exercise + behavioral therapy, 48	Metformin + glimepiride + diet + exercise + behavioral therapy, 47	4 (fixed) 1500 (fixed)	1500 (fixed) 2 (fixed)	26.6 (1.3) 24.5 (1.1) -2.1	26.8 (1.5) 25.2 (1.4) -1.6	-0.5	<0.01 vs. baseline	<0.05 vs. baseline	
Metformin vs. Second Generation Sulfonylurea											
Tosi, 2003 ⁵⁵	kg/m ²	Metformin, 19	Glibenclamide, 20	500 (esc) 3000	5 (esc) 15	NR NR -0.51 (0.83)	NR NR 0.27 (0.88)	-0.78	<0.02 vs. GP2		
Lawrence, 2004 ⁵⁴	kg/m ²	Metformin, 20	Gliclazide, 20	500 bid (esc) 1000 tid	80 (esc) 160 bid	29.2 [#] (28.1-31.6) ^{##} 28.6 [#] (27.3-NR) ^{##} -0.6	28.7 (28.3-34.4) [#] 30.6 [#] (28.0-NR) ^{##} 1.9	-2.5	<0.05 vs. baseline	<0.05 vs. baseline	
Rama-chandran, 2004 ⁵⁵	kg/m ²	Metformin + diet, 21	Glimepiride + diet, 18	250 (esc) 850	1 (esc) 2	25.7 (2.6) 25.5 (3) -0.2	24.6 (2.5) 25.3 (2.5) 0.7	-0.9	NR	<0.05 vs. baseline	
Charpentier, 2001 ⁸⁹	kg/m ²	Metformin + placebo, 75	Glimepiride + placebo, 150	850 tid (fixed)	1 (esc) 6	29.2 (range 20.1-39.9) 28.95 -0.25 (0.9)	29.3 (range 17.9-39.8) 29.58 0.28 (1.04)	-0.53	<0.001 vs. GP2		
Yama-nouchi, 2005 ⁵⁷	kg/m ²	Metformin + diet + exercise, 39	Glimepiride + diet + exercise, 37	750 (fixed)	1 (esc) 2	26.2 (3.8) 25.5 (4.2) -0.7	25.6 (3.5) 25.4 (4) -0.2	-0.5	NSG vs. baseline	NSG vs. baseline	

Appendix F: Evidence Table 8. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: body mass index

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2	Other
Derosa, 2004 ⁹⁰	kg/m ²	Metformin + placebo + diet + exercise, 75	Glimepiride + placebo + diet + exercise, 73	1000 (esc) 1000 tid	1 (esc) 2 bid	28.1 (1.5) 27.5 (0.9) -0.6 (-1.24, 0.33 [†])	27.6 (1.2) 26.9 (1) -0.7 (-1.35, 0.25 [†])	0.1	NSG vs. baseline	NSG vs. baseline	
Hermann, 1991 ⁹⁴	kg/m ²	Metformin + diet, 16	Glibenclamide + diet, 17	1000 (esc) 3000	3.5 (esc) 10.5	27 (3.0) 26.9 (2.8) -0.1	29.2 (4.3) 30.3 (4.8) 1.1	-1.2	NSG vs. baseline <0.001 vs. GP2	<0.001 vs. baseline	
Metformin vs. Meglitinide											
Derosa, 2003 ⁹⁷	kg/m ²	Metformin + diet + exercise, 56	Repaglinide + diet + exercise, 56	500 bid (esc) 2500	0.5 bid (esc) 4	24.7 (1.2) 24.1 -0.6 (-1.5, 1.2 [†])	25.2 (1.1) 25.1 -0.1 (-0.3, 0.19 [†])	-0.5	0.12 vs. baseline NSG vs. GP2	>0.2 vs. baseline	
Metformin vs. Metformin + Second Generation Sulfonylurea											
Tosi, 2003 ⁹⁶	kg/m ²	Metformin, 19	Metformin + glibenclamide, 41	500 (esc) 3000	400 (esc) 2400 2.5 (esc) 15	NR NR -0.51 (0.83)	NR NR 0.23 (1.10)	-0.74	<0.02 vs. GP2		
Charpentier, 2001 ⁸⁹	kg/m ²	Metformin + placebo, 75	Metformin + glimepiride, 147	850 tid (fixed)	850 tid (fixed) 1 (esc) 6	29.2 (range 20.1-39.9) 28.95 -0.25 (0.9)	29.5 (range 20.2-39.8) 29.71 0.21 (1.05)	-0.46	<0.002 vs. GP2		
Feinglos, 2005 ¹⁰⁴	kg/m ²	Metformin + placebo, 56	Metformin + glipizide, 56	at least 1000 (fixed)	at least 1000 (fixed) 2.5 (fixed)	32.1 (4.9) 31.5 -0.6	31.7 (4.4) 31.8 0.1	-0.7	< 0.0001 vs. GP2		

Appendix F: Evidence Table 8. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: body mass index

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2	Other
Hermann, 1991 ⁹⁴	kg/m ²	Metformin + diet, 16	Metformin + glibenclamide + diet, 11	1000 (esc) 3000	1000 (esc) 3000 10.5 (esc) 14	27 (3.0) 26.9 (2.8) -0.1	26.1 (3.6) 26.9 (3.8) 0.8	-0.9	NSG vs. baseline	<0.05 vs. baseline	
Hermann, 1991 ⁹⁴	kg/m ²	Metformin + diet, 16	Metformin + glibenclamide + diet, 12	1000 (esc) 3000	3000 (fixed) 3.5 (esc) 14	27 (3.0) 26.9 (2.8) -0.1	30.0 (6.5) 30.2 (6.5) 0.2	-0.3		NSG vs. baseline	
Second Generation Sulfonylurea vs. Meglitinide											
Derosa, 2003 ¹¹⁸	kg/m ²	Glimepiride + placebo, 62	Repaglinide + placebo, 62	1 (esc) 3 mean final dose	1 (esc) 2.5 mean final dose	26.4 (1) 25.9 (1.2) -0.5	26.1 (1.2) 26.2 (.8) 0.1	-0.6	NSG vs. GP2		
Second Generation Sulfonylurea vs. Second Generation Sulfonylurea + Thiazolidinedione											
Pfutzner, 2006 ¹²³	kg/m ²	Glimepiride + placebo	Rosiglitazone + glimepiride, 30	3 (fixed)	8 (fixed) 3 (fixed)	30 (3.4) 29.8 (3.4) -0.2	29.3 (4.8) 29.5 (4.8) 0.2	-0.4	NR	NR	
Pfutzner, 2006 ¹²³	kg/m ²	Glimepiride + placebo	Rosiglitazone + glimepiride, 30	3 (fixed)	4 (fixed) 3 (fixed)	30 (3.4) 29.8 (3.4) -0.2	27.7 (4.1) 27.7 (4.1) 0	-0.2	NR	NR	
Second Generation Sulfonylurea vs. Metformin + Second Generation Sulfonylurea											
Charpentier, 2001 ⁸⁹	kg/m ²	Glimepiride + placebo, 150	Metformin + glimepiride, 147	1 (esc) 6	850 tid (fixed) 1 (esc) 6	29.3 (range 17.9-39.8) 29.58 0.28 (1.04)	29.5 (range 20.2-39.8) 29.71 0.21 (1.05)	0.07	NSG vs. GP2		

Appendix F: Evidence Table 8. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: body mass index

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Tosi, 2003 ³⁵	kg/m ²	Glibenclamide, 20	Metformin + glibenclamide, 41	5 (esc) 15	400 (esc) 2400 2.5 (esc) 15	NR NR 0.27 (0.88)	NR NR 0.23 (1.10)	0.04	NR	NR	
Hermann, 1991 ⁹⁴	kg/m ²	Glibenclamide + diet, 17	Metformin + glibenclamide + diet, 11	3.5 (esc) 10.5	1000 (esc) 3000 10.5 (esc) 14.0	29.2 (4.3) 30.3 (4.8) 1.1	26.1 (3.6) 26.9 (3.8) 0.8	0.3	<0.001 vs. baseline	<0.05 vs. baseline	
Hermann, 1991 ⁹⁴	kg/m ²	Glibenclamide + diet, 17	Metformin + glibenclamide + diet, 12	3.5 (esc) 10.5	3000 (fixed) 3.5 (esc) 14.0	29.2 (4.3) 30.3 (4.8) 1.1	30 (6.5) 30.2 (6.5) 0.2	0.9	<0.001 vs. baseline	NSG vs. baseline	
Metformin vs. Placebo											
Rachmani, 2002 ¹⁵⁰	kg/m ²	Metformin continued + diet, 195	Metformin stopped + diet, 198	NR (NR)	NA	28.7 (SE 0.7) 29.1 0.4	28.4 (SE 0.6) 29.6 1.2	-0.8	NSG vs. baseline	<0.05 vs. baseline	
Manzella, 2004 ¹⁴⁸	kg/m ²	Metformin + diet, 60	Placebo + diet, 60	850 bid (fixed)	NA	29.5 (0.1) 29.1 (0.2) -0.4	29.2 (0.2) 29.5 (0.4) 0.3	-0.7	NSG vs. placebo		
Virtanen, 2003 ¹⁴³	kg/m ²	Metformin + diet, 13	Placebo + diet, 14	500 bid (esc) 1000 bid	NA	29.9 (SE 1.1) 29.2 (SE 1.1) -0.7	30.3 (SE 1.2) 30.3 (SE 1.2) 0	-0.7	<0.05 vs. GP2		

Appendix F: Evidence Table 8. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: body mass index

Author, year						GP1 BL mean (SD)	GP2 BL mean (SD)				
Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 final mean (SD) Mean diff from BL1	GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Del Prato, 2003 ¹⁴⁹	kg/m ²	Metformin + placebo, 279	Placebo, 138	850 (esc) 2550	NA	29.8 (4.2) 29.5 (4.3) -0.3	29.9 (3.9) 29.6 (4.0) -0.3	0	NR	NR	
Thiazolidinedione vs. Placebo											
Takagi, 2003 ⁷⁸	kg/m ²	Pioglitazone, 23	Control group (conventional antidiabetic therapy), 21	30 (fixed)	NR (NR)	25.6 (2.8) 25.3 (2.7) -0.3	24.5 (2.9) 24.1 (2.8) -0.4	0.1	0.2001 vs. GP2 final mean		
Nishio, 2006 ¹⁵¹	kg/m ²	Pioglitazone, 26	Control group (no placebo), 28	30 (fixed)	NA	24.6 (3.9) 24.7 (3.6) 0.1	24.6 (3.5) 24.5 (2.9) -0.1	0.2	0.901 vs. baseline 0.57 vs. GP2 final mean		
Virtanen, 2003 ¹⁴³	kg/m ²	Rosiglitazone + diet, 14	Placebo + diet, 14	2 bid (esc) 8 bid	NA	29.1 (SE 1) 29.3 (SE 1.1) 0.2	30.3 (SE 1.2) 30.3 (SE 1.2) 0	0.2	NSG vs. GP2		
Kim, 2005 ¹⁵²	kg/m ²	Rosiglitazone + diet + exercise, 60	Diet + exercise, 60	4 (fixed)	NA	23.9 (2.5) 24.4 (2.7) 0.5	24.5 (3) 24.5 (3) 0	0.5	<0.01 vs. baseline	NSG vs. baseline	
Alpha-Glucosidase Inhibitor vs. Placebo											
Rosenbaum, 2002 ¹⁵³	kg/m ²	Acarbose	Placebo	50 bid (esc) 100 tid	NA	30.3 (2.9) 29.8 (2.7) -0.5	31.7 (3.9) 31.5 (3.7) -0.2	-0.3	<0.05 vs. baseline	0.4 vs. baseline	

Appendix F: Evidence Table 8. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: body mass index

Comp = comparison; BL = baseline; GP = group; mg = milligrams; max = maximum; esc = escalated; diff = difference; NR = not reported; NSG = not significant; NA = not applicable; SD = standard deviation; SE = standard error; od = once daily; bid = twice daily; tid = three times daily; UKPDS = United Kingdom Prospective Diabetes Study; f/u = follow-up; vs = versus; kg/m² = kilograms per meter squared

* Number obtained from a figure

Median

Interquartile range

‡ 95% confidence interval

Appendix F: Evidence Table 9. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: systolic blood pressure

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2	Other
Thiazolidinedione vs. Metformin											
Hallsten, 2002 ⁵⁸	mmHg	Rosiglitazone + diet, 14	Metformin + diet, 13	2 bid (esc) 4 bid	500 bid (esc) 1000 bid	152 (5) 149 (4.5) -3	145 (4.1) 141.8 (4) -3.2	0.2			NSG vs. all groups
Pavo, 2003 ⁵⁹	mmHg	Pioglitazone + placebo, 100	Metformin + placebo, 91	30 (esc) 45	850 (esc) 2550	140.1 (SEM 15.4) 133.9 (SEM 1.2) -6.2	142.6 (SEM 14.2) 135.9 (SEM 1.2) -6.7	0.5	0.774 vs. GP2		
Yamanouchi, 2005 ⁵⁷	mmHg	Pioglitazone + diet + exercise, 38	Metformin + diet + exercise, 39	30 for women and 45 for men (fixed)	750 (fixed)	142.8 (17.1) 137.5 (19.5) -5.3	143.3 (18.8) 138 (14.8) -5.3	0	NSG vs. baseline and vs. GP2	NSG vs. baseline	
Natali, 2004 ¹⁴⁴	mmHg	Rosiglitazone	Metformin	4 bid (fixed)	500 tid (fixed)	129 (SEM 14) 135 -4 (2)	131 (SEM 14) 128 -3 (2)	-1 (-6, 3 [†])			
Schern-thaner, 2004 ⁵⁶	mmHg	Pioglitazone + placebo + diet	Metformin + placebo + diet	30 (esc) 45	850 (esc) 2550	NR NR NR	NR NR NR	NR	NSG vs. baseline	NSG vs. baseline	

Appendix F: Evidence Table 9. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: systolic blood pressure

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2	Other
Hanefeld, 2004 ⁶⁰ QUARTET study group	mmHg	Pioglitazone + unspecified sulfonylurea + placebo, 319	Metformin + unspecified sulfonylurea + placebo, 320	15 (esc) 45 NR	850 (esc) 850 tid NR	NR NR NR	NR NR NR	NR	NR	NR	No clinically relevant changes vs. baseline or between groups
Thiazolidinedione vs. Second Generation Sulfonylurea											
St John Sutto, 2002 ⁶⁷	mmHg	Rosiglitazone, 63	Glyburide (no trade drug specified), 66	4 bid (fixed)	NR (esc) 20	131.2 (SE 11.7) 131.1 -0.1 (SE 9.0)	129.5 (SE 13.5) 133.3 3.8 (SE 8.7)	-3.5	0.0219 vs. GP2 NSG vs. baseline	0.0006 vs. baseline	
Tan, 2004 ⁶⁶	mmHg	Pioglitazone, 91	Glibenclamide, 109	30 (esc) 45	1.75 (esc) 10.5	145.4 (20) 140.4 -5.0	142.9 (15.5) 137.6 -5.3	0.3	0.001 vs. baseline	<0.001 vs. baseline	
Nakamura, 2000 ⁶⁴	mmHg	Pioglitazone, 15	Glibenclamide, 15	30 (fixed)	5 (fixed)	122 (17) 116 (15) -6	122 (18) 124 (16) 2	-8	NR	NR	
Yanagawa, 2004 ⁶²	mmHg	Pioglitazone, 19	Gliclazide, 21	NR	NR	130 (12) NR NR	134 (17) NR NR	NR	NSG vs. GP2		

Appendix F: Evidence Table 9. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: systolic blood pressure

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2	Other
Yamanouchi, 2005 ⁵⁷	mmHg	Pioglitazone + diet + exercise, 38	Glimepiride + diet + exercise, 37	30 for women and 45 for men (fixed)	1.0 (esc) 2.0	142.8 (17.1) 137.5 (19.5) -5.3	141.3 (21.3) 137.2 (16.3) -4.1	-1.2	NSG vs. baseline and vs. GP2	NSG vs. baseline	
Langenfeld, 2005 ¹⁴⁶ Forst, 2005 ¹⁴⁵	mmHg	Pioglitazone, 89	Glimepiride, 84	45 (fixed)	1 (esc) 6	149 (21) 141 (16) -8	148 (20) 147 (19) 1	-9	<0.0001 vs. baseline <0.01 vs. GP2	NSG vs. baseline	
Thiazolidinedione vs. Alpha-Glucosidase Inhibitor											
Goke, 2002 ⁷⁵ German Pioglitazone Study Group	mmHg	Pioglitazone, 129	Acarbose, 136	45 (fixed)	50 (esc) 300	145.2 (19) 139.6 -5.6 (17.7)	141.5 (18.8) 141.9 0.4 (18.4)	6.0	<0.001 vs. GP2		
Nakamura, 2000 ⁶⁴	mmHg	Pioglitazone, 15	Voglibose, 15	30 (fixed)	0.6 (fixed)	122 (17) 116 (15) -6	118 (16) 122 (18) 4	-10	NSG vs. baseline	NSG vs. baseline	
Metformin vs. Second Generation Sulfonylurea											
Amador-Licona, 2000 ⁸⁵	mmHg	Metformin, 28	Glibenclamide, 23	850 (esc) NR	5 (esc) NR	120 115 -5 (2.7, 7.8 [†])	120 130 10	-15	0.002 vs. baseline	NSG vs. baseline	
Hermann, 1994 ⁸⁷	mmHg	Metformin + diet, 19	Glyburide + diet, 19	1000 (esc) 3000	3.5 (esc) 10.5	150 (SE 4) 152 (SE 3) 2.4 (SE 2.5)	141 (SE 3) 140 (SE 3) -1 (SE 2)	3	>0.1 vs. baseline	>0.1 vs. baseline	>0.1 all group comparison

Appendix F: Evidence Table 9. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: systolic blood pressure

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2	Other
Charpentier, 2001 ⁸⁹	mmHg	Metformin + placebo, 75	Glimepiride + placebo, 150	850 tid (fixed)	1 (esc) 6	142 (11) 141.35 -0.65	137 (12) 138.6 1.6	-2.25	NR	NR	Treatment effect p=0.811
Yamanouchi, 2005 ⁸⁷	mmHg	Metformin + diet + exercise, 39	Glimepiride + diet + exercise, 37	750 (fixed)	1 (esc) 2	143.3 (18.8) 138 (14.8) -5.3	141.3 (21.3) 137.2 (16.3) -4.1	-1.2	NSG vs. baseline and vs. GP2	NSG vs. baseline	
Derosa, 2004 ³⁰	mmHg	Metformin + placebo + diet + exercise, 75	Glimepiride + placebo + diet + exercise, 73	1000 (esc) 1000 tid	1 (esc) 2 bid	129 (5) 125 (3) -4	128 (5) 129 (4) 1	-3	NR	NR	
DeFronzo, 1995 ⁸⁸	mmHg	Metformin	Glyburide (no trade drug specified) + placebo	500 (esc) 2500	5 bid (esc) 10 bid	NR NR NR	NR NR NR	NR	NSG vs. baseline	NSG vs. baseline	
Second Generation Sulfonylurea vs. Metformin + Second Generation Sulfonylurea											
Charpentier, 2001 ⁸⁹	mmHg	Glimepiride + placebo, 150	Metformin + glimepiride, 147	1 (esc) 6	850 tid (fixed) 1 (esc) 6	137 (12) 138.6 1.6 (12.76)	140 (12) 139.86 -0.14(13.2)	1.74	NR	NR	Treatment effect p=0.811
Hermann, 1994 ⁸⁷	mmHg	Glyburide + diet, 19	Metformin + glyburide + diet, 17	3.5 (esc) 10.5	2000 + 7 (esc) 3000 + 14	141 140 (SE 3) -1 (SE 2.0)	146 144 (SE 4) 2	1	>0.1 vs. baseline	>0.1 vs. baseline	>0.1 all group comparison

Appendix F: Evidence Table 9. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: systolic blood pressure

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Hermann, 1994 ⁸⁷	mmHg	Glyburide + diet, 19	Metformin + glyburide + diet, 11	3.5 (esc) 10.5	1000 + 10.5 (esc) 3000 + 14	141 140 (SE 3) -1 (SE 2.0)	142 149 (SE 5) -7	-8	>0.1 vs. baseline	>0.1 vs. baseline	>0.1 all group compari- son
Hermann, 1994 ⁸⁷	mmHg	Glyburide + diet, 19	Metformin + glyburide + diet, 46	3.5 (esc) 10.5	500 (esc) 1500 1.75 (esc) 5.25	141 140 (SE 3) -1 (SE 2.0)	143 144 (SE 3) 1 (SE 2.4)	-2	>0.1 vs. baseline	>0.1 vs. baseline	>0.1 all group compari- son
Hermann, 1994 ⁸⁷	mmHg	Glyburide + diet, 19	Metformin + glyburide + diet, 12	3.5 (esc) 10.5	3000 + 3.5 (fixed + esc) 14	141 140 (SE 3) -1 (SE 2.0)	144 152 (SE 5) -8	-9	>0.1 vs. baseline	>0.1 vs. baseline	>0.1 all group compari- son
1998 ¹²⁸ UKPDS, 3 year f/u	mmHg	Glibenclamide + diet, 300	Metformin + glibenclamide + diet, 291	10 (fixed)	500 (esc) 2500 10 (fixed)	NR NR 0.72 (-1.17, 2.61 [†])	NR NR 2.51 (0.69, 4.34 [†])	-1.8	NSG vs. GP2		
Gregorio, 1999 ¹²⁹	mmHg	Glibenclamide or gliclazide, 85	Metformin + glibenclamide or metformin + gliclazide, 89	10 (esc) 15 120 (esc) 240	850 (esc) 1700 NR (fixed) NR (fixed)	165.4 (2.74) 163.5 (2.45) -1.9	157.6 (2.51) 154.4 (2.26) -3.2	1.3	NSG vs. baseline	NSG vs. baseline	
DeFronzo, 1995 ⁸⁸	mmHg	Glyburide (no trade drug specified) + placebo	Metformin + glyburide (no trade drug specified)	5 bid (esc) 10 bid	500 (esc) 2500 10 (esc) 20	NR NR NR	NR NR NR	NR	NSG vs. GP2		

Appendix F: Evidence Table 9. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: systolic blood pressure

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2	Other
Other Comparisons											
Hermann, 1994 ⁸⁷	mmHg	Metformin + diet, 19	Metformin + glyburide + diet, 17	1000 (esc) 3000	2000 + 7 (esc) 3000 + 14	150 152 (SE 3) 2.4 (SE 2.5)	146 144 (SE 4) -0.5	-4	>0.1 vs. baseline	>0.1 vs. baseline	>0.1 all group comparison
Hermann, 1994 ⁸⁷	mmHg	Metformin + diet, 19	Metformin + glyburide + diet, 11	1000 (esc) 3000	1000 + 10.5 (esc) 3000 + 14	150 152 (SE 3) 2.4 (SE 2.5)	142 149 (SE 5) 5.9	5	>0.1 vs. baseline	>0.1 vs. baseline	>0.1 all group comparison
Hermann, 1994 ⁸⁷	mmHg	Metformin + diet, 19	Metformin + glyburide + diet, 46	1000 (esc) 3000	500 (esc) 1500 1.75 (esc) 5.25	150 (SE 4) 152 (SE 3) 2.4 (SE 2.5)	143 (SE 3) 144 (SE 3) 1 (SE 2.4)	1	>0.1 vs. baseline	>0.1 vs. baseline	>0.1 all group comparison
Hermann, 1994 ⁸⁷	mmHg	Metformin + diet, 19	Metformin + glyburide + diet, 12	1000 (esc) 3000	3000 + 3.5 (fixed + esc) 14	150 152 (SE 3) 2.4 (SE 2.5)	144 152 (SE 5) 8.8	6	>0.1 vs. baseline	>0.1 vs. baseline	>0.1 all group comparison
Charpentier, 2001 ⁸⁹	mmHg	Metformin + placebo, 75	Metformin + glimepiride, 147	850 tid (fixed)	850 tid (fixed) 1 (esc) 6	142 (11) 141.35 -0.65 (12.22)	140 (12) 139.86 -0.14 (13.2)	-0.51	NR	NR	Treatment effect p=0.811
DeFronzo, 1995 ⁸⁸	mmHg	Metformin + placebo	Metformin + glyburide (no trade drug specified)	500 (esc) 2500	500 (esc) 2500 10 (esc) 20	NR NR NR	NR NR NR	NR	NSG vs. baseline and vs. GP2	NSG vs. baseline	

Appendix F: Evidence Table 9. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: systolic blood pressure

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Wolffenbuttel, 1999 ¹¹⁷	mmHg	Glyburide (no trade drug specified) + placebo, 109	Repaglinide, 211	1.75 (esc) 10.5	1.5 (esc) 12	146 143 -3	147 142 -5	2	NSG vs. GP2		
Derosa, 2003 ¹¹⁸	mmHg	Glimepiride + placebo, 62	Repaglinide + placebo, 62	1 (esc) 3 mean final dose	1 (esc) 2.5 mean final dose	128 (5) 129 (4) 1	129 (4) 128 (5) -1	2	NSG vs. GP2		
Goldberg, 2005 ⁵²	mmHg	Rosiglitazone + diet, 366	Pioglitazone + diet, 369	4 (esc) 8	30 (esc) 45	NR NR NR	NR NR NR	NR	NSG vs. GP2		
Pfutzner, 2006 ¹²³	mmHg	Glimepiride + placebo	Rosiglitazone + glimepiride	3 (fixed)	8 (fixed) 3 (fixed)	142 (13) 140 (14) -2	141 (82) 141 (81) 0	-2	NR	NR	
Pfutzner, 2006 ¹²³	mmHg	Glimepiride + placebo	Rosiglitazone + glimepiride	3 (fixed)	4 (fixed) 3 (fixed)	142 (13) 140 (14) -2	139 (16) 137 (17) -2	0	NR	NR	
Derosa, 2005 ⁷²	mmHg	Rosiglitazone + metformin + diet + exercise + behavioral therapy, 48	Metformin + glimepiride + diet + exercise + behavioral therapy, 47	4 (fixed) 1500 (fixed)	1500 (fixed) 2 (fixed)	131.6 (4) 126.2 (3.6) -5.4	131.4 (4.2) 128.2 (3.7) -3.2	-2.2	<0.05 vs. baseline and vs. GP2		
Derosa, 2003 ⁹⁷	mmHg	Metformin + diet + exercise, 56	Repaglinide + diet + exercise, 56	500 bid (esc) 2500	0.5 bid (esc) 4	125 (6.5) 126 (5.1) 1	124 (6.9) 121 (7.1) -3	4	NSG vs. GP2		

Appendix F: Evidence Table 9. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: systolic blood pressure

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2	Other
Nakamura, 2000 ⁶⁴	mmHg	Glibenclamide, 15	Voglibose, 15	5 (fixed)	0.6 (fixed)	122 (18) 124 (16) 2	118 (16) 122 (18) 4	-2	NSG vs. baseline	NSG vs. baseline	
Thiazolidinedione vs. Placebo											
Nishio, 2006 ¹⁵¹	mmHg	Pioglitazone, 26	Control group (no placebo), 28	30 (fixed)	NA	126.9 (19.4) 125.1 (23.4) -1.8	131.7 (16.9) 133.2 (19.6) 1.5	-3.3	NSG vs. baseline and vs. GP2	NSG vs. baseline	
Hallsten, 2002 ⁵⁸	mmHg	Rosiglitazone + diet, 14	Placebo + diet, 14	2 bid (esc) 8 bid	NA	152 (5) 149 (4.5) -3	147.2 (3.2) 144.4 (3.8) -2.8	-0.2	NR	NR	NSG vs. all groups
Kim, 2005 ¹⁵²	mmHg	Rosiglitazone + diet + exercise, 60	Diet + exercise, 60	4 (fixed)	NA	139.8 (17.7) 137.4 (18) -2.4	143.9 (17.7) 142 (22) -1.9	-0.5	NSG vs. baseline	NSG vs. baseline	
Natali, 2004 ¹⁴⁴	mmHg	Rosiglitazone	Placebo	4 bid (fixed)	NA	129 (SEM 14) 125 -4 (2)	132 (SEM 18) 132.03 0.3 (2)	-5 (-10, 0.4 [†])			
Metformin vs. Placebo											
Grant, 1996 ¹⁵⁴	NR	Metformin	Placebo	1500 (fixed)	NA	NR NR NR	NR NR NR	NR	NSG vs. GP2		

Appendix F: Evidence Table 9. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: systolic blood pressure

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Grant, 1996 ¹⁵⁴	NR	Metformin	Placebo	1500 (esc) 3000	NA	NR NR NR	NR NR NR	NR	NSG vs. GP2		
Rachmani, 2002 ¹⁵⁰	mmHg	Metformin continued + diet, 195	Metformin stopped + diet, 198	NR	NA	143 (6) 144 1	144 (5) 147 3	-2	NSG vs. GP2		
Teupe, 1991 ¹⁵⁵	mmHg	Metformin + diet, 25	Diet, 29	NR (esc) 1700	NA	160 (23) 150 (17) -10 (-7.4% [†])	168 (26) 148 (21) -20 (-12% [†])	10	<0.05	<0.05	
Hallsten, 2002 ⁵⁸	mmHg	Metformin + diet, 13	Placebo + diet, 14	500 bid (esc) 1000 bid	NA	145 (4.1) 141.8 (4) -3.2	147.2 (3.2) 144.4 (3.8) -2.8	-0.4	NR	NR	NSG vs. all groups
DeFronzo, 1995 ⁸⁸	mmHg	Metformin	Placebo	850 (esc) 850 tid	NA	NR NR NR	NR NR NR	NR	NSG vs. baseline	NSG vs. baseline	
Natali, 2004 ¹⁴⁴	mmHg	Metformin	Placebo	500 tid (fixed)	NA	131 (SEM 14) 128 -3 (2)	132 (SEM 18) 132.03 0.3 (2)	-3.3	NR	NR	

Appendix F: Evidence Table 9. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: systolic blood pressure

Author, year				Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	
Study group	Units	Comp group 1, N	Comp group 2, N								Other
Alpha-Glucosidase Inhibitor vs. Placebo											
Rosenbaum, 2002 ¹⁵³	mmHg	Acarbose, 20	Placebo, 20	50 bid (esc) 100 tid	NA	140.2 (16.2) 134 (11.9) -6.2	148.5 (13) 140.7 (12) -7.8	1.6	0.13 vs. baseline	0.02 vs. baseline	

Comp = comparison; BL = baseline; GP = group; mg = milligrams; max = maximum; esc = escalated; diff = difference; mmHg = millimeters of mercury; NR = not reported; NSG = not significant; NA = not applicable; SD = standard deviation; SE = standard error; SEM = standard error of the mean; bid = twice daily; tid = three times daily; UKPDS = United Kingdom Prospective Diabetes Study; f/u = follow-up; vs = versus

[†] Percent change from baseline

[‡] 95% confidence interval

Appendix F: Evidence Table 10. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: diastolic blood pressure

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Thiazolidinedione vs. Metformin											
Pavo, 2003 ⁵⁹	mmHg	Pioglitazone + placebo, 100	Metformin + placebo, 91	30 (esc) 45	850 (esc) 2550	87 (8.5) 83.1 -3.9 (0.6)	88 (8.2) 84.1 -3.9 (0.6)	0	0.979 vs. GP2		
Yamanouchi, 2005 ⁵⁷	mmHg	Pioglitazone + diet + exercise, 38	Metformin + diet + exercise, 39	30 for women and 45 for men (fixed)	750 (fixed)	85.3 (9.8) 80.5 (7.8) -4.8	86.3 (10.1) 82.7 (8.7) -3.6	-1.2	NSG vs. baseline and vs. GP2	NSG vs. baseline	
Hallsten, 2002 ⁵⁸	mmHg	Rosiglitazone + diet, 14	Metformin + diet, 13	2 bid (esc) 4 bid	500 bid (esc) 1000 bid	90.5 (SE 2.1) 84.2 (2.4) -6.3	91.4 (SE 2.5) 85.5 (2.6) -5.9	-0.4			NSG vs. all groups
Natali, 2004 ¹⁴⁴	mmHg	Rosiglitazone	Metformin	4 bid (fixed)	500 tid (fixed)	72 (SEM 6) 74 -2 (1)	75 (SEM 9) 76 -1 (1)	-4 (-7, - 1 [†])	<0.05 vs. GP2		
Schern-thaner, 2004 ⁵⁶	mmHg	Pioglitazone + placebo + diet, 48	Metformin + placebo + diet, 47	30 (esc) 45	850 (esc) 2550	NR NR NR	NR NR NR	NR	NSG vs. baseline	NSG vs. baseline	
Thiazolidinedione vs. Second Generation Sulfonylurea											
Tan, 2004 ⁶⁵	mmHg	Pioglitazone, 91	Glibenclamide, 109	30 (esc) 45	1.75 (esc) 10.5	87 (10.3) 82.7 -4.3	85.8 (9.3) 83.3 -2.5	-2.3	<0.001 vs. baseline	<0.001 vs. baseline	

Appendix F: Evidence Table 10. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: diastolic blood pressure

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2	Other
Nakamura, 2000 ⁶⁴	mmHg	Pioglitazone, 15	Glibenclamide, 15	30 (fixed)	5 (fixed)	76 (14) 72 (12) -4	78 (14) 79 (12) 1.0	-5	NR	NR	
Yanagawa, 2004 ⁶²	mmHg	Pioglitazone, 19	Gliclazide, 21	NR	NR	80.7 NR NR	81 (10) NR NR	NR	NSG vs. GP2		
Yamanouchi, 2005 ⁵⁷	mmHg	Pioglitazone + diet + exercise, 38	Glimepiride + diet + exercise, 37	30 for women and 45 for men (fixed)	1.0 (esc) 2.0	85.3 (9.8) 80.5 (7.8) -4.8	84.9 (7.7) 80.1 (8.3) -4.8	0	NSG vs. GP2		
Langenfeld, 2005 ¹⁴⁶ Forst, 2005 ¹⁴⁵	mmHg	Pioglitazone, 89	Glimepiride, 84	45 (fixed)	1 (esc) 6	87 (12) 84 (10) -3	85 (10) 87 (10) 2.0	-5	<0.001 vs. baseline and vs. GP2	NSG vs. baseline	
St John Sutton, 2002 ⁶⁷	mmHg	Rosiglitazone, 63	Glyburide (no trade drug specified), 66	4 bid (fixed)	NR (esc) 20	78 (SE 7.7) 75.7 -2.3 (SE 5.6)	76.3 (SE 7.7) 77 0.7 (SE 5.3)	-2.7	0.0046 vs. GP2 0.0016 vs. baseline	0.2801 vs. baseline	
Thiazolidinedione vs. Alpha-Glucosidase Inhibitor											
Goke, 2002 ⁷⁵	mmHg	Pioglitazone, 129	Acarbose, 136	45 (fixed)	50 (esc) 300	84.8 (10.6) 81.8 -3	84.4 (11.2) 83.2 -1.2	-1.8	0.078 vs. GP2		
German Pioglitazone Study Group											

Appendix F: Evidence Table 10. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: diastolic blood pressure

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2	Other
Nakamura, 2000 ⁶⁴	mmHg	Pioglitazone, 15	Voglibose, 15	30 (fixed)	0.6 (fixed)	76 (14) 72 (12) -4	78 (12) 80 (14) 2.0	-6	NSG vs. baseline	NSG vs. baseline	
Metformin vs. Second Generation Sulfonylurea											
Amador-Licona, 2000 ⁸⁵	mmHg	Metformin, 28	Glibenclamide, 23	850 (esc) NR	5 (esc) NR	75 70 -3.93 (-5.92, -1.94 [†])	70 80 10.0	-13.93	0.009 vs. baseline	0.16 vs. baseline	
Hermann, 1994 ⁸⁷	mmHg	Metformin + diet, 19	Glyburide + diet, 19	1000 (esc) 3000	3.5 (esc) 10.5	85 (SE 2) 85 (SE 1) 0.6 (SE 1.2)	84 (SE 1) 84 (SE 2) 0.5 (SE 1.2)	-0.1	>0.1 vs. baseline	>0.1 vs. baseline	>0.1 all group comparison
Charpentier, 2001 ⁸⁹	mmHg	Metformin + placebo, 75	Glimepiride + placebo, 150	850 tid (fixed)	1 (esc) 6	81 (7) 81.15 0.15 (9.22)	80 (7) 80.68 0.68 (8.25)	-0.53	NR	NR	0.502 all group comparison
Yamanouchi, 2005 ⁸⁷	mmHg	Metformin + diet + exercise, 39	Glimepiride + diet + exercise, 37	750 (fixed)	1 (esc) 2	86.3 (10.1) 82.7 (8.7) -3.6	84.9 (7.7) 80.1 (8.3) -4.8	1.2	NSG vs. baseline and vs. GP2	NSG vs. baseline	
Derosa, 2004 ⁹⁰	mmHg	Metformin + placebo + diet + exercise, 75	Glimepiride + placebo + diet + exercise, 73	1000 (esc) 1000 tid	1 (esc) 2 bid	86 (3) 83 (3) -3	85 (4) 86 (4) 1	-4	NR	NR	

Appendix F: Evidence Table 10. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: diastolic blood pressure

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2	Other
DeFronzo, 1995 ⁸⁸	mmHg	Metformin	Glyburide (no trade drug specified) + placebo	500 (esc) 2500	5 bid (esc) 10 bid	NR NR NR	NR NR NR	NR	NSG vs. baseline	NSG vs. baseline	
Metformin vs. Metformin + Second Generation Sulfonylurea											
Hermann, 1994 ⁸⁷	mmHg	Metformin + diet, 19	Metformin + glyburide + diet, 17	1000 (esc) 3000	2000 (esc) 3000 7.0 (esc) 14.0	85 (SE 2) 85 (SE 1) 0.6 (SE 1.2)	83 (SE 1) 85 (SE 1) 2	-1.4	>0.1 vs. baseline	>0.1 vs. baseline	>0.1 all group comparison
Hermann, 1994 ⁸⁷	mmHg	Metformin + diet, 19	Metformin + glyburide + diet, 46	1000 (esc) 3000	500 (esc) 1500 1.75 (esc) 5.25	85 (SE 2) 85 (SE 1) 0.6 (SE 1.2)	83 (SE 1) 85 (SE 1) 2.1	-1.5	>0.1 vs. baseline	>0.1 vs. baseline	>0.1 all group comparison
Hermann, 1994 ⁸⁷	mmHg	Metformin + diet, 19	Metformin + glyburide + diet, 12	1000 (esc) 3000	3000 (fixed) 3.5 (esc) 14.0	85 85 (SE 1) 0.6	83 85 (SE 2) 2	-1.4	>0.1 vs. baseline	>0.1 vs. baseline	>0.1 all group comparison
Hermann, 1994 ⁸⁷	mmHg	Metformin + diet, 19	Metformin + glyburide + diet, 11	1000 (esc) 3000	1000 (esc) 3000 10.5 (esc) 14.0	85 85 (SE 1) 0.6	85 83 (SE 3) -2	2.6	>0.1 vs. baseline	>0.1 vs. baseline	>0.1 all group comparison
Charpentier, 2001 ⁸⁹	mmHg	Metformin + placebo, 75	Metformin + glimepiride, 147	850 tid (fixed)	850 tid (fixed) 1 (esc) 6	81 (7) 81.15 0.15	81 (7) 80.31 -0.69	0.84	NR	NR	0.502 all group comparison

Appendix F: Evidence Table 10. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: diastolic blood pressure

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2	Other
DeFronzo, 1995 ⁸⁸	mmHg	Metformin + placebo	Metformin + glyburide (no trade drug specified)	500 (esc) 2500	500 (esc) 2500 10 (esc) 20	NR NR NR	NR NR NR	NR	NSG vs. baseline and vs. GP2	NSG vs. baseline	
Second Generation Sulfonylurea vs. Metformin + Second Generation Sulfonylurea											
Hermann, 1994 ⁸⁷	mmHg	Glyburide + diet, 19	Metformin + glyburide + diet, 17	3.5 (esc) 10.5	2000 (esc) 3000 7.0 (esc) 14.0	84 84 (SE 2) 0.5	85 83 (SE 2) -2	-2.5	>0.1 vs. baseline	>0.1 vs. baseline	>0.1 all group comparison
Hermann, 1994 ⁸⁷	mmHg	Glyburide + diet, 19	Metformin + glyburide + diet, 11	3.5 (esc) 10.5	1000 (esc) 3000 10.5 (esc) 14	84 84 (SE 2) 0.5	85 83 (SE 3) -2	2.5	>0.1 vs. baseline	>0.1 vs. baseline	>0.1 all group comparison
Hermann, 1994 ⁸⁷	mmHg	Glyburide + diet, 19	Metformin + glyburide + diet, 46	3.5 (esc) 10.5	500 (esc) 1500 1.75 (esc) 5.25	84 (SE 1) 84 (SE 2) 0.5 (SE 1.2)	83 (SE 1) 85 (SE 1) 2.1 (SE 1.3)	-1.6	>0.1 vs. baseline	>0.1 vs. baseline	>0.1 all group comparison
Hermann, 1994 ⁸⁷	mmHg	Glyburide + diet, 19	Metformin + glyburide + diet, 12	3.5 (esc) 10.5	3000 (fixed) 3.5 (esc) 14	84 84 (SE 2) 0.5	83 85 (SE 2) 2	-1.5	>0.1 vs. baseline	>0.1 vs. baseline	>0.1 all group comparison
1998 ¹²⁸ UKPDS, 3 year f/u	mmHg	Glibenclamide + diet, 300	Metformin + glibenclamide + diet, 291	10 (fixed)	500 (esc) 2500 10 (fixed)	NR NR -1.66	NR NR -1.54	-0.12	0.0043 vs. baseline NSG vs. GP2	0.0068 vs. baseline	

Appendix F: Evidence Table 10. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: diastolic blood pressure

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2	Other
Charpentier, 2001 ⁸⁹	mmHg	Glimepiride + placebo, 150	Metformin + glimepiride, 147	1 (esc) 6	850 tid (fixed) 1 (esc) 6	80 (7) 80.68 0.68 (8.25)	81 (7) 80.31 -0.69 (7.91)	1.37	NR	NR	0.502 all group comparison
Gregorio, 1999 ¹²⁹	mmHg	Glibenclamide or gliclazide, 85	Metformin + glibenclamide or metformin + gliclazide, 89	10 (esc) 15 120 (esc) 240	850 (esc) 1700 NR (fixed) NR (fixed)	78.63 (SE 2.1) 78.33 (SE 1.86) -0.3	80.23 (SE 2.22) 82.21 (SE 1.95) 1.98	-2.01	NSG vs. baseline	NSG vs. baseline	
DeFronzo, 1995 ⁸⁸	mmHg	Glyburide (no trade drug specified) + placebo	Metformin + glyburide (no trade drug specified)	5 bid (esc) 10 bid	500 (esc) 2500 10 (esc) 20	NR NR NR	NR NR NR	NR	NSG vs. GP2		
Other Comparisons											
Wolffenbuttel, 1999 ¹¹⁷	mmHg	Glyburide (no trade drug specified) + placebo, 109	Repaglinide, 211	1.75 (esc) 10.5	1.5 (esc) 12	83 83 0	86 84 -2.0	2	NSG vs. GP2		
Derosa, 2003 ¹¹⁸	mmHg	Glimepiride + placebo, 62	Repaglinide + placebo, 62	1 (esc) 3 mean final dose	1 (esc) 2.5 mean final dose	85 (3) 85 (5) 0	85 (4) 84 (4) -1	-1	NSG vs. GP2		
Goldberg, 2005 ⁵²	mmHg	Rosiglitazone + diet, 366	Pioglitazone + diet, 369	4 (esc) 8	30 (esc) 45	NR NR NR	NR NR NR	NR	NSG vs. GP2		

Appendix F: Evidence Table 10. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: diastolic blood pressure

Author, year						GP1 BL mean (SD)	GP2 BL mean (SD)				
Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 final mean (SD) Mean diff from BL1	GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Hanefeld, 2004 ⁶⁰ QUARTET study group	mmHg	Pioglitazone + unspecified sulfonylurea + placebo, 319	Metformin + unspecified sulfonylurea + placebo, 320	15 (esc) 45 NR	850 (esc) 850 tid NR	NR NR NR	NR NR NR	NR	NR	NR	No clinically relevant changes vs. baseline or between groups
Pfutzner, 2006 ¹²³	mmHg	Glimepiride + placebo	Rosiglitazone + glimepiride	3 (fixed)	8 (fixed) 3 (fixed)	83 (7) 83 (9) 0	82 (9) 82 (9) 0.0	0	NR	NR	
Pfutzner, 2006 ¹²³	mmHg	Glimepiride + placebo	Rosiglitazone + glimepiride	3 (fixed)	4 (fixed) 3 (fixed)	83 (7) 83 (9) 0	82 (9) 82 (7) 0.0	0	NR	NR	
Derosa, 2003 ⁹⁷	mmHg	Metformin + diet + exercise, 56	Repaglinide + diet + exercise, 56	500 bid (esc) 2500	0.5 bid (esc) 4	81 (4.5) 80 (4.5) -1	80 (4.1) 81 (5.1) 1.0	-2	NSG vs. GP2		
Nakamura, 2000 ⁶⁴	mmHg	Glibenclamide, 15	Voglibose, 15	5 (fixed)	0.6 (fixed)	78 (14) 79 (12) 1	78 (12) 80 (14) 2.0	-1	NR	NR	
Thiazolidinedione vs. Placebo											
Nishio, 2006 ¹⁵¹	mmHg	Pioglitazone, 26	Control group (no placebo), 28	30 (fixed)	NA	74.3 (7.5) 73.5 (8.8) -0.8	74.1 (11.1) 74.6 (9.9) 0.5	-1.3	NSG vs. baseline and vs. GP2	NSG vs. baseline	

Appendix F: Evidence Table 10. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: diastolic blood pressure

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Hallsten, 2002 ⁵⁸	mmHg	Rosiglitazone + diet, 14	Placebo + diet, 14	2 bid (esc) 8 bid	NA	90.5 (SE 2.1) 84.2 (SE 2.4) -6.3	85.1 (SE 2.3) 85.4 (SE 2.7) 0.3	-6.6	NR	NR	NSG all group comparis on
Kim, 2005 ¹⁵²	mmHg	Rosiglitazone + diet + exercise, 60	Diet + exercise, 60	4 (fixed)	NA	83.4 (10.5) 80.5 (10.3) -2.9	86.1 (15.4) 84.4 (14) -1.7	-1.2	<0.05 vs. baseline	NSG vs. baseline	
Natali, 2004 ¹⁴⁴	mmHg	Rosiglitazone	Placebo	4 bid (fixed)	NA	72 (SEM 6) 70 -2 (1)	76 (SEM 8) 76.1 0.1 (1)	-2.1 (-5, 1 ⁺)			
Metformin vs. Placebo											
Natali, 2004 ¹⁴⁴	mmHg	Metformin	Placebo	500 tid (fixed)	NA	75 (SEM 9) 74 -1 (1)	76 (SEM 8) 76.1 0.1 (1)	-1.1	NR	NR	
Rachmani, 2002 ¹⁵⁰	mmHg	Metformin continued + diet, 195	Metformin stopped + diet, 198	NR	NA	82 (SE 2) 80 -2	83 (SE 2) 80 -3.0	1	NSG vs. baseline and vs. GP2	<0.05 vs. baseline	
Teupe, 1991 ¹⁵⁵	mmHg	Metformin + diet, 25	Diet, 29	NR (esc) 1700	NA	92 (9) 89 (6) -3	95 (15) 87 (10) -8.0	5	<0.05 vs. baseline	<0.05 vs. baseline	

Appendix F: Evidence Table 10. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: diastolic blood pressure

Author, year				Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Study group	Units	Comp group 1, N	Comp group 2, N								
Hallsten, 2002 ⁵⁸	mmHg	Metformin + diet, 13	Placebo + diet, 14	500 bid (esc) 1000 bid	NA	91.4 (SE 2.5) 85.5 (SE 2.6) -5.9	85.1 (SE 2.3) 85.4 (SE 2.7) 0.3	-6.2			NSG vs. all groups
DeFronzo, 1995 ⁵⁸	mmHg	Metformin + placebo	Placebo	850 (esc) 850 tid	NA	NR NR NR	NR NR NR	NR	NSG vs. GP2		
Alpha-Glucosidase Inhibitor vs. Placebo											
Rosenbaum, 2002 ¹⁵³	mmHg	Acarbose, 20	Placebo, 20	50 bid (esc) 100 tid	NA	82.5 (7.3) 80.9 (4.5) -1.6	87.6 (5.5) 84.2 (5.4) -3.4	1.8	0.32 vs. baseline	0.01 vs. baseline	

Comp = comparison; BL = baseline; GP = group; mg = milligrams; max = maximum; esc = escalated; diff = difference; mmHg = millimeters of mercury; NR = not reported; NSG = not significant; NA = not applicable; SD = standard deviation; SE = standard error; SEM = standard error of the mean; bid = twice daily; tid = three times daily; UKPDS = United Kingdom Prospective Diabetes Study; f/u = follow-up; vs = versus

‡ 95% confidence interval

Appendix F: Evidence Table 11. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: low density lipoprotein

Author, year Study group	Outcome (calc or meas) Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Thiazolidinedione vs. Thiazolidinedione										
Goldberg, 2005 ⁵²	(meas) mg/dL	Rosiglitazone + diet, 356	Pioglitazone + diet, 363	4 (esc) 8	30 (esc) 45	109.1 (SE 1.4) 130.4 21.3 (SE 1.6)	107.1 (SE 1.3) 119.4 12.3 (SE 1.6)	9	< 0.05 vs. baseline <0.001 vs. GP2	< .05 vs. baseline
Khan, 2002 ⁵¹	(calc) mg/dL	Rosiglitazone, 60	Pioglitazone, 67	2-8 (fixed)	15-45 (fixed)	105.9 (29.7) 103.9 -2	116.2 (38) 98.2 -18	16	NSG vs. baseline <0.01 vs. GP2	<0.01 vs. baseline
Derosa, 2005 ¹⁵⁶	(calc) mg/dL	Rosiglitazone + glimepiride + diet + exercise, 42	Pioglitazone + glimepiride + diet + exercise, 45	4 (fixed) 4 (fixed)	15 (fixed) 4 (fixed)	121 (17) 141 (20) 20	125 (15) 110 (13) -15	-35	<0.05 vs. GP2	
Thiazolidinedione vs. Metformin										
Schern-thaner, 2004 ⁵⁶	(calc) mg/dL	Pioglitazone + placebo + diet	Metformin + placebo + diet	30 (esc) 45	850 up to 3 times/day (esc) 2550	138.84 149.37 10.53	138.84 134.16 -4.68	15.21	0.001 vs. GP2	
Lawrence, 2004 ⁵⁴	(meas) mg/dL	Pioglitazone, 20	Metformin, 20	30 (esc) 45	500 bid (esc) 1000 tid	194.2 (43.2) 202.4 (46.9) 8.2	200.5 (42.6) 200.9 (50.5) 0.4	7.8	NR	NR
Pavo, 2003 ⁵⁹	(calc) mg/dL	Pioglitazone + placebo, 100	Metformin + placebo, 91	30 (esc) 45	850 (esc) 2550	NR NR 6.24	NR NR -7.02	13.26	0.055 vs. baseline 0.003 vs. GP2	0.04 vs. baseline

Appendix F: Evidence Table 11. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: low density lipoprotein

Author, year Study group	Outcome (calc or meas) Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Hanefeld, 2004 ⁶⁰ QUARTET study group Betteridge, 2005 ¹⁵⁷	(meas) mg/dL	Pioglitazone + unspecified sulfonylurea + placebo, 319	Metformin + unspecified sulfonylurea + placebo, 320	15 (esc) 45 NR	850 (esc) 850 tid NR	139.23 (33.54) 142.74 (1.56) 3.12	139.62 (35.58) 132.99 (1.56) -6.24	9.36	0.0002 vs. GP2	
Natali, 2004 ¹⁴⁴	(meas) mg/dL	Rosiglitazone	Metformin	4 bid (fixed)	500 tid (fixed)	120 (SE 29) 131 11	118 (SE 25) 120 2	10 (-4, 23 [†])	NSG vs. GP2	
Virtanen, 2003 ¹⁴³	(meas) mg/dL	Rosiglitazone + diet, 14	Metformin + diet, 13	2 bid (esc) 4 bid	500 bid (esc) 1000 bid	113.1 (SE 7.8) 136.5 (SE 7.8) 23.4	109.2 (SE 7.8) 101.4 (SE 7.8) -7.8	31.2	NR	NR
Thiazolidinedione vs. Second Generation Sulfonylurea										
Pfutzner, 2005 ⁶⁸ Forst, 2005 ¹⁴⁵ Langenfeld, 2005 ¹⁴⁶	(meas) mg/dL	Pioglitazone, 89	Glimepiride, 84	45 (fixed)	1 (esc) 6	136 (29) 133 (31) -3	137 (25) 129 (27) -8	5	NSG vs. GP2	
Matthews, 2005 ⁷⁰ Betteridge, 2005 ¹⁵⁷ (52 week data)	(meas) mg/dL	Pioglitazone + metformin, 317	Gliclazide + metformin, 313	15 (esc) 45 NR	80 (esc) 320 NR	130.26 (38.22) 140.66 10.4	127.92 (36.27) 123.72 -4.2	14.6		<0.001 vs. GP1

Appendix F: Evidence Table 11. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: low density lipoprotein

Author, year Study group	Outcome (calc or meas) Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Betteridge, 2005 ¹⁵⁷ (104 week data)	(meas) mg/dL	Pioglitazone + metformin, 317	Gliclazide + metformin, 313	15 (esc) 45 NR	80 (esc) 320 NR	130.26 (38.22) 132.99 2.73	127.92 (36.27) 120.12 -7.8	10.53		<0.001 vs. GP1
Charbonnel, 2005 ⁶³	(meas) mg/dL	Pioglitazone	Gliclazide	NR (esc) 45	NR (esc) 320	137.28 141.96 4.68	136.5 129.87 -6.63	11.31 (7.8, 14.04 [†])	<0.001 vs. GP2	
Tan, 2004 ⁶⁵	(calc) mg/dL	Pioglitazone, 91	Glibendamide, 109	30 (esc) 45	1.75 (esc) 10.5	141.18 146.64 5.46	135.72 134.55 -1.17	6.63	NSG vs. baseline	NSG vs. baseline
Lawrence, 2004 ⁵⁴	(meas) mg/dL	Pioglitazone, 20	Gliclazide, 20	30 (esc) 45	80 od (esc) 160 bid	194.2 (43.2) 202.4 (46.9) 8.2	196.6 (62.3) 194.9 (64.6) -1.7	9.9	NSG vs. baseline	NSG vs. baseline
St John Sutto, 2002 ⁶⁷	(meas) mg/dL	Rosiglitazone, 63	Glyburide (no trade drug specified), 66	4 bid (fixed)	NR (esc) 20	140.2 146.5 6.3; 7.7 [#]	135.4 126.5 -8.9	15.2	NR	NR
Thiazolidinedione + Metformin vs. Metformin + Second Generation Sulfonylurea										
Derosa, 2005 ^{72 158}	(meas) mg/dL	Rosiglitazone + metformin + diet + exercise + behavioral therapy, 48	Metformin + glimepiride + diet + exercise + behavioral therapy, 47	4 (fixed) 1500 (fixed)	1500 (fixed) 2 (fixed)	116 (15) 120 (17) 4	118 (13) 102 (11) -16	20		<0.05 vs. baseline and vs. GP1

Appendix F: Evidence Table 11. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: low density lipoprotein

Author, year Study group	Outcome (calc or meas) Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Garber, 2006 ⁷¹	(calc) mg/dL	Rosiglitazone + metformin + diet, 99	Metformin + glibenclamide + diet, 110	4 (esc) 8 1500-2000 (esc) 2000	1000 (esc) 2000 5 (esc) 10	116 125 9 (35)	119 115 -4 (26)	14 (-6, 22 [†])	NSG vs. GP2	
Thiazolidinedione vs. Meglitinide										
Raskin, 2004 ⁷⁴	(meas) mg/dL	Rosiglitazone, 29	Repaglinide, 25	2 bid (esc) 4 bid	0.5 tid if HbA1c≤8%, 1 tid if HbA1c>8% (esc) 4 tid	125 (23.5) 139 (34.3) 14	124 (33.8) 123 (32.3) -1	15	NR	NR
Jovanovic, 2004 ⁷³	(meas) mg/dL	Pioglitazone, 21	Repaglinide, 35	30 (fixed)	0.5 tid if HbA1c≤8%, 1 tid if HbA1c>8% (esc) 4 tid	106 (37) 116 (42) 10	124 (36) 118 (38) -6	16	NR	NR
Other Thiazolidinedione Comparisons										
Goke, 2002 ⁷⁵ German Pioglitazone Study Group	(meas) mg/dL	Pioglitazone, 129	Acarbose, 136	45 (fixed)	50 (esc) 100 tid	137.4 (36.1) 136.9 0.5 (30.7)	141.9 (36.8) 146.46 4.56 (27.6)	-4	0.124 vs. GP2	
McCluskey, 2004 ⁷⁶	(calc) mg/dL	Rosiglitazone + placebo, 15	Rosiglitazone + glimepiride, 24	4 or 8 (fixed)	4 or 8 fixed 2 (esc) 8	60.9 (SE 4.4) 60.8 -0.1 (SE 3.4)	58 (SE 3.3) 58.2 0.2 (SE 2.3)	-0.3	NSG vs. GP2	
Metformin vs. Second Generation Sulfonylurea										
Derosa, 2004 ³⁰	(meas) mg/dL	Metformin + placebo + diet + exercise, 75	Glimepiride + placebo + diet + exercise, 73	1000 (esc) 1000 tid	1 (esc) 2 bid	144 (20) 130 (25) -14 (-42, -8 [†])	135 (20) 130 (15) -5 (2.8, 9.6 [†])	-9	<0.05 vs. baseline	

Appendix F: Evidence Table 11. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: low density lipoprotein

Author, year Study group	Outcome (calc or meas) Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Lawrence, 2004 ⁵⁴	(meas) mg/dL	Metformin, 20	Gliclazide, 20	500 bid (esc) 1000 tid	80 (esc) 160 bid	200.5 (42.6) 200.9 (50.5) 0.4	196.6 (62.3) 194.9 (64.6) -1.7	2.1	NSG vs. baseline	NSG vs. baseline
Garber, 2003 ⁸⁰	(meas) mg/dL	Metformin, 164	Glyburide (no trade drug specified), 151	500 (esc) 2000	2.5 (esc) 10	122.7 (3.2) 117 -5.7	122.2 (3.2) 124.5 2.3	-8	<0.05 vs. baseline	NSG vs. baseline
Goldstein, 2003 ⁸²	(meas) mg/dL	Metformin, 67	Glipizide	500 (esc) 2000	15 bid (fixed)	109.7 (35.2) 102.5 -7.2 (-15, 0.6 [†])	111.2 (34.6) 110.8 -0.4 (-6.7, 5.8 [†])	-6.8	NR	NR
Blonde, 2002 ⁸¹	NR	Metformin, 153	Glyburide (no trade drug specified), 164	500 (esc) 2000	10 bid (fixed)	NR NR NR	NR NR NR	NR	NSG vs. GP2	
Marre, 2002 ⁸⁴	(meas) mg/dL	Metformin, 104	Glibenclamide, 103	500 (esc) 2000	5 (esc) 20	148.2 (SE 39) 136.5 -11.7 (SE 31.2)	152.1 (SE 42.9) 148.2 -3.9 (SE 39)	-7.8	NSG vs. GP2	
Hermann, 1991 ¹⁵⁹	(calc) mg/dL	Metformin + diet, 28	Glibenclamide + diet, 28	1000 (esc) 3000	3.5 (esc) 10.5	NR NR -0.78 (SE 3.9)	NR NR 5.07 (SE 7.41)	-5.85	NR	NR

Appendix F: Evidence Table 11. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: low density lipoprotein

Author, year Study group	Outcome (calc or meas) Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Campbell, 1994 ⁸³	(calc) mg/dL	Metformin, 24	Glipizide, 24	500 bid (esc) 3000	5 (esc) 30	4.65 (1.07) 4.58 (1.19) -0.07	4.51 (1.26) 4.99 (1.16) 0.48	-0.55	NSG vs. GP2	
DeFronzo, 1995 ⁸⁸	(calc) mg/dL	Metformin + placebo, 210	Glyburide (no trade drug specified) + placebo, 209	500 (esc) 2500	5 bid (esc) 10 bid	134 (SE 3) 129 (SE 3) -6 (SE 2)	136 (SE 3) 141 (SE 3) 3 (SE 2)	-9	0.009 vs. GP2	
Hermann, 1994 ⁸⁷	(calc) mg/dL	Metformin + diet, 19	Glyburide + diet, 19	1000 (esc) 3000	3.5 (esc) 10.5	142.74 (SE 9.75) 131.82 (SE 8.97) -5.85 (SE 2.73)	153.27 (SE 5.46) 157.56 (SE 5.07) 4.68 (SE 3.51)	-10.53	0.052 vs. baseline 0.086 comparis on of all study groups	>0.1 vs. baseline
Metformin vs. Thiazolidinedione + Metformin										
Weissman, 2005 ¹⁰⁰	(calc) mg/dL	Metformin, 277	Rosiglitazone + metformin, 268	1000 (esc) 2000	4 (esc) 8 1000 (fixed)	105.1 (103.4, 106.8 [†]) 101.6 (99.7, 103.6 [†]) -3.5	106.3 (104.5, 108.2 [†]) 118.5 (116.3, 120.7 [†]) 12.2	-15.7	NR	NR
Bailey, 2005 ¹⁰¹	(meas) mg/dL	Metformin, 215	Rosiglitazone + metformin, 220	2500 (esc) 3000	4 (esc) 8 2000 (fixed)	111.9 (109.7, 114.1 [†]) 114.9 (112.6, 117.2 [†]) 3	109.5 (107.1, 111.8 [†]) 125.9 (122.9, 128.9 [†]) 16.4	-13.4	NR	NR

Appendix F: Evidence Table 11. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: low density lipoprotein

Author, year Study group	Outcome (calc or meas) Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Gomez-Perez, 2002 ¹⁰²	(calc) mg/dL	Metformin + placebo, 34	Rosiglitazone + metformin, 36	2500 (fixed)	2500 (fixed) 4 bid (fixed)	116 (27.7) 115 -1 (20.9)	106.9 (25.7) 123.5 16.6 (24.7)	-15.9 (-4.73, -27 [†])	<0.05 vs. GP2	
Gomez-Perez, 2002 ¹⁰²	(calc) mg/dL	Metformin + placebo, 34	Rosiglitazone + metformin, 35	2500 (fixed)	2500 (fixed) 2 bid (fixed)	116 (27.7) 115 -1 (20.9)	108.2 (30) 114.3 6.1 (22.5)	-7.1	NSG vs. GP2	
Fonseca, 2000 ¹⁰³	(calc) mg/dL	Metformin + placebo, 104	Rosiglitazone + metformin, 108	2500 (fixed)	4 (fixed) 2500 (fixed)	118.17 (34.32) 122.07 (37.83) 3.9	116.61 (30.42) 134.94 (33.54) 18.33	-14.04		<0.0001 vs. GP1
Fonseca, 2000 ¹⁰³	(calc) mg/dL	Metformin + placebo, 104	Rosiglitazone + metformin, 102	2500 (fixed)	8 (fixed) 2500 (fixed)	118.17 (34.32) 122.07 (37.83) 3.9	113.49 (32.76) 134.55 (40.56) 21.06	-17.16		<0.0001 vs. GP1
Metformin vs. Metformin + Second Generation Sulfonylurea										
Garber, 2003 ⁸⁰	(meas) mg/dL	Metformin, 164	Metformin + glyburide (no trade drug specified), 171	500 (esc) 2000	250 (esc) 1000 1.25 (esc) 5	122.7 (3.2) 115 -5.7	118.3 (3.5) 122.8 4.5	-10.2	<0.05 vs. baseline	<0.05 vs. baseline
Goldstein, 2003 ³²	(meas) mg/dL	Metformin, 67	Metformin + glipizide	500 (esc) 2000	500 (esc) 2000 5 (esc) 20	109.7 (35.2) 102.5 -7.2 (-15, 0.6 [†])	119.7 (29.5) 119.5 -0.2 (-6.7, 6.3 [†])	-7	NR	NR

Appendix F: Evidence Table 11. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: low density lipoprotein

Author, year Study group	Outcome (calc or meas) Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Blonde, 2002 ⁸¹	NR	Metformin, 153	Metformin + glyburide (no trade drug specified), 160	500 (esc) 2000	500 (esc) 2000 2.5 (esc) 10	NR NR NR	NR NR NR	NR	NSG vs. GP2	
Blonde, 2002 ⁸¹	NR	Metformin, 153	Metformin + glyburide (no trade drug specified), 162	500 (esc) 2000	500 (esc) 2000 5 (esc) 20	NR NR NR	NR NR NR	NR	NSG vs. GP2	
Marre, 2002 ⁸⁴	(meas) mg/dL	Metformin, 104	Metformin + glibenclamide, 101	500 (esc) 2000	500 (esc) 2000 2.5 (esc) 10	148.2 (39) 136.5 -11.7 (31.2)	152.1 (42.9) 144.3 -7.8 (27.3)	-3.9	NSG vs. baseline and vs. GP2	NSG vs. baseline
Marre, 2002 ⁸⁴	(meas) mg/dL	Metformin, 104	Metformin + glibenclamide, 103	500 (esc) 2000	500 (esc) 2000 5 (esc) 20	148.2 (39) 136.5 -11.7 (31.2)	152.1 (35.1) 144.3 -7.8 (27.3)	-3.9	NSG vs. baseline and vs. GP2	NSG vs. baseline
Hermann, 1994 ⁸⁷	(calc) mg/dL	Metformin + diet, 19	Metformin + glyburide + diet, 46	1000 (esc) 3000	500 (esc) 1500 1.75 (esc) 5.25	142.74 (SE 9.75) 131.82 (SE 8.97) -5.85 (SE 2.73)	143.13 (SE 5.46) 139.62 (SE 4.68) -2.73 (SE 2.34)	-3.12	NR	NR
Hermann, 1991 ¹⁵⁹	(calc) mg/dL	Metformin + diet, 28	Metformin + glibenclamide + diet, 60	1000 (esc) 3000	3000 (fixed) 1.75 (esc) 14	NR NR 0.78 (SE 3.9)	NR NR -6.24 (SE 2.34)	7.02	<0.05 vs. GP2	

Appendix F: Evidence Table 11. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: low density lipoprotein

Author, year Study group	Outcome (calc or meas) Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
DeFronzo, 1995 ⁸⁸	(calc) mg/dL	Metformin + placebo, 210	Metformin + glyburide (no trade drug specified), 213	500 (esc) 2500	500 (esc) 2500 10 (esc) 20	134 (SE 3) 129 (SE 3) -6 (SE 2)	137 (SE 3) 128 (SE 3) -8 (SE 2)	2	NSG vs. GP2	
Other Metformin Comparisons										
Fujioka, 2003 ¹⁰⁵	(meas) mg/dL	Metformin + placebo + diet, 71	Metformin XR + placebo + diet, 71	1000 (esc) 1500	1000 (esc) 2000	122 (30) 118 -4 (-9, 1 [†])	116 (34) 110 -6 (-11, -1 [†])	2	NR	NR
Fujioka, 2003 ¹⁰⁵	(meas) mg/dL	Metformin + placebo + diet, 71	Metformin XR + placebo + diet, 75	1000 (esc) 1500	1000 (esc) 1500	122 (30) 118 -4 (-9, 1 [†])	124 (33) 118 -6 (-11, -1 [†])	2	NR	NR
Derosa, 2003 ⁹⁷	(meas) mg/dL	Metformin + diet + exercise, 56	Repaglinide + diet + exercise, 56	500 bid (esc) 2500	0.5 bid (esc) 4	132.21 (26.13) 117 -15.21 (-34.32, -8.19 [†])	127.14 (25.35) 115.05 -12.09 (-29.05, 20.28 [†])	-3.12	<0.05 vs. baseline >0.05 vs. GP2	0.065 vs. baseline
Second Generation Sulfonylurea vs. Meglitinide										
Derosa, 2003 ¹¹⁸	(calc) mg/dL	Glimepiride + placebo, 62	Repaglinide + placebo, 62	1 (esc) 3 mean final dose	1 (esc) 2.5 mean final dose	142 (24) 136 (25) -6	139 (22) 132 (18) -7	1	NSG vs. GP2	
Vakkilainen, 2002 ¹²²	NR	Glibenclamide + placebo, 20	Nateglinide + placebo, 23	5 (esc) 10	120 tid (fixed)	NR NR NR	NR NR NR	NR	NSG vs. baseline	NSG vs. baseline

Appendix F: Evidence Table 11. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: low density lipoprotein

Author, year	Outcome (calc or meas)	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Study group	Units									
Marbury, 1999 ¹¹⁶	(meas) mg/dL	Glyburide (no trade drug specified) + placebo	Repaglinide	2.5 (esc) 15	0.5 (esc) 12	NR NR -6.51	NR NR -5.03	-1.48 (-6.499, 3.532 [†])	NSG vs. GP2	
Second Generation Sulfonylurea vs. Thiazolidinedione + Second Generation Sulfonylurea										
Rosenstock, 2006 ¹²⁴	(calc) %	Glipizide + placebo, 57	Rosiglitazone + glipizide, 90	10 (esc) 20	4 (fixed) 10 (esc) 20	NR NR -1.30% [†]	NR NR 3.30% [†]	-4.60%	NR	NR
Baksi, 2004 ¹²⁵	(meas) mg/dL	Gliclazide, 187	Rosiglitazone + gliclazide, 189	160 (esc) 320	160 (fixed) 4 bid (fixed)	117 [#] 117 [#] 0	124.8 [#] 136.5 [#] 11.7	-11.7 (-14, -7.7 [†])		
Kerenyi, 2004 ¹²⁵	(meas) mg/dL	Glibenclamide + diet, 130	Rosiglitazone + glibenclamide + diet, 132	7.5 (esc) 15	4 bid (fixed) 7.5 (fixed)	123.63 115.05 -8.58	125.19 136.11 10.92	-19.50	NR	NR
Second Generation Sulfonylurea vs. Metformin + Second Generation Sulfonylurea										
Garber, 2003 ³⁰	(meas) mg/dL	Glyburide (no trade drug specified), 151	Metformin + glyburide (no trade drug specified), 171	2.5 (esc) 10	250 (esc) 1000 1.25 (esc) 5	122.2 (3.2) 124.5 2.3	118.3 (3.5) 122.5 4.5	-2.2	NSG vs. baseline	<0.05 vs. baseline
Goldstein, 2003 ³²	(meas) mg/dL	Glipizide	Metformin + glipizide	30 (fixed)	500 (esc) 2000 5 (esc) 20	111.2 (34.6) 110.8 -0.4 (-6.7, 5.8 [†])	119.7 (29.5) 119.5 -0.2 (-6.7, 6.3 [†])	-0.2	NSG vs. baseline	NSG vs. baseline

Appendix F: Evidence Table 11. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: low density lipoprotein

Author, year Study group	Outcome (calc or meas) Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Marre, 2002 ³⁴	(meas) mg/dL	Glibenclamide, 103	Metformin + glibenclamide, 101	5 (esc) 20	500 (esc) 2000 2.5 (esc) 10	152.1 (42.9) 148.2 -3.9 (39)	152.1 (42.9) 144.3 -7.8 (27.3)	3.9	NSG vs. baseline and vs. GP2	NSG vs. baseline
Marre, 2002 ³⁴	(meas) mg/dL	Glibenclamide, 103	Metformin + glibenclamide, 103	5 (esc) 20	500 (esc) 2000 5 (esc) 20	152.1 (42.9) 148.2 -3.9 (39)	152.1 (35.1) 144.3 -7.8 (27.3)	3.9	NSG vs. baseline and vs. GP2	NSG vs. baseline
Hermann, 1994 ³⁷	(calc) mg/dL	Glyburide + diet, 19	Metformin + glyburide + diet, 17	3.5 (esc) 10.5	2000 (esc) 3000 7.0 (esc) 14.0	153.27 (SE 5.46) 157.56 (SE 5.07) 4.68 (SE 3.51)	157.56 144.69 (SE 7.41) -12.48 (SE 4.68)	17.16		0.019 vs. baseline
Hermann, 1991 ¹⁵⁹	(calc) mg/dL	Glibenclamide + diet, 28	Metformin + glibenclamide + diet, 60	3.5 (esc) 14	500 (esc) 3000 1.75 (esc) 14	NR NR 5.07 (SE 7.41)	NR NR -6.24 (SE 2.34)	11.31	<0.05 vs. GP2	
DeFronzo, 1995 ⁸⁸	(calc) mg/dL	Glyburide + placebo, 209	Metformin + glyburide, 213	5 bid (esc) 10 bid	500 (esc) 2500 10 (esc) 20	136 (SE 3) 141 (SE 3) 3 (SE 2)	137 (SE 3) 128 (SE 3) -8 (SE 2)	11	0.001 vs. GP2	

Appendix F: Evidence Table 11. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: low density lipoprotein

Author, year Study group	Outcome (calc or meas) Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Gregorio, 1999 ¹²⁹	(calc) mg/dL	Glibenclamide or gliclazide, 85	Metformin + glibenclamide or metformin + gliclazide, 89	10 (esc) 15 120 (esc) 240	850 (esc) 1700 NR (fixed) NR (fixed)	169.26 (SE 4.68) 164.58 (5.46) -4.68	176.28 (SE 5.46) 161.46 (SE 4.68) -14.82	10.14	<0.05 vs. baseline	
Pioglitazone vs. Placebo										
Nishio, 2006 ¹⁵¹	(meas) mg/dL	Pioglitazone, 26	Control group (no placebo), 28	30 (fixed)	NA	123.24 (30.81) 118.17 (37.44) -5.07	116.22 (22.62) 115.83 (25.35) -0.39	-4.68	0.352 vs. baseline 0.865 between final means	
Smith, 2005 ¹⁶¹	(meas) mg/dL	Pioglitazone + diet, 21	Placebo + diet, 21	30 (esc) 45	NA	107.4 (32.97) 125.69 18.29 (26.86)	103.51 (23.22) 110.29 6.78 (18.97)	11.51	0.3538 vs. placebo	
Saad, 2004 ¹⁶⁴	(meas) %	Pioglitazone, 22	Placebo, 20	45 (fixed)	NA	NR NR 11.60% [†]	NR NR 0.20% [†]	11.4%	NR	NR
Takagi, 2003 ⁷⁵	(calc) mg/dL	Pioglitazone, 23	Control group (conventional antidiabetic therapy), 21	30 (fixed)	NR	134 (24) 136 (16) 2	144 (29) 134 (28) -10	12	0.9813 between- group differenc e at f/u	
Rosenblatt, 2001 ¹⁶²	(calc) mg/dL	Pioglitazone, 101	Placebo, 96	30 (NR)	NA	129.87 (35.49) 136.1 4.8% (2.5% ^{†*})	134.94 (37.05) 141.68 5% (2.5% ^{†*})	-.051	NSG vs. baseline	NSG vs. baseline

Appendix F: Evidence Table 11. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: low density lipoprotein

Author, year Study group	Outcome (calc or meas) Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Aronoff, 2000 ¹⁶⁵	(calc) mg/dL	Pioglitazone, 67	Placebo, 66	7.5 (fixed)	NA	122.9 (4.52) 127.2 (3.68) -4.3	138.8 (4.54) 141.9 (5.1) -3.1	1.2	NSG vs. GP2	
Aronoff, 2000 ¹⁶⁵	(calc) mg/dL	Pioglitazone, 64	Placebo, 66	15 (fixed)	NA	131.9 (4.64) 138.2 (4.52) -6.3	138.8 (4.54) 141.9 (5.1) -3.1	3.2	NSG vs. GP2	
Aronoff, 2000 ¹⁶⁵	(calc) mg/dL	Pioglitazone, 74	Placebo, 66	30 (fixed)	NA	135.6 (4.33) 139.4 (5.1) 3.8	138.8 (4.54) 141.9 (5.1) 3.7	0.7	NSG vs. GP2	
Aronoff, 2000 ¹⁶⁵	(calc) mg/dL	Pioglitazone, 65	Placebo, 66	45 (fixed)	NA	126.8 (4.6) 135.4 (4.43) -8.6	138.8 (4.54) 141.9 (5.1) -3.1	5.5	NSG vs. GP2	
Kipnes, 2001 ¹⁶⁶	(calc) mg/dL	Pioglitazone + unspecified sulfonylurea, 155	Unspecified sulfonylurea + placebo, 151	30 (fixed) NR (fixed)	NR (fixed)	127 (121, 132 [†]) 130 (126, 134 [†]) 3	124 (118, 130 [†]) 131 (127, 135 [†]) 7	-4	NSG vs. GP2	
Kipnes, 2001 ¹⁶⁶	(calc) mg/dL	Pioglitazone + unspecified sulfonylurea, 150	Unspecified sulfonylurea + placebo, 151	15 (fixed) NR (fixed)	NR (fixed)	124 (118, 130 [†]) 128 (124, 132 [†]) 4	124 (118, 130 [†]) 131 (127, 135 [†]) 7	-3	NSG vs. GP2	

Appendix F: Evidence Table 11. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: low density lipoprotein

Author, year Study group	Outcome (calc or meas) Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Einhom, 2000 ¹⁶⁰	(calc) mg/dL	Pioglitazone + metformin + diet, 129	Metformin + placebo + diet, 125	30 (fixed) NR (NR)	NR (NR)	119.3 (3.07) 128.5 7.7% [†]	118 (6.9) 132 11.9% [†]	4.2%	<0.05 vs. baseline	
Tseng, 2005 ¹⁴⁰	(meas) %	Pioglitazone + unspecified sulfonylurea, 23	Unspecified sulfonylurea + placebo, 25	30 (fixed) NR (NR)	NR (NR)	NR NR 12.3% [†]	NR NR 2.20% [†]	10.1% [†]	>0.05 vs. baseline	>0.05 vs. baseline
Rosiglitazone vs. Placebo										
Kim, 2005 ¹⁵²	(meas) mg/dL	Rosiglitazone + diet + exercise, 60	Diet + exercise, 60	4 (fixed)	NA	121.29 (40.95) 126.36 (34.32) 5.07	120.12 (32.76) 117.78 (32.37) -2.34	7.41	>0.05 vs. baseline	>0.05 vs. baseline
Natali, 2004 ¹⁴⁴	(meas) mg/dL	Rosiglitazone	Placebo	4 bid (fixed)	NA	120 (SE 29) 131 11	124 (SE 26) 121 -3	13 (-2, 20 [†])	NSG vs. GP2	
Virtanen, 2003 ¹⁴³	(meas) mg/dL	Rosiglitazone + diet, 14	Placebo + diet, 14	2 bid (esc) 8 bid	NA	113.1 (SE 7.8) 136.5 (SE 28) 23.4	97.5 (SE 7.8) 105.3 (SE 7.8) 7.8	15.6	<0.05 vs. placebo	
Lebovitz, 2001 ¹⁶⁹	(meas) mg/dL	Rosiglitazone, 169	Placebo, 158	4 bid (fixed)	NA	125.19 (37.05) 148.98 23.79 (31.59)	122.85 (37.44) 128.43 5.85 (25.35)	18.21	<0.05 vs. baseline	<0.05 vs. baseline

Appendix F: Evidence Table 11. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: low density lipoprotein

Author, year Study group	Outcome (calc or meas) Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Lebovitz, 2001 ¹⁶⁹	(meas) mg/dL	Rosiglitazone, 166	Placebo, 158	2 bid (fixed)	NA	122.07 (34.71) 138.84 16.77 (27.3)	122.85 (37.44) 128.43 5.85 (25.35)	11.19	<0.05 vs. baseline	<0.05 vs. baseline
Patel, 1999 ¹⁶⁷	(calc) mg/dL	Rosiglitazone, 79	Placebo, 74	2.0 bid (fixed)	NA	125.6 142.5 16.9 (SE 2.52)	130.2 131.8 1.6 (SE 2.6)	15.3 (6.9, 23.8 [†])	0.0001 vs. GP2	
Patel, 1999 ¹⁶⁷	(calc) mg/dL	Rosiglitazone, 79	Placebo, 74	1.0 bid (fixed)	NA	126.3 129.6 3.3 (SE 2.6)	130.2 131.8 1.6 (SE 2.6)	1.7 (-6.8, 10.2 [†])	NSG vs. GP2	
Patel, 1999 ¹⁶⁷	(calc) mg/dL	Rosiglitazone, 72	Placebo, 74	0.25 bid (fixed)	NA	127.8 130.8 3 (SE 2.69)	130.2 131.8 1.6 (SE 2.6)	1.4 (-7.3, 10.1 [†])	NSG vs. GP2	
Patel, 1999 ¹⁶⁷	(calc) mg/dL	Rosiglitazone, 70	Placebo, 74	0.05 bid (fixed)	NA	121.3 122.0 0.7 (SE 2.73)	130.2 131.8 1.6 (SE 2.6)	-0.9 (-9.6, 7.9 [†])	NSG vs. GP2	
Phillips, 2001 ¹⁶⁸	(calc) mg/dL	Rosiglitazone, 146	Placebo, 97	2 bid (fixed)	NA	131.04 [#] 145.08 [#] 9.5% [¶] (6.2%, 13.3% [†])	127.92 [#] 125.19 [#] 1.7% [¶] (1.6%, 4.9% [†])	7.4% ^{¶¶} (1.7%, 13.6% [†])	<0.05 vs. GP2	

Appendix F: Evidence Table 11. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: low density lipoprotein

Author, year Study group	Outcome (calc or meas) Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Phillips, 2001 ¹⁶⁸	(calc) mg/dL	Rosiglitazone, 128	Placebo, 97	4 od (fixed)	NA	125.97 [#] 140.4 [#] 10.6% [¶] (7.1%, 14.4% [‡])	127.92 [#] 125.19 [#] 1.7% [¶] (1.6%, 4.9% [‡])	8.7% ^{¶¶} (2.8%, 14.7% [‡])	<0.05 vs. GP2	
Phillips, 2001 ¹⁶⁸	(calc) mg/dL	Rosiglitazone, 113	Placebo, 97	8 od (fixed)	NA	130.26 [#] 151.32 [#] 18.3% [¶] (12.6%, 24.2% [‡])	127.92 [#] 125.19 [#] 1.7% [¶] (1.6%, 4.9% [‡])	16.5% [¶] (8.3%, 24.7% [‡])	<0.05 vs. GP2	
Phillips, 2001 ¹⁶⁸	(calc) mg/dL	Rosiglitazone, 128	Placebo, 97	4 bid (fixed)	NA	125.97 [#] 141.18 [#] 14.3% [¶] (10.3%, 18.6% [‡])	127.92 [#] 125.19 [#] 1.7% [¶] (1.6%, 4.9% [‡])	12.2% [¶] (5.7%, 18.8% [‡])	<0.05 vs. GP2	
Vongthava- ravat, 2002 ¹⁷⁰	(calc) mg/dL	Rosiglitazone + unspecified sulfonylurea + diet, 164	Unspecified sulfonylurea + diet, 170	2 bid (fixed)	NR	130 (SE 3.3) 135 (SE 3.9) 5	130 (SE 3) 125 (SE 2.4) -5	10	NR	NR
Wolffen-buttel, 2000 ¹⁷¹	(calc) mg/dL	Rosiglitazone + unspecified sulfonylurea, 183	Unspecified sulfonylurea + placebo, 192	2 bid (fixed) NR (fixed)	NR (fixed)	140.4 (31.2) 148.2 (39) 7.8	140.4 (31.2) 140.4 (31.2) 0	7.8	0.0006 vs. baseline	0.9664 vs. baseline 0.0030 vs. GP1

Appendix F: Evidence Table 11. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: low density lipoprotein

Author, year Study group	Outcome (calc or meas) Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Wolffen-buttel, 2000 ¹⁷¹	(calc) mg/dL	Rosiglitazone + unspecified sulfonylurea, 199	Unspecified sulfonylurea + placebo, 192	1 bid (fixed) NR (fixed)	NR (fixed)	132.6 (35.1) 136.5 (35.1) 3.9	140.4 (31.2) 140.4 (31.2) 0	3.9	0.1747 vs. baseline 0.7921 vs. GP2	0.9664 vs. baseline
Barnett, 2003 ¹⁷²	NR	Rosiglitazone + unspecified sulfonylurea, 84	Unspecified sulfonylurea + placebo, 87	4 bid (fixed) NR (NR)	NR (NR)	NR NR NR	NR NR NR	NR	NSG vs. baseline	NSG vs. baseline
Metformin vs. Placebo										
Natali, 2004 ¹⁴⁴	(meas) mg/dL	Metformin	Placebo	500 tid (fixed)	NA	118 (SE 29) 120 2 (SE 6)	124 (SE 26) 121 -3 (SE 2)	5	NR	NR
Virtanen, 2003 ¹⁴³	(meas) mg/dL	Metformin + diet, 13	Placebo + diet, 14	500 bid (esc) 1000 bid	NA	109.2 (SE 7.8) 101.4 (SE 7.8) -7.8	97.5 (SE 7.8) 105.3 (SE 7.8) 7.8	-15.6	>0.05 vs. GP2	
Rachmani, 2002 ¹⁵⁰	(meas) mg/dL	Metformin continued + diet, 195	Metformin stopped + diet, 198	NR	NA	139.62 (SE 7.8) 138.84 -0.78	140.4 (SE 3.9) 143.52 3.12	-3.9	NSG vs. baseline NSG vs. GP2	
DeFronzo, 1995 ⁸⁸	(calc) mg/dL	Metformin, 143	Placebo, 146	850 (esc) 850 tid	NA	136 (SE 3) 123 (SE 3) -11 (SE 3)	138 (SE 3) 135 (SE 3) -2 (SE 2)	-9	0.019 vs. GP2	
Second Generation Sulfonylurea vs. Placebo										

Appendix F: Evidence Table 11. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: low density lipoprotein

Author, year	Outcome (calc or meas)	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Study group	Units									
Rosenstock, 1996 ¹⁸⁹	NR	Glimepiride	Placebo, 66	4 bid (fixed) or 8 od (fixed) or 16 od (fixed) or 8 bid (fixed)	NA	NR NR NR	NR NR NR	NR	0.018 vs. GP2	
Repaglinide vs. Placebo										
Goldberg, 1998 ¹³⁹	(meas) mg/dL	Repaglinide, 56	Placebo, 23	0.25 tid (esc) 8.0	NA	NR NR 15.21	NR NR 11.7	1.326	0.718 vs. GP2	
Alpha-Glucosidase Inhibitor vs. Placebo										
Hasche, 1999 ¹³⁸	(calc) mg/dL	Acarbose + diet, 28	Placebo + diet, 32	50 bid (esc) 100 tid	NA	159.7 (31.2) 151.6 (30.5) -8.1	170 (31.9) 163.6 (38.2) -6.4	-1.7	NR	NR
Rosenbaum, 2002 ¹⁵³	(calc) mg/dL	Acarbose, 20	Placebo, 20	50 bid (esc) 100 tid	NA	300.3 (66.3) 288.6 (66.3) -11.7	327.6 (97.5) 319.8 (54.6) -7.8	-3.9	0.34 vs. baseline	0.47 vs. baseline
Other Second Generation Sulfonylurea Comparisons										
Schern-thaner, 2004 ¹⁰⁶	(calc) mg/dL	Glimepiride + existing medications + diet, 440	Gliclazide + existing medications + diet, 405	1 (esc) 6	30 (esc) 120	124.8 124.8 0	128.7 124.8 -3.9	3.9	NSG vs. baseline	NSG vs. baseline

Calc = calculated; Meas = measured; Comp = comparison; BL = baseline; GP = group; mg = milligrams; dL = deciliter; max = maximum; esc = escalated; diff = difference; NR = not reported; NSG = not significant; NA = not applicable; SD = standard deviation; SE = standard error; od = once daily; bid = twice daily; tid = three times daily; HbA1c = hemoglobin A1c; f/u = follow-up; XR = extended release; vs = versus

* Number obtained from a figure

† Percent change from baseline

‡ 95% confidence interval

Appendix F: Evidence Table 11. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: low density lipoprotein

Median

¶ Median percent change from baseline

¶¶ Median percent difference from placebo

Appendix F: Evidence Table 12. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: high density lipoprotein

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Thiazolidinedione vs. Thiazolidinedione											
Khan, 2002 ⁵¹	mg/dL	Rosiglitazone, 60	Pioglitazone, 67	2-8 (fixed)	15-45 (fixed)	45.3 (15.2) 48.6 1.5*	44.7 (15.6) 46.7 2.0*	-0.5	NSG vs. baseline and vs. GP2	NSG vs. baseline	
Goldberg, 2005 ⁵²	mg/dL	Rosiglitazone + diet, 356	Pioglitazone + diet, 363	4 (esc) 8	30 (esc) 45	39.8 (SE 0.6) 42.2 2.4 (SE 0.5)	38.8 (SE 0.5) 44 5.2 (SE 0.5)	-2.8	<0.001 vs. GP2		
Derosa, 2005 ¹⁵⁶	mg/dL	Rosiglitazone + glimepiride + diet + exercise, 42	Pioglitazone + glimepiride + diet + exercise, 45	4 (fixed) 4 (fixed)	15 (fixed) 4 (fixed)	42 (5) 43 (4) 1	40 (4) 46 (5) 6	-5	NSG vs. baseline	<0.05 vs. baseline and vs. GP1	
Thiazolidinedione vs. Metformin											
Natali, 2004 ¹⁴⁴	mg/dL	Rosiglitazone	Metformin	4 bid (fixed)	500 tid (fixed)	46 (SEM 9) 50 4	46 (SEM 15) 49 3	0.4 (-5, 6 ⁺)	NSG vs. GP2		
Virtanen, 2003 ¹⁴³	mg/dL	Rosiglitazone + diet	Metformin + diet	2 bid (esc) 4 bid	500 bid (esc) 1000 bid	42.9 (SE 3.9) 46.8 (SE 3.9) 3.9	42.9 (SE 3.9) 46.8 (SE 3.9) 3.9	0	NSG vs. baseline	NSG vs. baseline	
Lawrence, 2004 ⁵⁴	mg/dL	Pioglitazone, 20	Metformin, 20	30 (esc) 45	500 bid (esc) 1000 tid	49.6 (11.8) 52.7 (11.1) 3.1	48.7 (9.4) 46.8 (8.5) -1.9	5	<0.05 vs. baseline 0.026 vs. GP2	NSG vs. baseline	

Appendix F: Evidence Table 12. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: high density lipoprotein

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Pavo, 2003 ⁵⁹	mg/dL	Pioglitazone + placebo, 100	Metformin + placebo, 91	30 (esc) 45	850 (esc) 2550	NR NR 8.58	NR NR 5.07	3.51	0.02 vs. GP2		
Ramachan- dran, 2004 ⁵⁵	mg/dL	Pioglitazone + diet, 23	Metformin + diet, 21	15 (esc) 30	250 (esc) 850	38.22 (5.85) 42.9 (7.8) 4.68	39 (7.8) 42.9 (11.7) 3.9	0.78	<0.01 vs. baseline		
Schern-thaner, 2004 ⁵⁶	mg/dL	Pioglitazone + placebo + diet	Metformin + placebo + diet	30 (esc) 45	850 up to 3 times/day (esc) 2550	44.07 50.31 6.24	44.07 47.19 3.12	3.12	0.001 vs. GP2		
Yamanouchi, 2005 ⁵⁷	mg/dL	Pioglitazone + diet + exercise, 38	Metformin + diet + exercise, 39	30 for women and 45 for men (fixed)	750 (fixed)	53.82 (4.68) 58.11 (3.51) 4.29	51.87 (3.51) 51.48 (4.68) -0.39	4.68	NSG vs. baseline and vs. GP2	NSG vs. baseline	
Hanefeld, 2004 ⁶⁰ QUARTET study group Betteridge, 2005 ¹⁵⁷	mg/dL	Pioglitazone + unspecified sulfonylurea + placebo, 319	Metformin + unspecified sulfonylurea + placebo, 320	15 (esc) 45 NR	850 (esc) 850 tid NR	42.51 (9.36) 48.75 (0.39) 6.24	43.29 (10.53) 46.41 (0.39) 3.12	3.12	<0.0001 vs. GP2		

Appendix F: Evidence Table 12. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: high density lipoprotein

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Thiazolidinedione vs. Second Generation Sulfonylurea											
Pfutzner, 2005 ⁶⁸ Forst, 2005 ¹⁴⁵ Langenfeld, 2005 ¹⁴⁶	mg/dL	Pioglitazone, 89	Glimepiride, 84	45 (fixed)	1 (esc) 6	46 (11) 54 (13) 8	46 (14) 47 (12) 1	7	0.001 vs. GP2		
Tan, 2004 ⁶⁵	mg/dL	Pioglitazone, 91	Glibenclamide, 109	30 (esc) 45	1.75 (esc) 10.5	46.02 54.21 8.19	43.68 44.85 1.17	7.02	<0.001 vs. baseline and vs. GP2	NSG vs. baseline	
Charbonnel, 2005 ⁶³	mg/dL	Pioglitazone	Gliclazide	NR (esc) 45	NR (esc) 320	40.17 48.75 8.58	40.56 42.9 2.34	6.24 (5.07, 6.63 [†])	<0.001 vs. baseline and vs. GP2	NSG vs. baseline	
Lawrence, 2004 ⁵⁴	mg/dL	Pioglitazone, 20	Gliclazide, 20	30 (esc) 45	80 od (esc) 160 bid	49.6 (11.8) 52.7 (11.1) 3.1	49.5 (9.8) 48.3 (10.1) -1.2	4.3	<0.05 vs. baseline	NSG vs. baseline	
Yanagawa, 2004 ⁶²	mg/dL	Pioglitazone, 19	Gliclazide, 21	NR	NR	57 (13) NR NR	50 (14) NR NR	NR	NSG vs. GP2		
Ramachan- dran, 2004 ⁵⁵	mg/dL	Pioglitazone + diet, 23	Glimepiride + diet, 18	15 (esc) 30	1 (esc) 2	38.22 (5.85) 42.9 (7.8) 4.68	37.05 (11.7) 42.9 (7.8) 5.85	-1.17	<0.01 vs. baseline	NSG vs. baseline	

Appendix F: Evidence Table 12. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: high density lipoprotein

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2	Other
Yamanouchi, 2005 ⁵⁷	mg/dL	Pioglitazone + diet + exercise, 38	Glimepiride + diet + exercise, 37	30 for women and 45 for men (fixed)	1.0 (esc) 2.0	53.82 (4.68) 58.11 (3.51) 4.29	52.65 (4.29) 52.26 (4.29) -0.39	4.68	NSG vs. baseline and vs. GP2	NSG vs. baseline	
Betteridge, 2005 ¹⁵⁷	mg/dL	Pioglitazone + metformin, 317	Metformin + gliclazide, 313	15 (esc) 45 NR	80 (esc) 320 NR	42.9 (9.75) 52.65 9.75 (SEM 0.30)	42.51 (8.97) 45.72 3.21 (SEM 0.39)	6.54	NR	NR	
Thiazolidinedione + Metformin vs. Second Generation Sulfonylurea + Metformin											
Garber, 2006 ¹¹	mg/dL	Rosiglitazone + metformin + diet, 117	Metformin + glibenclamide + diet, 122	4 (esc) 8 1500-2000 (esc) 2000	1000 (esc) 2000 5 (esc) 10	45 48 3 (10)	47 45 -2 (10)	4 (1, 7 [†])	<0.05 vs. GP2		
Derosa, 2005 ¹⁵⁸	mg/dL	Rosiglitazone + metformin + diet + exercise + behavioral therapy, 48	Metformin + glimepiride + diet + exercise + behavioral therapy, 47	4 (fixed) 1500 (fixed)	1500 (fixed) 2 (fixed)	42 (4) 44 (3) 2	43 (5) 43 (4) 0	2	NSG vs. GP2		
Thiazolidinedione vs. Meglitinide											
Raskin, 2004 ⁷⁴	mg/dL	Rosiglitazone, 37	Repaglinide, 37	2 bid (esc) 4 bid	0.5 tid if HbA1c≤8%, 1 tid if HbA1c>8% (esc) 4 tid	39.9 (10.6) 42.5 (11.3) 2.6	39.2 (10.5) 40.5 (11.5) 1.3	1.3	NR	NR	
Jovanovic, 2004 ⁷³	mg/dL	Pioglitazone, 26	Repaglinide, 35	30 (fixed)	0.5 tid if HbA1c≤8%, 1 tid if HbA1c>8% (esc) 4 tid	41 (8.8) 47.2 (9.4) 6.2	45.4 (12.5) 44.6 (11.8) -0.8	7	NR	NR	

Appendix F: Evidence Table 12. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: high density lipoprotein

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2	Other
Thiazolidinedione vs. Alpha-Glucosidase Inhibitor											
Goke, 2002 ⁷⁶	mg/dL	Pioglitazone, 129	Acarbose, 136	45 (fixed)	50 (esc) 100 tid	41.4 (12.8)	43.5 (27.9)	8.6	<0.001 vs. GP2		
German Pioglitazone Study Group						49.2	42.7				
						7.8	-0.8				
Other Thiazolidinedione Comparisons											
Choi, 2004 ⁷⁷	mg/dL	Rosiglitazone + diet, 38	Upitration of existing medications, 45	8 (other) 4	NR (esc)	39.39 (10.92)	41.34 (10.92)	1.17	<0.05 vs. baseline	NSG vs. baseline	
						43.68 (8.19)	44.46 (10.53)		NSG vs. GP2		
						4.29 (8.19)	3.12 (8.58)				
Metformin vs. Second Generation Sulfonylurea											
Garber, 2003 ⁸⁰	mg/dL	Metformin, 164	Glyburide (no trade drug specified), 151	500 (esc) 2000	2.5 (esc) 10	42.3 (0.9)	41.6 (1)	-0.9	NSG vs. baseline	NSG vs. baseline	
						41.9	42.1				
						-0.4	0.5				
Goldstein, 2003 ⁸²	mg/dL	Metformin, 67	Glipizide	500 (esc) 2000	15 bid (fixed)	42.3 (9.7)	43.5 (9.8)	0	NSG vs. baseline	NSG vs. baseline	
						42.7	43.9				
						0.4	0.4				
Campbell, 1994 ⁸³	mg/dL	Metformin, 24	Glipizide, 24	500 bid (esc) 3000	5 (esc) 30	35.88 (11.31)	36.27 (8.58)	1.17	NSG vs. GP2		
						37.05 (11.31)	36.27 (8.58)				
						1.17	0				

Appendix F: Evidence Table 12. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: high density lipoprotein

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Marre, 2002 ⁸⁴	mg/dL	Metformin, 104	Glibenclamide, 103	500 (esc) 2000	5 (esc) 20	46.8 (11.7) 47.97 1.17	46.8 (11.7) 47.19 0.39	0.78	NSG vs. baseline and vs. GP2	NSG vs. baseline	
Amador- Licona, 2000 ⁸⁵	mg/dL	Metformin, 28	Glibenclamide, 23	850 (esc) NR	5 (esc) NR	31.98 (8.97) 35.49 (8.97) 3.51	36.66 (7.02) 39 (10.92) 2.34	1.17	0.0001 vs. baseline	0.01 vs. baseline	
Lawrence, 2004 ⁵⁴	mg/dL	Metformin, 20	Gliclazide, 20	500 bid (esc) 1000 tid	80 (esc) 160 bid	48.7 (9.4) 46.8 (8.5) -1.9	49.5 (9.8) 48.3 (10.1) -1.2	-0.7	NSG vs. baseline and vs. GP2	NSG vs. baseline	
Ramachan- dran, 2004 ⁵⁵	mg/dL	Metformin + diet, 21	Glimepiride + diet, 18	250 (esc) 850	1 (esc) 2	39 (7.8) 42.9 (11.7) 3.9	37.05 (11.7) 42.9 (7.8) 5.85	-1.95	NSG vs. baseline	NSG vs. baseline	
Hermann, 1994 ⁸⁷	mg/dL	Metformin + diet, 19	Glyburide + diet, 19	1000 (esc) 3000	3.5 (esc) 10.5	31.59 (SE 2.34) 30.03 (SE 1.56) 0.78 (SE 0.78)	34.71 (SE 1.95) 35.88 (SE 1.95) 1.17 (SE 0.78)	-0.39	>0.1 vs. baseline and vs. GP2	>0.1 vs. baseline	
DeFronzo, 1995 ⁸⁸	mg/dL	Metformin + placebo, 210	Glyburide (no trade drug specified) + placebo, 209	500 (esc) 2500	5 bid (esc) 10 bid	37 (SE 1) 39 (SE 1) 2	37 (SE 1) 38 (SE 1) 1	1	NR	NR	

Appendix F: Evidence Table 12. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: high density lipoprotein

Author, year						GP1 BL mean (SD)	GP2 BL mean (SD)				
Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 final mean (SD) Mean diff from BL1	GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Charpentier, 2001 ⁸⁹	mg/dL	Metformin + placebo, 75	Glimepiride + placebo, 150	850 tid (fixed)	1 (esc) 6	46.41 (13.65) 48.36 1.95	45.24 (12.87) 45.63 0.39	1.56	NR	NR	0.14 all group com- parison
Yamanouchi, 2005 ⁵⁷	mg/dL	Metformin + diet + exercise, 39	Glimepiride + diet + exercise, 37	750 (fixed)	1 (esc) 2	51.87 (3.51) 51.48 (4.68) -0.39	52.65 (4.29) 52.26 (4.29) -0.39	0	NSG vs. baseline and vs. GP2	NSG vs. baseline	
Derosa, 2004 ⁹⁰	mg/dL	Metformin + placebo + diet + exercise, 75	Glimepiride + placebo + diet + exercise, 73	1000 (esc) 1000 tid	1 (esc) 2 bid	43 (5) 45 (4) 2	42 (4) 44 (6) 2	0	NSG vs. baseline and vs. GP2	NSG vs. baseline	
Blonde, 2002 ⁸¹	NR	Metformin, 153	Glyburide (no trade drug specified), 164	500 (esc) 2000	10 bid (fixed)	NR NR NR	NR NR NR	NR	NSG vs. GP2		
Metformin vs. Thiazolidinedione + Metformin											
Weissman, 2005 ¹⁰⁰	mg/dL	Metformin, 302	Rosiglitazone + metformin, 309	1000 (esc) 2000	4 (esc) 8 1000 (fixed)	43.7 45.3 1.6	45 49.1 4.1	-2.5	NR	NR	
Bailey, 2005 ¹⁰¹	mg/dL	Metformin, 230	Rosiglitazone + metformin, 245	2500 (esc) 3000	4 (esc) 8 2000 (fixed)	47.2 46.4 -0.8	45.3 47.1 1.8	-2.6	<0.05 vs. baseline	<0.05 vs. baseline	

Appendix F: Evidence Table 12. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: high density lipoprotein

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2	Other
Fonseca, 2000 ¹⁰³	mg/dL	Metformin + placebo, 112	Rosiglitazone + metformin, 110	2500 (fixed)	8 (fixed) 2500 (fixed)	44.46 (10.92) 46.8 (11.31) 2.34	46.8 (14.43) 53.04 (16.38) 6.24	-3.9		0.0002 vs. GP1	
Fonseca, 2000 ¹⁰³	mg/dL	Metformin + placebo, 112	Rosiglitazone + metformin, 116	2500 (fixed)	4 (fixed) 2500 (fixed)	44.4 (10.92) 46.8 (11.31) 2.4	46.02 (11.31) 51.48 (13.26) 5.46	-3.06		0.0002 vs. GP1	
Gomez-Perez, 2002 ¹⁰²	mg/dL	Metformin + placebo, 34	Rosiglitazone + metformin, 35	2500 (fixed)	2500 (fixed) 2 bid (fixed)	49.4 (11.9) 48.9 -0.5 (7.2)	51.5 (10) 56.7 5.2 (7)	-5.7		<0.05 vs. GP1	
Gomez-Perez, 2002 ¹⁰²	mg/dL	Metformin + placebo, 34	Rosiglitazone + metformin, 36	2500 (fixed)	2500 (fixed) 4 bid (fixed)	49.4 (11.9) 48.9 -0.5 (7.2)	51.5 (10.9) 57.9 6.4 (7)	-6.9		<0.05 vs. GP1	
Metformin vs. Metformin + Second Generation Sulfonylurea											
Garber, 2003 ⁸⁰	mg/dL	Metformin, 164	Metformin + glyburide (no trade drug specified), 171	500 (esc) 2000	250 (esc) 1000 1.25 (esc) 5	42.3 (0.9) 41.9 -0.4	41.3 (0.9) 42.1 0.8	-1.2	NSG vs. baseline	NSG vs. baseline	
Goldstein, 2003 ⁸²	mg/dL	Metformin, 67	Metformin + glipizide	500 (esc) 2000	500 (esc) 2000 5 (esc) 20	42.3 (9.7) 42.7 0.4	43.2 (10.0) 44.1 0.9	-0.5	NSG vs. baseline	NSG vs. baseline	

Appendix F: Evidence Table 12. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: high density lipoprotein

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Marre, 2002 ⁸⁴	mg/dL	Metformin, 104	Metformin + glibenclamide, 103	500 (esc) 2000	500 (esc) 2000 5 (esc) 20	46.8 (11.7) 58.5 1.17	50.7 (11.7) 50.7 0	1.17	NSG vs. baseline and vs. GP2	NSG vs. baseline	
Marre, 2002 ⁸⁴	mg/dL	Metformin, 104	Metformin + glibenclamide, 101	500 (esc) 2000	500 (esc) 2000 2.5 (esc) 10	46.8 (11.7) 47.97 1.17	46.8 (15.6) 47.19 0.39	0.78	NSG vs. baseline and vs. GP2	NSG vs. baseline	
Hermann, 1994 ⁸⁷	mg/dL	Metformin + diet, 19	Metformin + glyburide, 46	1000 (esc) 3000	500 (esc) 1500 1.75 (esc) 5.25	31.59 (SE 2.34) 30.03 (SE 1.56) 0.78 (SE 0.78)	35.49 (SE 1.56) 37.05 (SE 1.95) 1.56 (SE 1.17)	-0.78	>0.1 vs. baseline and vs. GP2	>0.1 vs. baseline	
DeFronzo, 1995 ⁸⁸	mg/dL	Metformin + placebo, 210	Metformin + glyburide (no trade drug specified), 213	500 (esc) 2500	500 (esc) 2500 10 (esc) 20	37 (SE 1) 39 (SE 1) 2	39 (SE 1) 40 (SE 1) 1	1	NR	NR	
Charpentier, 2001 ⁸⁹	mg/dL	Metformin + placebo, 75	Metformin + glimepiride, 147	850 tid (fixed)	850 tid (fixed) 1 (esc) 6	46.41 (13.65) 60.06 0.24 (9.36)	46.41 (12.09) 45.24 -1.17 (9.87)	3.12	NR	NR	0.14 all group com- parison
Blonde, 2002 ⁸¹	NR	Metformin, 153	Metformin + glyburide (no trade drug specified), 160	500 (esc) 2000	500 (esc) 2000 2.5 (esc) 10	NR NR NR	NR NR NR	NR	NSG vs. GP2		

Appendix F: Evidence Table 12. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: high density lipoprotein

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Blonde, 2002 ⁸¹	NR	Metformin, 153	Metformin + glyburide (no trade drug specified), 162	500 (esc) 2000	500 (esc) 2000 5 (esc) 20	NR NR NR	NR NR NR	NR	NSG vs. GP2		
Feinglos, 2005 ¹⁰⁴	NR	Metformin + placebo, 56	Metformin + glipizide, 56	at least 1000 (fixed)	at least 1000 (fixed) 2.5 (fixed)	NR NR NR	NR NR NR	NR	NSG vs. baseline and vs. GP2	NSG vs. baseline	
Other Metformin Comparisons											
Derosa, 2003 ⁹⁷	mg/dL	metformin + diet + exercise, 56	repaglinide + diet + exercise, 56	500 bid (esc) 2500	0.5 bid (esc) 4	46.41 (8.19) 45.24 -1.17	42.51 (7.02) 45.63 3.12	-4.29	NSG vs. GP2		
Fujioka, 2003 ¹⁰⁵	mg/dL	Metformin + placebo + diet, 71	Metformin XR + placebo + diet, 71	1000 (esc) 1500	1000 (esc) 2000	42 (9) 44 2	45 (11) 43 -2	4	NSG vs. baseline	NSG vs. baseline	
Fujioka, 2003 ¹⁰⁵	mg/dL	Metformin + placebo + diet, 71	Metformin XR + placebo + diet, 75	1000 (esc) 1500	1000 (esc) 1500	42 (9) 44 2	42 (10) 42 0	2	NSG vs. baseline	NSG vs. baseline	
Second Generation Sulfonylurea vs. Second Generation Sulfonylurea											
Inukai, 2005 ¹¹¹	mg/dL	Glimepiride, 120	Glibenclamide or glizalazide, 52	1 or 2 (esc) 6	2.5 (fixed) 40 (fixed)	53.3 (13.6) 52.3 (12.9) -1	52.3 (15.5) 52.2 (14) -0.1	-0.9	NSG vs. GP2		

Appendix F: Evidence Table 12. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: high density lipoprotein

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Baba, 1983 ¹³³	mg/dL	Glibenclamide, 131	Glidazide, 146	2.5 (esc) 10	40 (esc) 160	NR NR NR	NR NR NR	NR	NSG vs. GP2		
Second Generation Sulfonylurea vs. Meglitinide											
Wolffen-buttel, 1999 ¹¹⁷	mg/dL	Glyburide (no trade drug specified) + placebo, 109	Repaglinide, 211	1.75 (esc) 10.5	1.5 (esc) 12	45.63 (12.48) 45.63 (12.48) 0	44.85 (14.82) 46.02 (14.43) 1.17	-1.17	NSG vs. baseline	NSG vs. baseline	
Marbury, 1999 ¹¹⁶	mg/dL	Glyburide (no trade drug specified) + placebo, 216	Repaglinide, 115	2.5 (esc) 15	0.5 (esc) 12	NR NR -0.13	NR NR -0.81	0.68 (- 0.8, 2.15 [†])	NSG vs. baseline and vs. GP2	NSG vs. baseline	
Derosa, 2003 ¹¹⁸	mg/dL	Glimepiride + placebo, 62	Repaglinide + placebo, 62	1 (esc) 3 mean final dose	1 (esc) 2.5 mean final dose	44 (5) 43 (6) -1	43 (7) 45 (7) 2	-3	NSG vs. GP2		
Madsbad, 2001 ¹¹⁹	mg/dL	Glipizide + placebo, 81	Repaglinide, 175	5 (esc) 15	0.5 (esc) 4	NR NR 0.78	NR NR 0	1.17 (1.56, - 3.5 [†])	NSG vs. baseline and vs. GP2	NSG vs. baseline	
Landgraf, 1999 ¹²¹	mg/dL	Glibenclamide + placebo	Repaglinide	1.75, 3.5, 7.0, or 10.5 (esc) 10.5	0.5, 1.0, 2.0, or 4.0 tid (esc) 4 tid	NR NR 1.11 (SE 0.03)	NR NR 1.15 (SE 0.03)	-0.04		0.005 vs. GP1	

Appendix F: Evidence Table 12. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: high density lipoprotein

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2	Other
Vakkilainen, 2002 ¹²²	NR	Glibenclamide + placebo, 20	Nateglinide + placebo, 23	5 (esc) 10	120 tid (fixed)	NR NR NR	NR NR NR	NR	NSG vs. baseline	NSG vs. baseline	
Second Generation Sulfonylurea vs. Thiazolidinedione + Second Generation Sulfonylurea											
Kerenyi, 2004 ¹²⁵	mg/dL	Glibenclamide + diet, 138	Rosiglitazone + glibenclamide + diet, 143	7.5 (esc) 15	4 bid (fixed) 7.5 (fixed)	46.02 53.04 7.02	47.19 54.21 7.02	0 NSG vs. GP2	<0.05 vs. baseline NSG vs. GP2	<0.05 vs. baseline	
Baksi, 2004 ¹²⁶	mg/dL	Gliclazide, 201	Rosiglitazone + gliclazide, 204	160 (esc) 320	160 (fixed) 4 bid (fixed)	46.8 [#] 50.7 [#] 6.8 [†]	50.7 [#] 50.7 [#] 0 [†]	6.8% [†]	<0.05 vs. baseline	NSG vs. baseline	
Rosenstock, 2006 ¹²⁴	%	Glipizide + placebo, 57	Rosiglitazone + glipizide, 90	10 (esc) 20	4 (fixed) 10 (esc) 20	NR NR 1.6 [†]	NR NR 2.7 [†]	-1.1%	NR	NR	
Second Generation Sulfonylurea vs. Metformin + Second Generation Sulfonylurea											
Garber, 2003 ⁸⁰	mg/dL	Glyburide (no trade drug specified), 151	Metformin + glyburide (no trade drug specified), 171	2.5 (esc) 10	250 (esc) 1000 1.25 (esc) 5	41.6 (1) 42.1 0.5	41.3 (0.9) 42.1 0.8	-0.3	NSG vs. baseline	NSG vs. baseline	
DeFronzo, 1995 ⁸⁸	mg/dL	Glyburide (no trade drug specified) + placebo, 209	Metformin + glyburide (no trade drug specified), 213	5 bid (esc) 10 bid	500 (esc) 2500 10 (esc) 20	37 (SE 1) 38 (SE 1) 1	39 (SE 1) 40 (SE 1) 1	0	NR	NR	

Appendix F: Evidence Table 12. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: high density lipoprotein

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Charpentier, 2001 ⁸⁹	mg/dL	Glimepiride + placebo, 150	Metformin + glimepiride, 147	1 (esc) 6	850 tid (fixed) 1 (esc) 6	45.24 (12.87) 45.63 0.39	46.41 (12.09) 45.24 -1.17	1.56	NR	NR	0.14 all group com- parison
Goldstein, 2003 ⁸²	mg/dL	Glipizide	Metformin + glipizide	30 (fixed)	500 (esc) 2000 5 (esc) 20	43.5 (9.8) 43.9 0.4	43.2 (10) 44.1 0.9	-0.5	NSG vs. baseline	NSG vs. baseline	
Marre, 2002 ⁸⁴	mg/dL	Glibenclamide, 103	Metformin + glibenclamide, 103	5 (esc) 20	500 (esc) 2000 5 (esc) 20	46.8 (11.7) 47.19 0.39	50.7 (11.7) 50.7 0	0.39	NSG vs. baseline and vs. GP2	NSG vs. baseline	
Marre, 2002 ⁸⁴	mg/dL	Glibenclamide, 103	Metformin + glibenclamide, 101	5 (esc) 20	500 (esc) 2000 2.5 (esc) 10	46.8 (11.7) 47.19 0.39	46.8 (15.6) 47.19 0.39	0	NSG vs. baseline and vs. GP2	NSG vs. baseline	
Hermann, 1994 ⁸⁷	mg/dL	Glyburide + diet, 19	Metformin + glyburide + diet, 46	3.5 (esc) 10.5	500 (esc) 1500 1.75 (esc) 5.25	34.71 (SE 1.95) 35.88 (SE 1.95) 1.17 (SE 0.78)	35.49 (SE 1.56) 37.05 (SE 1.95) 1.56 (SE 1.17)	-0.39	>0.1 vs. baseline and vs. GP2	>0.1 vs. baseline and vs. GP2	
Gregorio, 1999 ¹²⁹	mg/dL	Glibenclamide or gliclazide, 85	Metformin + glibenclamide or metformin + gliclazide, 89	10 (esc) 15 120 (esc) 240	850 (esc) 1700 NR (fixed) NR (fixed)	38.22 (SE 1.56) 42.9 (SE 1.17) 4.68	36.66 (SE 1.95) 37.44 (SE 1.17) 0.78	3.9	<0.02 vs. baseline		

Appendix F: Evidence Table 12. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: high density lipoprotein

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Blonde, 2002 ⁸¹	NR	Glyburide (no trade drug specified), 164	Metformin + glyburide (no trade drug specified), 160	10 bid (fixed)	500 (esc) 2000 2.5 (esc) 10	NR NR NR	NR NR NR	NR	NSG vs. GP2		
Blonde, 2002 ⁸¹	NR	Glyburide (no trade drug specified), 164	Metformin + glyburide (no trade drug specified), 162	10 bid (fixed)	500 (esc) 2000 5 (esc) 20	NR NR NR	NR NR NR	NR	NSG vs. GP2		
Pioglitazone vs. Placebo											
Rosenblatt, 2001 ¹⁶²	mg/dL	Pioglitazone, 101	Placebo, 96	30 (NR)	NA	40.17 (10.53) 46.5 15.8 [†]	39.78 (10.92) 40.07 3 [†]	12.8 [†]	0.0065 vs. GP2		
Herz, 2003 ¹⁶³	mg/dL	Pioglitazone, 95	Placebo, 96	30 (fixed)	NA	44.46 51.8 16 [†]	46.8 51.0 9 [†]	7 [†]	0.028 vs. GP2		
Herz, 2003 ¹⁶³	mg/dL	Pioglitazone, 96	Placebo, 96	45 (fixed)	NA	44.07 52.9 20 [†]	46.8 51.0 9 [†]	11 [†]	<0.001 vs. GP2		
Saad, 2004 ¹⁶⁴	%	Pioglitazone, 26	Placebo, 29	45 (fixed)	NA	NR NR 15.1 [†]	NR NR 2.7 [†]	12.4 [†]	NSG vs. GP2		

Appendix F: Evidence Table 12. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: high density lipoprotein

Author, year						GP1 BL mean (SD)	GP2 BL mean (SD)				
Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 final mean (SD) Mean diff from BL1	GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Nishio, 2006 ¹⁵¹	mg/dL	Pioglitazone, 26	Control group (no placebo), 28	30 (fixed)	NA	44.07 (11.7) 42.51 (12.09) -1.56	42.12 (10.92) 42.51 (11.7) 0.39	-1.95	NSG vs. baseline and vs. GP2	NSG vs. baseline	
Aronoff, 2000 ¹⁶⁵	mg/dL	Pioglitazone, 79	Placebo, 79	7.5 (fixed)	NA	40.5 (SE 1.24) 43.4 (SE 1.31) 2.9	41.7 (SE 1.24) 44.3 (SE 1.25) 2.6 (SE 2.03)	0.3	<=0.05 vs. baseline	<=0.05 vs. baseline	
Aronoff, 2000 ¹⁶⁵	mg/dL	Pioglitazone, 77	Placebo, 79	45 (fixed)	NA	40.7 (SE 1.25) 47.8 (SE 1.56) 7.1	41.7 (SE 1.24) 44.3 (SE 1.25) 2.6 (SE 2.03)	4.5	<=0.05 vs. baseline and GP2	<=0.05 vs. baseline	
Aronoff, 2000 ¹⁶⁵	mg/dL	Pioglitazone, 79	Placebo, 79	15 (fixed)	NA	40.4 (SE 1.24) 45.4 (SE 1.19) 5	41.7 (SE 1.24) 44.3 (SE 1.25) 2.6 (SE 2.03)	2.4	<=0.05 vs. baseline	<=0.05 vs. baseline	
Aronoff, 2000 ¹⁶⁵	mg/dL	Pioglitazone, 83	Placebo, 79	30 (fixed)	NA	40.8 (SE 1.21) 45 (SE 1.25) 4.2	41.7 (SE 1.24) 44.3 (SE 1.25) 2.6 (SE 2.03)	1.6	<=0.05 vs. baseline	<=0.05 vs. baseline	
Smith, 2005 ¹⁶¹	mg/dL	Pioglitazone + diet, 21	Placebo + diet, 21	30 (esc) 45	NA	47.45 (14.34) 55.22 7.77 (5.22)	46.9 (10.05) 48.34 1.44 (3.77)	6.33	0.0003 vs. GP2		

Appendix F: Evidence Table 12. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: high density lipoprotein

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2	Other
Einhom, 2000 ¹⁶⁰	mg/dL	Pioglitazone + metformin + diet, 158	Metformin + placebo + diet, 143	30 (fixed) NR (NR)	NR (NR)	42.9 (0.95) 53.1 10.2	42.1 (1) 43.6 1.5	8.7	<=0.05 vs. GP2		
Tseng, 2005 ¹⁴⁰	%	Pioglitazone + unspecified sulfonylurea, 23	Unspecified sulfonylurea + placebo, 25	30 (fixed) NR (NR)	NR (NR)	NR NR 15.5 [†]	NR NR -2.8 [†]	18.3 [†]	<0.01 vs. baseline	NSG vs. baseline	
Kipnes, 2001 ¹⁶⁶	mg/dL	Pioglitazone + unspecified, 171	Unspecified sulfonylurea + placebo, 175	15 (fixed) NR (fixed)	NR (fixed)	41 44 3	43 41 -2	5	<0.05 vs. GP2		
Kipnes, 2001 ¹⁶⁶	mg/dL	Pioglitazone + unspecified sulfonylurea, 179	Unspecified sulfonylurea + placebo, 175	30 (fixed) NR (fixed)	NR (fixed)	42 46 4	43 41 -2	6	<0.05 vs. GP2		
Rosiglitazone vs. Placebo											
Natali, 2004 ¹⁴⁴	mg/dL	Rosiglitazone	Placebo	4 bid (fixed)	NA	46 (SEM 9) 50 4 (3)	45 (SEM 12) 46 1 (1)	3 (-4, 9 [†])	NSG vs. GP2		
Patel, 1999 ¹⁶⁷	mg/dL	Rosiglitazone, 72	Placebo, 74	0.25 bid (fixed)	NA	48.5 49.7 1.2 (SE 0.80)	47.6 49.7 2.1 (SE 0.79)	-0.9 (-3.5, 1.7 [†])	NSG vs. GP2		

Appendix F: Evidence Table 12. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: high density lipoprotein

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Patel, 1999 ¹⁶⁷	mg/dL	Rosiglitazone, 79	Placebo, 74	1.0 bid (fixed)	NA	48.4 50.3 1.9 (SE 0.77)	47.6 49.7 2.1 (SE 0.79)	-0.3 (-2.8, 2.3 [†])	NSG vs. GP2		
Patel, 1999 ¹⁶⁷	mg/dL	Rosiglitazone, 79	Placebo, 74	2.0 bid (fixed)	NA	48.0 53.6 5.6 (SE 0.76)	47.6 49.7 2.1 (SE 0.79)	3.5 (0.9, 6.0 [†])	0.0009 vs. GP2		
Patel, 1999 ¹⁶⁷	mg/dL	Rosiglitazone, 70	Placebo, 74	0.05 bid (fixed)	NA	47.1 47.1 -0.1 (SE 0.82)	47.6 49.7 2.1 (SE 0.79)	-2.3 (-4.9, 0.4 [†])	NSG vs. GP2		
Virtanen, 2003 ¹⁴³	mg/dL	Rosiglitazone + diet	Placebo + diet	2 bid (esc) 8 bid	NA	42.9 (SE 3.9) 46.8 (SE 3.9) 3.9	46.8 (SE 3.9) 46.02 (SE 3.9) 3.9	0	NSG vs. baseline and vs. GP2	NSG vs. baseline	
Kim, 2005 ¹⁵²	mg/dL	Rosiglitazone + diet + exercise, 60	Diet + exercise, 60	4 (fixed)	NA	44.85 (9.36) 45.63 (10.14) 0.78	46.41 (10.53) 46.02 (11.31) -0.39	1.17	NSG vs. baseline	NSG vs. baseline	
Phillips, 2001 ¹⁶⁸	mg/dL	Rosiglitazone, 156	Placebo, 110	2 bid (fixed)	NA	46.41 [#] 50.31 [#] 3.9	42.51 [#] 47.58 [#] 5.07	-1.17	<0.05 vs. baseline	NSG vs. baseline	

Appendix F: Evidence Table 12. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: high density lipoprotein

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Phillips, 2001 ¹⁶⁸	mg/dL	Rosiglitazone, 140	Placebo, 110	8 od (fixed)	NA	43.29 [#] 47.58 [#] 4.29	42.51 [#] 47.58 [#] 5.07	-0.78	<0.05 vs. baseline	NSG vs. baseline	
Phillips, 2001 ¹⁶⁸	mg/dL	Rosiglitazone, 143	Placebo, 110	4 bid (fixed)	NA	42.51 [#] 48.36 [#] 5.85	42.51 [#] 47.58 [#] 5.07	0.78	<0.05 vs. baseline	NSG vs. baseline	
Phillips, 2001 ¹⁶⁸	mg/dL	Rosiglitazone, 169	Placebo, 110	4 od (fixed)	NA	44.46 [#] 48.36 [#] 3.9	42.51 [#] 47.58 [#] 5.07	-1.17	<0.05 vs. baseline	NSG vs. baseline	
Lebovitz, 2001 ¹⁶⁹	mg/dL	Rosiglitazone, 169	Placebo, 158	4 bid (fixed)	NA	42.51 (10.14) 46.79 4.29 (8.97)	43.29 (13.26) 45.63 2.34 (7.41)	1.95	<0.05 vs. baseline	<0.05 vs. baseline	
Lebovitz, 2001 ¹⁶⁹	mg/dL	Rosiglitazone, 166	Placebo, 158	2 bid (fixed)	NA	42.51 (9.75) 46.8 4.29 (7.02)	43.29 (13.26) 45.63 2.34 (7.41)	1.95	<0.05 vs. baseline	<0.05 vs. baseline	
Vong- thavaravat, 2002 ¹⁷⁰	mg/dL	Rosiglitazone + unspecified sulfonylurea + diet, 164	Unspecified sulfonylurea + diet, 170	2 bid (fixed)	NR	41 (SE 0.9) 45 (SE 1) 4	44 (SE 1) 46 (SE 1) 2	2	NR	NR	

Appendix F: Evidence Table 12. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: high density lipoprotein

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2	Other
Wolffen-buttel, 2000 ¹⁷¹	mg/dL	Rosiglitazone + unspecified sulfonylurea, 199	Unspecified sulfonylurea + placebo, 192	1 bid (fixed) NR (fixed)	NR (fixed)	42.9 (11.7) 46.8 (11.7) 3.9	46.8 (15.6) 46.8 (11.7) 0	3.9	0.0043 vs. baseline NSG vs. GP2	0.3858 vs. baseline	
Wolffen-buttel, 2000 ¹⁷¹	mg/dL	Rosiglitazone + unspecified sulfonylurea, 183	Unspecified sulfonylurea + placebo, 192	2 bid (fixed) NR (fixed)	NR (fixed)	42.9 (11.7) 46.8 (11.7) 3.9	46.8 (15.6) 46.8 (11.7) 0	3.9	<0.0001 vs. baseline 0.0019 vs. GP2	0.3858 vs. baseline	
Barnett, 2003 ¹⁷²	mg/dL	Rosiglitazone + unspecified sulfonylurea, 84	Unspecified sulfonylurea + placebo, 87	4 bid (fixed) NR (NR)	NR (NR)	NR NR NR	NR NR NR	NR	NSG vs. GP2		
Metformin vs. Placebo											
Natali, 2004 ¹⁴⁴	mg/dL	Metformin	Placebo	500 tid (fixed)	NA	46 (SEM 15) 49 3 (2)	45 (SEM 12) 46 1 (1)	2	NR	NR	
DeFronzo, 1995 ⁸⁸	mg/dL	Metformin, 143	Placebo, 146	850 (esc) 850 tid	NA	39 (SE 1) 40 (SE 1) 1	41 (SE 1) 41 (SE 1) 0	1	NR	NR	
Schneider, 1991 ¹⁷³	mg/dL	Metformin, 18	Placebo, 16	850 (esc) 1700	NA	47 (22) 49 (21) 2	38 (13) 43 (10) 5	-3	NSG vs. baseline	NSG vs. baseline	

Appendix F: Evidence Table 12. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: high density lipoprotein

Author, year						GP1 BL mean (SD)	GP2 BL mean (SD)				
Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 final mean (SD) Mean diff from BL1	GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	Other
Rachmani, 2002 ¹⁵⁰	mg/dL	Metformin continued + diet, 195	Metformin stopped + diet, 198	NR	NA	38.22 (SE 1.17) 40.95 2.73	40.95 (SE 0.78) 40.95 0	2.73	<0.05 vs. baseline and vs. GP2	NSG vs. baseline	
Virtanen, 2003 ¹⁴³	mg/dL	Metformin + diet	Placebo + diet	500 bid (esc) 1000 bid	NA	42.9 (SE 3.9) 46.8 (SE 3.9) 3.9	46.8 (SE 3.9) 50.7 (SE 3.9) 3.9	0	NSG vs. baseline and vs. GP2	NSG vs. baseline	
Del Prato, 2003 ¹⁴⁹	mg/dL	Metformin + placebo, 233	Placebo, 115	850 (esc) 2550	NA	44.46 (11.7) 47.97 (13.65) 3.51	44.85 (11.31) 46.02 (11.7) 1.17	2.34	NR	NR	
Alpha-Glucosidase Inhibitor vs. Placebo											
Rosenbaum, 2002 ¹⁵³	mg/dL	Acarbose, 20	Placebo, 20	50 bid (esc) 100 tid	NA	85.8 (23.4) 85.8 (15.6) 0	78 (15.6) 74.1 (15.6) -3.9	3.9	0.56 vs. baseline	0.44 vs. baseline	
Hasche, 1999 ¹³⁸	mg/dL	Acarbose + diet, 28	Placebo + diet, 32	50 bid (esc) 100 tid	NA	49.2 (9.2) 50.7 (14.2) 1.5	46.1 (9.9) 44.7 (7.8) -1.4	2.9	NR	NR	
Second Generation Sulfonylurea vs. Placebo											
Simonson, 1997 ¹³⁶	mg/dL	Glipizide GITS, 278	Placebo, 69	5, 10, 15, 20, 40, or 60 (fixed)	NA	37 37 0	37 36 -1	1	NR	NR	

Appendix F: Evidence Table 12. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: high density lipoprotein

Author, year				Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2	
Study group	Units	Comp group 1, N	Comp group 2, N								Other
Repaglinide vs. Placebo											
Goldberg, 1998 ¹³⁹	mg/dL	Repaglinide, 56	Placebo, 23	0.25 tid (esc) 8.0	NA	NR NR -1.17	NR NR -1.17	-0.31	0.873 vs. GP2		

Comp = comparison; BL = baseline; GP = group; mg = milligrams; dL = deciliter; esc = escalated; max = maximum; diff = difference; NR = not reported; NSG = not significant; NA = not applicable; SD = standard deviation; SE = standard error; SEM = standard error of the mean; od = once daily; bid = twice daily; tid = three times daily; HbA1c = hemoglobin A1c; f/u = follow-up; XR = extended release; GITS = gastrointestinal therapeutic system; vs = versus

* Number obtained from figure

† Percent change from baseline

‡ 95% confidence interval

Median

|| Article states a mean change of baseline as 1.11 mmol/L and 1.15 mmol/L for GP1 and GP2 respectively. We suspect that there may be a reporting error, and therefore have recorded these values as mg/dL.

¶ Median percent difference between groups.

Appendix F: Evidence Table 13. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: triglycerides

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2
Thiazolidinedione vs. Thiazolidinedione										
Khan, 2002 ⁵¹	mg/dL	Rosiglitazone, 60	Pioglitazone, 67	2-8 (fixed)	15-45 (fixed)	236 (222) 242 6*	181 (110.1) 166 -15*	21	NSG vs. baseline	NSG vs. baseline
Goldberg, 2005 ⁵²	mg/dL	Rosiglitazone + diet, 356	Pioglitazone + diet, 363	4 (esc) 8	30 (esc) 45	235.3 (SE 6.6) 248.4 13.1 (SE 7.8)	257.8 (SE 8.2) 205.9 -51.9 (SE 7.8)	65	NSG vs. baseline	<0.05 vs. baseline and vs. GP1
Derosa, 2005 ⁵³	mg/dL	Rosiglitazone + glimepiride + diet + exercise, 42	Pioglitazone + glimepiride + diet + exercise, 45	4 (fixed) 4 (fixed)	15 (fixed) 4 (fixed)	162.87 (29.37) 192.24 (32.04) 29.37	156.65 (35.6) 121.93 (28.48) -34.71	64.08	<0.05 vs. baseline and GP2	p<0.05 vs. baseline
Thiazolidinedione vs. Metformin										
Lawrence, 2004 ⁵⁴	mg/dL	Pioglitazone, 20	Metformin, 20	30 (esc) 45	500 bid (esc) 1000 tid	203 (149) 176 (115) -27	202 (110) 175.6 (114.4) -6.4	-0.6	NSG vs. baseline and vs. GP2	
Pavo, 2003 ⁵⁹	mg/dL	Pioglitazone + placebo, 100	Metformin + placebo, 91	30 (esc) 45	850 (esc) 2550	NR NR -80.99	NR NR -56.07	-24.92	0.001 vs. baseline	0.03 vs. baseline
Hanefeld, 2004 ⁶⁰ QUARTET study group	mg/dL	Pioglitazone + unspecified sulfonylurea + placebo, 319	Metformin + unspecified sulfonylurea + placebo, 320	15 (esc) 45 NR	850 (esc) 850 tid NR	219.83 (150.41) 178.89 (5.34) -40.94	211.82 (153.08) 191.35 (5.34) -20.47	-20.47	0.008 vs. GP2	

Appendix F: Evidence Table 13. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: triglycerides

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Rama- chandran, 2004 ⁵⁵	mg/dL	Pioglitazone + diet, 23	Metformin + diet, 21	15 (esc) 30	250 (esc) 850	258.1 (213.6) 195.8 (124.6) -62.3	249.2 (222.5) 222.5 (160.2) -26.7	-35.6	<0.05 vs. baseline	
Schemth- aner, 2004 ⁵⁶	mg/dL	Pioglitazone + placebo + diet	Metformin + placebo + diet	30 (esc) 45	850 up to 3 times/day (esc) 2550	234.96 180.67 -54.29	232.29 205.59 -26.7	-27.59	0.001 vs. GP2	
Yamanouchi, 2005 ⁵⁷	mg/dL	Pioglitazone + diet + exercise, 38	Metformin + diet + exercise, 39	30 for women and 45 for men (fixed)	750 (fixed)	219.83 (112.14) 185.12 (96.12) -39.16	205.59 (101.46) 197.58 (94.34) -8.01	-31.15	NSG vs. baseline and vs. GP2	NSG vs. baseline
Natali, 2004 ¹⁴⁴	mg/dL	Rosiglitazone	Metformin	4 bid (fixed)	500 tid (fixed)	142 (SEM 7.3) 178 36 (32)	196 (SEM 251) 152 -44 (41)	47	NSG vs. GP2	
Virtanen, 2003 ¹⁴³	mg/dL	Rosiglitazone + diet, 14	Metformin + diet, 13	2 bid (esc) 4 bid	500 bid (esc) 1000 bid	151.3 (SE 17.8) 133.5 (SE 17.8) -17.8	106.8 (SE 8.9) 115.7 (SE 17.8) 8.9	-26.7	NSG vs. GP2	
Thiazolidinedione vs. Second Generation Sulfonylurea										

Appendix F: Evidence Table 13. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: triglycerides

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Pfutzner, 2005 ⁶⁸	mg/dL	Pioglitazone, 89	Glimepiride, 84	45 (fixed)	1 (esc) 6	190 (109) 168 (102) -22	202 (111) 185 (106) -17	-5	<0.005 vs. baseline NSG vs. GP2	<0.001 vs. baseline
Tan, 2004 ⁶⁵	mg/dL	Pioglitazone, 91	Glibenclamide, 109	15 (esc) 45	2 (esc) 8	182.45 150.41 -32.04	202.03 199.36 -2.67	-29.37	<0.05 vs. baseline and 0.019 vs. GP2	NS
Charbonnel, 2005 ⁶³	mg/dL	Pioglitazone	Gliclazide	NR (esc) 45	NR (esc) 320	232.29 190.46 -45.39	249.2 203.81 -39.16	-6.23 (-22.25, 8.9 [†])	0.413 vs. GP2	
Lawrence, 2004 ⁶⁴	mg/dL	Pioglitazone, 20	Gliclazide, 20	30 (esc) 45	80 od (esc) 160 bid	203 (149) 176 (115) -27	157 (93.14) 167.6 (94) 10.6	-37.6	NSG vs. baseline and vs. GP2	NSG vs. baseline
Yanagawa, 2004 ⁶²	mg/dL	Pioglitazone, 19	Gliclazide, 21	NR	NR	140 (72) NR NR	164 (134) NR NR	NR	F-statistic = 1.4; NSG vs. GP2	
Rama- chandran, 2004 ⁶⁵	mg/dL	Pioglitazone + diet, 23	Glimepiride + diet, 18	15 (esc) 30	1 (esc) 2	258.1 (213.6) 195.8 (124.6) -62.3	195.8 (124.6) 151.3 (80.1) -44.5	-17.8	<0.05 vs. baseline	<0.05 vs. baseline

Appendix F: Evidence Table 13. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: triglycerides

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Yamanouchi, 2005 ⁵⁷	mg/dL	Pioglitazone + diet + exercise, 38	Glimepiride + diet + exercise, 37	30 for women and 45 for men (fixed)	1.0 (esc) 2.0	219.83 (112.14) 185.12 (96.12) -34.71	234.07 (121.93) 229.62 (112.14) -4.45	-30.26	NSG vs. baseline and vs. GP2	NSG vs. baseline
Betteridge, 2005 ¹⁵⁷	mg/dL	Pioglitazone + existing metformin, 317	Gliclazide + existing metformin, 313	15 (esc) 45 NR	80 (esc) 320 NR	258.1 (172.66) 192.24 -65.86 (SEM 6.23)	247.42 (168.21) 229.62 -17.8 (SEM 6.23)	-48.06	<0.001 vs. baseline	
St John Sutto, 2002 ⁶⁷	mg/dL	Rosiglitazone, 63	Glyburide (no trade drug specified), 66	4 bid (fixed)	NR (esc) 20	226.6 223.8 -2.8	189.6 175.8 -13.8	11	NSG vs. baseline	NSG vs. baseline
Thiazolidinedione + Metformin vs. Second Generation Sulfonylurea + Metformin										
Garber, 2006 ⁷¹	mg/dL	Rosiglitazone + metformin + diet, 116	Metformin + glibenclamide + diet, 120	4 (esc) 8 1500-2000 (esc) 2000	1000 (esc) 2000 5 (esc) 10	218 238 21 (113)	226 238 12 (133)	9 (-22, 40)	NSG vs. GP2	
Derosa, 2005 ⁷²	mg/dL	Rosiglitazone + metformin + diet + exercise + behavioral therapy, 48	Metformin + glimepiride + diet + exercise + behavioral therapy, 47	4 (fixed) 1500 (fixed)	1500 (fixed) 2 (fixed)	186 (28) 129 (18) -57	178 (23) 137 (20) -41	-16	NSG and vs. GP2	
Thiazolidinedione vs. Meglitinide										

Appendix F: Evidence Table 13. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: triglycerides

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Raskin, 2004 ⁷⁴	mg/dL	Rosiglitazone, 37	Repaglinide, 37	2 bid (esc) 4 bid	0.5 tid if HbA1c≤8%, 1 tid if HbA1c>8% (esc) 4 tid	245 (211) 246 (174) 1	306 (246) 284 (211) -22	23	NR	NR
Jovanovic, 2004 ⁷³	mg/dL	Pioglitazone, 26	Repaglinide, 35	30 (fixed)	0.5 tid if HbA1c≤8%, 1 tid if HbA1c>8% (esc) 4 tid	291 (232) 200 (99) -91	174 (80) 179 (78) 5	-96	NR	NR
Thiazolidinedione vs. Alpha-Glucosidase Inhibitor										
Goke, 2002 ⁷⁵ German Pioglitazone Study Group	mg/dL	Pioglitazone, 129	Acarbose, 136	45 (fixed)	50 (esc) 100 tid	275.3 (240.4) 204.2 -71.1 (184.1)	322 (339.9) 283.9 -38.1 (171.3)	-33	0.001 vs. GP2	
Other Thiazolidinedione Comparisons										
Takagi, 2003 ⁷⁶	mg/dL	Pioglitazone + existing medications, 23	Uptitration of existing medications, 21	30 (fixed) NR	NR (NR)	173 (91) 143 (78) -30	162 (47) 162 (57) 0	-30	NSG vs. GP2	
Choi, 2004 ⁷⁷	mg/dL	Rosiglitazone + existing medications, 45	Uptitration of existing medications, 38	8 (other) 4	NR (esc)	168.21 (61.41) 119.26 (39.16) -48.95 (49.84)	160.2 (55.18) 127.27 (61.41) -25.81 (50.73)	-23.14	<.001 vs. baseline	
Metformin vs. Second Generation Sulfonylurea										
Garber, 2003 ⁸⁰	mg/dL	Metformin, 164	Glyburide (no trade drug specified), 151	500 (esc) 2000	2.5 (esc) 10	256.8 (26.7) 217.2 -39.6	236.3 (19.1) 221.2 -15.1	-24.5	NSG vs. baseline	NS vs. baseline

Appendix F: Evidence Table 13. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: triglycerides

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Goldstein, 2003 ⁸²	mg/dL	Metformin, 67	Glipizide	500 (esc) 2000	15 bid (fixed)	218.7 (120.2) 217.1 -1.6 (-25.3, 22 [†])	213.8 (127.2) 273.6 59.8 (22.5, 97.1 [†])	-70.4	<0.05 vs. baseline	<0.05 vs. baseline
Campbell, 1994 ⁸³	mg/dL	Metformin, 24	Glipizide, 24	500 bid (esc) 3000	5 (esc) 30	191.35 (130.83) 202.92 (163.76) 11.57	183.34 (61.41) 205.59 (108.58) 22.25	-10.68	NSG vs. baseline	
Marre, 2002 ⁸⁴	mg/dL	Metformin, 104	Glibenclamide, 103	500 (esc) 2000	5 (esc) 20	204.7 (169.1) 186.9 -17.8 (89)	204.7 (151.3) 204.7 0 (133.5)	-17.8	NSG vs. GP2	
Amador- Licona, 2000 ⁸⁵	mg/dL	Metformin, 28	Glibenclamide, 23	850 (esc) NR	5 (esc) NR	195.8 (81.88) 178 (65.86) -17.8	174.44 (81.88) 166.43 (97.9) -8.01	-10.68	0.04 vs. baseline	0.67 vs. baseline
Lawrence, 2004 ⁸⁴	mg/dL	Metformin, 20	Gliclazide, 20	500 bid (esc) 1000 tid	80 (esc) 160 bid	202 (110) 175.6 (114.4) -26.4	157 (93.14) 167.6 (94) 10.6	-37	NSG vs. baseline and vs. GP2	NSG vs. baseline

Appendix F: Evidence Table 13. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: triglycerides

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Noury, 1991 ⁸⁶	mg/dL	Metformin, 30	Gliclazide, 27	1700 (fixed)	80 (esc) 240	199.36 (226.06) 177.11 (135.28) -22.25	150.41 (99.68) 179.78 (161.98) 29.37	-51.62	NSG vs. baseline and vs. GP2	NSG vs. baseline
Rama- chandran, 2004 ⁵⁵	mg/dL	Metformin + diet, 21	Glimepiride + diet, 18	250 (esc) 850	1 (esc) 2	249.2 (222.5) 222.5 (160.2) -26.7	195.8 (124.6) 151.3 (80.1) -44.5	17.8		<0.05 vs. baseline
Hermann, 1994 ⁸⁷	mg/dL	Metformin + diet, 19	Glyburide + diet, 19	1000 (esc) 3000	3.5 (esc) 10.5	179.78 (SE 18.69) 173.55 (SE 14.24) -6.23 (SE 12.46)	178.89 (SE 32.93) 186.9 (SE 31.15) 8.01 (SE 11.57)	-14.24	>0.1 vs. GP2	
DeFronzo, 1995 ⁸⁸	mg/dL	Metformin + placebo, 210	Glyburide (no trade drug specified) + placebo, 209	500 (esc) 2500	5 bid (esc) 10 bid	231 (SE 12) 221 (SE 13) -16 (SE 7)	210 (SE 8) 227 (SE 11) 21 (SE 9)	-37	0.001 vs. GP2	
Charpentier, 2001 ⁸⁹	mg/dL	Metformin + placebo, 75	Glimepiride + placebo, 150	850 tid (fixed)	1 (esc) 6	171.77 (119.26) 185.12 13.35 (104.13)	189.57 (143.29) 200.25 10.68 (108.58)	2.67	0.029 for all treatment groups in study	

Appendix F: Evidence Table 13. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: triglycerides

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2
Yamanouchi, 2005 ⁵⁷	mg/dL	Metformin + diet + exercise, 39	Glimepiride + diet + exercise, 37	750 (fixed)	1 (esc) 2	205.59 (101.46) 197.58 (94.34) -8.01	234.07 (121.93) 229.62 (112.14) -4.45	-3.56	NSG vs. baseline and vs. GP2	NSG vs. baseline
Derosa, 2004 ³⁰	mg/dL	Metformin + placebo + diet + exercise, 75	Glimepiride + placebo + diet + exercise, 73	1000 (esc) 1000 tid	1 (esc) 2 bid	180 (25) 165 (25) -15	160 (20) 145 (25) -15	0	NSG vs. baseline	NSG vs. baseline
Blonde, 2002 ⁸¹	NR	Metformin, 153	Glyburide (no trade drug specified), 164	500 (esc) 2000	10 bid (fixed)	NR NR NR	NR NR NR	NR	NSG vs. baseline	NSG vs. baseline
Metformin vs. Meglitinide										
Derosa, 2003 ⁹⁷	mg/dL	Metformin + diet + exercise, 56	Repaglinide + diet + exercise, 56	500 bid (esc) 2500	0.5 bid (esc) 4	176.22 (4.806) 152.19 -24.03 (-55.18, -15.13 [†])	156.64 (52.51) 140.62 -16.02 (-38.27, 17.8 [†])	-8.01	<0.05 vs. baseline NSG vs. GP2	0.065 vs. baseline
Metformin vs. Alpha-Glucosidase Inhibitor										
Willms, 1999 ⁹⁹	mg/dL	Metformin, 27	Acarbose, 31	850 bid (fixed)	100 tid (fixed)	NR NR -24.03 [#]	NR NR -36.49 [#]	12.5	NR	NR
Metformin vs. Thiazolidinedione + Metformin										

Appendix F: Evidence Table 13. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: triglycerides

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Weissman, 2005 ¹⁰⁰	mg/dL	Metformin, 266	Rosiglitazone + metformin, 271	1000 (esc) 2000	4 (esc) 8 1000 (fixed)	179.2 176.8 (170.9, 182.9 [†]) -2.4	184.8 196.6 (189.2, 204.2 [†]) 11.8	-14.2	NSG vs. baseline	NSG vs. baseline
Bailey, 2005 ¹⁰¹	mg/dL	Metformin, 230	Rosiglitazone + metformin, 245	2500 (esc) 3000	4 (esc) 8 2000 (fixed)	180.8 (175.5, 186.3 [†]) 167.5 (161.8, 173.4 [†]) -13.3	189.3 (183.5, 195.2 [†]) 189.4 (183.1, 195.9 [†]) 0.1	-13.4	<0.05 vs. baseline	NSG vs. baseline
Fonseca, 2000 ¹⁰³	mg/dL	Metformin + placebo, 113	Rosiglitazone + metformin, 116	2500 (fixed)	4 (fixed) 2500 (fixed)	246.53 (194.91) 247.42 (159.31) 0.89	226.06 (138.84) 233.18 (139.73) 7.12	-6.23		0.73 vs. GP1
Fonseca, 2000 ¹⁰³	mg/dL	Metformin + placebo, 113	Rosiglitazone + metformin, 110	2500 (fixed)	8 (fixed) 2500 (fixed)	246.53 (194.91) 247.42 (159.31) 0.89	228.73 (184.23) 228.73 (166.43) 0	0.89		0.56 vs. GP1
Gomez-Perez, 2002 ¹⁰²	mg/dL	Metformin + placebo, 34	Rosiglitazone + metformin, 36	2500 (fixed)	4 bid (fixed) 2500 (fixed)	227.2 (126.8) 233.4 6.2	204.4 (113.3) 199.9 -4.5	10.7	NR	NR

Appendix F: Evidence Table 13. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: triglycerides

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Gomez-Perez, 2002 ¹⁰²	mg/dL	Metformin + placebo, 34	Rosiglitazone + metformin, 35	2500 (fixed)	2 bid (fixed) 2500 (fixed)	227.2 (126.8) 233.4 6.2	199.6 (133.2) 193.8 -5.8	12	NR	NR
Metformin vs. Metformin + Second Generation Sulfonylurea										
Garber, 2003 ⁸⁰	mg/dL	Metformin, 164	Metformin + glyburide (no trade drug specified), 171	500 (esc) 2000	250 (esc) 1000 1.25 (esc) 5	256.8 (26.7) 217.2 -39.6	248.4 (26.2) 196.4 -52	12.4	NSG vs. baseline	<0.05 vs. baseline
Goldstein, 2003 ⁸²	mg/dL	Metformin, 67	Metformin + glipizide,	500 (esc) 2000	500 (esc) 2000 5 (esc) 20	218.7 (120.2) 217.1 -1.6 (-25.3, 22 [†])	237.5 (192.2) 256 18.5 (-16.8, 53.7 [†])	-20.1	NSG vs. baseline	NSG vs. baseline
Marre, 2002 ⁸⁴	mg/dL	Metformin, 104	Metformin + glibenclamide, 103	500 (esc) 2000	500 (esc) 2000 5 (esc) 20	204.7 (169.1) 186.9 -17.8 (89)	213.6 (160.2) 195.8 -17.8 (151.3)	0	NSG vs. GP2	
Marre, 2002 ⁸⁴	mg/dL	Metformin, 104	Metformin + glibenclamide, 101	500 (esc) 2000	500 (esc) 2000 2.5 (esc) 10	204.7 (169.1) 186.9 -17.8 (89)	222.5 (284.8) 178 -44.5 (186.9)	26.7	NSG vs. GP2	
Hermann, 1994 ⁸⁷	mg/dL	Metformin + diet, 19	Metformin + glyburide, 46	1000 (esc) 3000	500 (esc) 1500 1.75 (esc) 5.25	179.78 (SE 18.69) 173.55 (SE 14.24) 8.01 (SE 12.46)	175.33 (SE 20.47) 168.21 (SE 17.8) 5.34 (SE 11.57)	2.67	>0.1 vs. baseline and vs. GP2	>0.1 vs. baseline

Appendix F: Evidence Table 13. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: triglycerides

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
DeFronzo, 1995 ⁸⁸	mg/dL	Metformin + placebo, 210	Metformin + glyburide (no trade drug specified), 213	500 (esc) 2500	500 (esc) 2500 10 (esc) 20	231 (SE 12) 221 (SE 13) -16 (SE 7)	216 (SE 10) 194 (SE 9) -20 (SE 7)	4	NR	NR
Charpentier, 2001 ⁸⁹	mg/dL	Metformin + placebo, 75	Metformin + glimepiride, 147	850 tid (fixed)	850 tid (fixed) 1 (esc) 6	171.77 (119.26) 185.12 13.35 (104.13)	169.99 (110.36) 167.32 -2.67 (93.45)	16.02		0.029 all group compar- ison
Blonde, 2002 ⁸¹	NR	Metformin, 153	Metformin + glyburide (no trade drug specified), 160	500 (esc) 2000	500 (esc) 2000 2.5 (esc) 10	NR NR NR	NR NR NR	NR	NSG vs. GP2	
Blonde, 2002 ⁸¹	NR	Metformin, 153	Metformin + glyburide (no trade drug specified), 162	500 (esc) 2000	500 (esc) 2000 5 (esc) 20	NR NR NR	NR NR NR	NR	NSG vs. GP2	
Feinglos, 2005 ¹⁰⁴	NR	Metformin + placebo, 56	Metformin + glipizide, 56	at least 1000 (fixed)	at least 1000 (fixed) 2.5 (fixed)	NR NR NR	NR NR NR	NR	NSG vs. baseline and vs. GP2	NSG vs. baseline
Second Generation Sulfonylurea vs. Second Generation Sulfonylurea										
Inukai, 2005 ¹¹¹	mg/dL	Glibenclamide or gliclazide, 52	Glimepiride, 120	2.5 (fixed) 40 (fixed)	1 or 2 (esc) 6	143.4 (120.3) 146.2 (100.3) 2.8	149.6 (118.8) 136.4 (84.6) -13.2	16	0.66 vs. baseline	0.08 vs. baseline

Appendix F: Evidence Table 13. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: triglycerides

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Baba, 1983 ¹³³	mg/dL	Glibenclamide, 131	Gliclazide, 146	2.5 (esc) 10	40 (esc) 160	135* 136* 1	133* 132* -1	2	NSG vs. GP2	
Schemth- aner, 2004 ¹⁰⁶	mg/dL	Glimepiride + existing oral diabetes medications + diet, 440	Gliclazide + existing oral diabetes medications + diet, 405	1 (esc) 6	30 (esc) 120	204.7 195.8 -8.9	195.8 186.9 -8.9	0	NSG vs. baseline	NSG vs. baseline
Second Generation Sulfonylurea vs. Meglitinide										
Wolffen-but- tel, 1999 ¹¹⁷	mg/dL	Glyburide (no trade drug specified) + placebo, 109	Repaglinide, 211	1.75 (esc) 10.5	1.5 (esc) 12	163.76 [#] 174.44 [#] 10.68	170.88 [#] 178 [#] 7.12	3.56	NSG vs. baseline	NSG vs. baseline
Marbury, 1999 ¹¹⁶	mg/dL	Glyburide (no trade drug specified) + placebo, 216	Repaglinide, 115	2.5 (esc) 15	0.5 (esc) 12	NR NR -6.45	NR NR 6.57	-13.02 (-31.24, 57.28 [†])	NSG vs. GP2	
Derosa, 2003 ¹¹⁸	mg/dL	Glimepiride + placebo, 62	Repaglinide + placebo, 62	1 (esc) 3 mean final dose	1 (esc) 2.5 mean final dose	170 (36) 155 (39) -15	153 (32) 135 (36) -18	3	NSG vs. GP2	
Madsbad, 2001 ¹¹⁹	mg/dL	Glipizide + placebo, 81	Repaglinide, 175	5 (esc) 15	0.5 (esc) 4	NR NR 3.56 (-23.14, 29.37 [†])	NR NR 3.56 (-14.24, 20.47 [†])	0 (-31.15, 31.15 [†])	NSG vs. GP2	

Appendix F: Evidence Table 13. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: triglycerides

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Vakkilainen, 2002 ¹²²	NR	Glibenclamide + placebo, 20	Nateglinide + placebo, 23	5 (esc) 10	120 tid (fixed)	NR NR NR	NR NR NR	NR	NSG vs. GP2	
Second Generation Sulfonylurea vs. Thiazolidinedione + Second Generation Sulfonylurea										
Rosenstock, 2006 ¹²⁴	%	Glipizide + placebo, 57	Rosiglitazone + glipizide, 90	10 (esc) 20	4 (fixed) 10 (esc) 20	NR NR -5.4 [†]	NR NR 9.5 [†]	-14.9	NR	NR
Kerenyi, 2004 ¹²⁵	mg/dL	Glibenclamide + diet, 139	Rosiglitazone + glibenclamide + diet, 144	7.5 (esc) 15	4 bid (fixed) 7.5 (fixed)	169.1 163.76 -5.34	173.55 166.43 -7.12	1.78	NSG vs. baseline	<0.05 vs. baseline
Baksi, 2004 ¹²⁶	mg/dL	Gliclazide, 201	Rosiglitazone + gliclazide, 205	160 (esc) 320	160 (fixed) 4 bid (fixed)	142.4 [#] 151.3 [#] 3.5 [†]	151.3 [#] 160.2 [#] 7.7 [†]	-4.2	NR	NR
Second Generation Sulfonylurea vs. Metformin + Second Generation Sulfonylurea										
Garber, 2003 ⁸⁰	mg/dL	Glyburide (no trade drug specified), 151	Metformin + glyburide (no trade drug specified), 171	2.5 (esc) 10	250 (esc) 1000 1.25 (esc) 5	236.3 (19.1) 22.12 -15.1	246.4 (26.2) 196.2 -52	36.9	NSG vs. baseline	<0.05 vs. baseline
DeFronzo, 1995 ⁸⁸	mg/dL	Glyburide (no trade drug specified) + placebo, 209	Metformin + glyburide (no trade drug specified), 213	5 bid (esc) 10 bid	500 (esc) 2500 10 (esc) 20	210 (SE 8) 227 (SE 11) 21 (SE 9)	216 (SE 10) 194 (SE 9) -20 (SE 7)	41	0.001 vs. GP2	

Appendix F: Evidence Table 13. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: triglycerides

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Charpentier, 2001 ⁸⁹	mg/dL	Glimepiride + placebo, 150	Metformin + glimepiride, 147	1 (esc) 6	850 tid (fixed) 1 (esc) 6	189.57 (143.29) 200.25 10.68 (108.58)	169.99 (110.36) 167.32 -2.67 (93.45)	13.35		0.029 all group compar- ison
Goldstein, 2003 ⁸²	mg/dL	Glipizide	Metformin + glipizide	30 (fixed)	500 (esc) 2000 5 (esc) 20	213.8 (127.2) 273.6 59.8	237.5 (192.2) 256 18.5	41.3	<0.05 vs. baseline	NSG vs. baseline
Marre, 2002 ⁸⁴	mg/dL	Glibenclamide, 103	Metformin + glibenclamide, 103	5 (esc) 20	500 (esc) 2000 5 (esc) 20	204.7 (151.3) 204.7 0 (133.5)	213.6 (160.2) 195.8 -17.8 (151.3)	17.8	NSG vs. baseline and vs. GP2	NSG vs. baseline and vs. GP2
Marre, 2002 ⁸⁴	mg/dL	Glibenclamide, 103	Metformin + glibenclamide, 101	5 (esc) 20	500 (esc) 2000 2.5 (esc) 10	204.7 (151.3) 204.7 0 (133.5)	222.5 (284.8) 178 -44.5 (186.9)	44.5	NSG vs. baseline and vs. GP2	NSG vs. baseline and vs. GP2
Hermann, 1994 ⁸⁷	mg/dL	Glyburide + diet, 19	Metformin + glyburide + diet, 46	3.5 (esc) 10.5	500 (esc) 1500 1.75 (esc) 5.25	178.89 (SE 32.93) 186.9 (SE 31.15) 7.12 (SE 11.57)	175.33 (SE 20.47) 168.21 (SE 17.8) 5.34 (SE 11.57)	1.78	>0.1 vs. baseline and vs. GP2	>0.1 vs. baseline

Appendix F: Evidence Table 13. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: triglycerides

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
1998 ¹²⁸ UKPDS, 3 year f/u	mg/dL	Glibenclamide + diet, 300	Metformin + glibenclamide + diet, 291	10 (fixed)	500 (esc) 2500 10 (fixed)	NR NR -14.24 (-51.62, 23.14 [†])	NR NR -5.34 (-18.69, 8.01 [†])	-8.9	NSG vs. baseline and vs. GP2	NSG vs. baseline
Gregorio, 1999 ¹²⁹	mg/dL	Glibenclamide or gliclazide, 85	Metformin + glibenclamide or metformin + gliclazide, 89	10 (esc) 15 120 (esc) 240	850 (esc) 1700 NR (fixed) NR (fixed)	169.99 (10.68) 162.87 (10.68) -7.12	172.66 (11.57) 166.43 (10.68) -6.23	-0.89	NSG vs. baseline	NSG vs. baseline
Other Comparisons										
Fujioka, 2003 ¹⁰⁵	mg/dL	Metformin + placebo + diet, 71	Metformin XR + placebo + diet, 75	1000 (esc) 1500	1000 (esc) 1500	181 (113) 182 1 (-14, 17)	187 (200) 221 34 (15, 53)	-33	NSG vs. baseline	<0.05 vs. baseline
Fujioka, 2003 ¹⁰⁵	mg/dL	Metformin + placebo + diet, 71	Metformin XR + placebo + diet, 71	1000 (esc) 1500	1000 (esc) 2000	199 (34) 200 1 (-14, 17)	201 (137) 243 42 (6, 78)	-41	NSG vs. baseline	<0.05 vs. baseline
McCluskey, 2004 ⁷⁶	mg/dL	Rosiglitazone + placebo, 11	Rosiglitazone + glimepiride, 23	4 or 8 (fixed)	4 or 8 fixed 2 (esc) 8	45.9 (SE 6.4) 67.5 21.6 (SE 13.7)	41.3 (SE 5) 33.8 -7.5 (SE 10)	29.1	NSG vs. GP2	
Pioglitazone vs. Placebo										

Appendix F: Evidence Table 13. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: triglycerides

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Rosenblatt, 2001 ¹⁶²	mg/dL	Pioglitazone, 101	Placebo, 96	30 (NR)	NA	357.78 (533.11) 304.83 -14.8% [†]	173.55 (347.1) 163.48 1.8% [†]	-0.65%	0.0178 vs. GP2	
Saad, 2004 ¹⁶⁴	mg/dL	Pioglitazone, 24	Placebo, 28	45 (fixed)	NA	315 (122) 214 -101	351 (168) 368 17	-118	<.05 vs. GP2	
Tseng, 2005 ¹⁴⁰	%	Pioglitazone + unspecified sulfonylurea, 23	Unspecified sulfonylurea + placebo, 25	30 (fixed) NR (NR)	NR (NR)	NR NR -16.6% [†]	NR NR 20% [†]	-36.6%	<0.05 vs. baseline	NSG vs. baseline
Herz, 2003 ¹⁶³	mg/dL	Pioglitazone, 96	Placebo, 96	45 (fixed)	NA	177.11 148.77 -16% [†]	153.08 154.6 1% [†]	-29.9	<0.001 vs. baseline 0.007 vs. GP2	
Herz, 2003 ¹⁶³	mg/dL	Pioglitazone, 95	Placebo, 96	30 (fixed)	NA	169.99 161.49 -5% [†]	153.08 154.6 1% [†]	-10	NSG vs. GP2	
Nishio, 2006 ¹⁵¹	mg/dL	Pioglitazone, 26	Control group (no placebo), 28	30 (fixed)	NA	97.01 (32.93) 151.3 (81.88) 54.29	133.5 (111.25) 142.4 (64.08) 8.9	45.39	NSG vs. baseline and vs. GP2	NSG vs. baseline

Appendix F: Evidence Table 13. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: triglycerides

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Aronoff, 2000 ¹⁶⁵	mg/dL	Pioglitazone, 77	Placebo, 79	45 (fixed)	NA	259.7 (SE 34.87) 218.9 (SE 14.24) -40.8	262.8 (SE 34.35) 252.7 (SE 20.71) -10.1	-30.7	<=0.05 vs. baseline	
Aronoff, 2000 ¹⁶⁵	mg/dL	Pioglitazone, 79	Placebo, 79	15 (fixed)	NA	283.8 (SE 34.4) 226 (SE 20.15) -57.8	262.8 (SE 34.35) 252.7 (SE 20.71) -10.1	-47.7	<=0.05 vs. baseline	
Aronoff, 2000 ¹⁶⁵	mg/dL	Pioglitazone, 80	Placebo, 79	7.5 (fixed)	NA	319 (SE 34.23) 264.1 (SE 33.08) -54.9	262.8 (SE 34.35) 252.7 (SE 20.71) -10.1	-44.8	<=0.05 vs. baseline	
Aronoff, 2000 ¹⁶⁵	mg/dL	Pioglitazone, 84	Placebo, 79	30 (fixed)	NA	261.1 (SE 33.44) 225.2 (SE 24.77) -35.9	262.8 (SE 34.35) 252.7 (SE 20.71) -10.1	-25.8	<=0.05 vs. baseline	
Smith, 2005 ¹⁶¹	mg/dL	Pioglitazone + diet, 21	Placebo + diet, 21	30 (esc) 45	NA	205.79 (182.61) 147.27 -58.52 (123.26)	221.96 (141.66) 219.6 -2.36 (59.87)	-56.16	0.0035 vs. GP2	

Appendix F: Evidence Table 13. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: triglycerides

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Einhom, 2000 ¹⁶⁰	mg/dL	Pioglitazone + existing metformin + diet, 161	Existing metformin + placebo + diet, 149	30 (fixed) NR (NR)	NR (NR)	298.9 (24.9) 289.2 -9.7	300.4 (25.86) 308.9 8.5	-18.2	≤0.05 vs. GP2	
Kipnes, 2001 ¹⁶⁶	mg/dL	Pioglitazone + existing unspecified sulfonylurea, 181	Unspecified sulfonylurea + placebo, 180	30 (fixed) NR (NR)	NR (NR)	260 198 -62	259 267 8	-70	<0.05 vs. baseline and vs. GP2	
Kipnes, 2001 ¹⁶⁶	mg/dL	Pioglitazone + existing unspecified sulfonylurea, 177	Unspecified sulfonylurea + placebo, 180	15 (fixed) NR (NR)	NR (NR)	272 230 -42	259 267 8	-50	<0.05 vs. baseline and vs. GP2	
Rosiglitazone vs. Placebo										
Barnett, 2003 ¹⁷²	mg/dL	Rosiglitazone + unspecified sulfonylurea, 84	Unspecified sulfonylurea + placebo, 87	4 bid (fixed) NR (NR)	NR (NR)	179.78 (91.67) NR NR	176.22 (94.34) NR NR	NR	NSG vs. GP2	
Natali, 2004 ¹⁴⁴	mg/dL	Rosiglitazone	Placebo	4 bid (fixed)	NA	142 (SEM 73) 178 36	155 (SEM 76) 161 6	30 (-40, 96 ⁺)	NSG vs. GP2	
Patel, 1999 ¹⁶⁷	mg/dL	Rosiglitazone, 79	Placebo, 74	1.0 bid (fixed)	NA	209.8 216.7 6.9	208 224.1 16.1	-9.3 (-60.0, 41.5 ⁺)	NSG vs. GP2	

Appendix F: Evidence Table 13. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: triglycerides

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Patel, 1999 ¹⁶⁷	mg/dL	Rosiglitazone, 79	Placebo, 74	2.0 bid (fixed)	NA	189.5 206.8 17.3	208 224.1 16.1	1.2 (-49.7, 52.0 [†])	NSG vs. GP2	
Patel, 1999 ¹⁶⁷	mg/dL	Rosiglitazone, 70	Placebo, 74	0.05 bid (fixed)	NA	217.9 244.6 26.7	208 224.1 16.1	10.6 (-41.6, 62.8 [†])	NSG vs. GP2	
Patel, 1999 ¹⁶⁷	mg/dL	Rosiglitazone, 72	Placebo, 74	0.25 bid (fixed)	NA	222.9 246.7 23.8	208 224.1 16.1	7.7 (-44.5, 62.8 [†])	NSG vs. GP2	
Phillips, 2001 ¹⁶⁸	mg/dL	Rosiglitazone, 158	Placebo, 110	2 bid (fixed)	NA	168.21 [#] 188.68 [#] 20.47	175.33 [#] 171.77 [#] -3.56	24.03	NSG vs. GP2	
Phillips, 2001 ¹⁶⁸	mg/dL	Rosiglitazone, 142	Placebo, 110	8 od (fixed)	NA	186.01 [#] 211.82 [#] 25.81	175.33 [#] 171.77 [#] -3.56	29.37	NSG vs. GP2	
Phillips, 2001 ¹⁶⁸	mg/dL	Rosiglitazone, 145	Placebo, 110	4 bid (fixed)	NA	161.98 [#] 188.68 [#] 26.7	175.33 [#] 171.77 [#] -3.56	30.26	NSG vs. GP2	
Phillips, 2001 ¹⁶⁸	mg/dL	Rosiglitazone, 158	Placebo, 110	4 od (fixed)	NA	194.02 [#] 194.02 [#] 0	175.33 [#] 171.77 [#] -3.56	3.56	NSG vs. GP2	

Appendix F: Evidence Table 13. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: triglycerides

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Lebovitz, 2001 ¹⁶⁹	mg/dL	Rosiglitazone, 166	Placebo, 158	2 bid (fixed)	NA	253.65 (299.04) NR NR	226.95 (179.78) NR NR	NR	NSG vs. GP2	
Lebovitz, 2001 ¹⁶⁹	mg/dL	Rosiglitazone, 169	Placebo, 158	4 bid (fixed)	NA	236.74 (157.53) NR NR	226.95 (179.78) NR NR	NR	NSG vs. GP2	
Virtanen, 2003 ¹⁴³	mg/dL	Rosiglitazone + diet, 14	Placebo + diet, 14	2 bid (esc) 8 bid	NA	151.3 (SE 17.8) 133.5 (SE 17.8) -17.8	169.1 (SE 62.3) 124.6 (SE 26.7) -44.5	26.7	>0.05 vs. GP2	
Kim, 2005 ¹⁵²	mg/dL	Rosiglitazone + diet + exercise, 60	Diet + exercise, 60	4 (fixed)	NA	211.82 (145.07) 210.93 (115.7) -0.89	189.57 (94.34) 184.23 (105.02) -5.34	4.45	NSG vs. baseline	NSG vs. baseline
Wolffen-buttel, 2000 ¹⁷¹	mg/dL	Rosiglitazone + unspecified sulfonylurea, 183	Unspecified sulfonylurea + placebo, 192	2 bid (fixed) NR (fixed)	NR (fixed)	178 (106.8) 195.8 (169.1) 17.8	160.2 (89) 169.1 (106.8) 8.9	8.9	0.0198 vs. baseline 0.1393 vs. GP2	0.4115 vs. baseline

Appendix F: Evidence Table 13. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: triglycerides

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2
Wolffen-buttel, 2000 ¹⁷¹	mg/dL	Rosiglitazone + unspecified sulfonylurea, 199	Unspecified sulfonylurea + placebo, 192	1 bid (fixed) NR (fixed)	NR (fixed)	169.1 (97.9) 204.7 (151.3) 35.6	160.2 (89) 169.1 (106.8) 8.9	26.7	<0.0001 vs. baseline 0.0020 vs. GP2	0.4115 vs. baseline
Metformin vs. Placebo										
Willms, 1999 ⁹⁹	mg/dL	Metformin, 27	Placebo, 29	850 bid (fixed)	NA	NR NR -24.03 [#]	NR NR 26.7 [#]	-50.73	NR	NR
Natali, 2004 ¹⁴⁴	mg/dL	Metformin	Placebo	500 tid (fixed)	NA	196 (SEM 251) 152 -44 (41)	155 (SEM 76) 161 6 (17)	-50	NR	NR
DeFronzo, 1995 ⁸⁸	mg/dL	Metformin, 143	Placebo, 146	850 (esc) 2550	NS (NR)	209 (SE 15) 193 (SE 10) -17 (SE 12)	185 (SE 9) 191 (SE 10) 6 (SE 7)	-22	NSG vs. GP2	
Grant, 1996 ¹⁵⁴	mg/dL	Metformin, 25	Placebo, 23	1500 (fixed)	NA	284.8 191.35 -93.45	NR NR NR	NR	0.06 vs. GP2	
Grant, 1996 ¹⁵⁴	mg/dL	Metformin, 27	Placebo, 23	1500 (esc) 3000	NA	257.21 201.14 -56.07	NR NR NR	NR	<0.05 vs. GP2	

Appendix F: Evidence Table 13. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: triglycerides

Author, year Study group	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for compar- isons with GP1	P-value for compar- isons with GP2
Doran, 1991 ²⁶⁰	mg/dL	Metformin, 30	Placebo, 30	500 (esc) 1000 tid	NA	240.3 [#] 231.4 [#] -8.9 [#]	204.7 [#] 222.5 [#] 17.8 [#]	-26.7	NR	NR
Schneider, 1991 ¹⁷³	mg/dL	Metformin, 18	Placebo, 16	850 (esc) 1700	NA	340 (207) 242 (156) -98	309 (168) 269 (85) -40	-58	0.009 vs. GP2	
Teupe, 1991 ¹⁵⁵	mg/dL	Metformin + diet, 25	Diet, 29	NR (esc) 1700	NA	177 (112) 212 (151) 35	142 (43) 193 (100) 51	-16	NR	NR
Manzella, 2004 ¹⁴⁸	mg/dL	Metformin + diet, 60	Placebo + diet, 60	850 bid (fixed)	NA	197.58 (35.6) 172.66 (13.35) -24.92	202.03 (17.8) 195.8 (9.79) -6.23	-18.69	<0.05 vs. GP2	
Virtanen, 2003 ¹⁴³	mg/dL	Metformin + diet, 13	Placebo + diet, 14	500 bid (esc) 1000 bid	NA	106.8 (SE 8.9) 115.7 (SE 17.8) 8.9	169.1 (SE 62.3) 124.6 (SE 26.7) -44.5	53.4	>0.05 vs. GP2	
Del Prato, 2003 ¹⁴⁹	mg/dL	Metformin + placebo, 234	Placebo, 115	850 (esc) 2550	NA	156.64 (102.35) 143.29 (90.78) -13.35	138.84 (88.11) 162.87 (152.19) 24.03	-37.38	NR	NR
Second Generation Sulfonylurea vs. Placebo										

Appendix F: Evidence Table 13. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: triglycerides

Author, year	Units	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL1 - mean diff BL2	P-value for comparisons with GP1	P-value for comparisons with GP2
Simonson, 1997 ¹³⁶	mg/dL	Glipizide GITS, 278	Placebo, 69	5, 10, 15, 20, 40, or 60 (fixed)	NA	168 154 -14	178 176 -2	-12	NR	NR
Meglitinide vs. Placebo										
Goldberg, 1998 ¹³⁹	mg/dL	Repaglinide, 62	Placebo, 30	0.25 tid (esc) 8.0	NA	NR NR -33.82	NR NR 13.35	-47.17	0.404 vs. GP2	
Alpha-Glucosidase Inhibitor vs. Placebo										
Willms, 1999 ⁹⁹	mg/dL	Acarbose, 31	Placebo, 29	100 tid (fixed)	NA	NR NR -36.49 [#]	NR NR 26.7 [#]	-63.19	NR	NR
Rosenbaum, 2002 ¹⁵³	mg/dL	Acarbose, 20	Placebo, 20	50 bid (esc) 100 tid	NA	7.9 (3.1) 8.6 (4.5) 0.7	10.8 (4.6) 10.3 (4.9) -0.5	1.2	0.37	0.45
Leonhardt, 1991 ²⁶³	mg/dL	Acarbose, 47	Placebo, 47	100 tid (fixed)	NA	195 (1.88) 177 -18	186 (1.58) 176 -10	-8	NR	NR
Hasche, 1999 ¹³⁸	mg/dL	Acarbose + diet, 28	Placebo + diet, 32	50 bid (esc) 100 tid	NA	186 174.8 -13.3 (78.8)	185.2 185 -0.1 (72.9)	-13.2	NR	NR

Appendix F: Evidence Table 13. Comparative effectiveness of oral diabetes medications on proximal clinical outcomes: triglycerides

Comp = comparison; BL = baseline; GP = group; mg = milligrams; dL = deciliter; esc = escalated; max = maximum; diff = difference; NR = not reported; NSG = not significant; NA = not applicable; SD = standard deviation; SE = standard error; SEM = standard error of the mean; od = once daily; bid = twice daily; tid = three times daily; HbA1c = hemoglobin A1c; f/u = follow-up; XR = extended release; GITS = gastrointestinal therapeutic system; vs = versus

* Number obtained from a figure

† Percent change from baseline

‡ 95% confidence interval

Median

Appendix F: Evidence Table 14. Quality of randomized controlled trials evaluating comparative effectiveness of oral diabetes medications on proximal clinical outcomes

Author, year	Randomized	Randomization scheme described	Double blinded	Blinding described	Withdrawals described	Quality score
Ramachandran, 2004 ⁵⁵	Yes	Not described	No	No	No	1
Rosenbaum, 2002 ¹⁵³	Yes	Not described	Yes	Not described	Yes	3
Nishio, 2006 ¹⁵¹	Yes	Not described	No	No	Yes	2
Weissman, 2005 ¹⁰⁰	Yes	Not described	Yes	Yes	Yes	4
Rosenstock, 2006 ¹²⁴	Yes	Not described	Yes	Not described	Yes	3
Bailey, 2005 ¹⁰¹	Yes	Yes	Yes	Not described	Yes	4
Pfutzner, 2006 ¹²³	Yes	Not described	Yes	Not described	Yes	3
Betteridge, 2005 ¹⁵⁷	Yes	Not described	Yes	Yes	No	3
Kardas, 2005 ¹¹⁴	Yes	Not described	No	No	Yes	2
Forst, 2005 ¹⁴⁵	Yes	Not described	No	No	No	1
Yamanouchi, 2005 ⁵⁷	Yes	Yes	No	No	Yes	3
Goldberg, 2005 ⁵²	Yes	Not described	Nr	Not described	No	1
Pfutzner, 2005 ⁶⁸	Yes	Not described	No	No	No	1
Derosa, 2005 ⁵³	Yes	Yes	Yes	Yes	Yes	5
Derosa, 2005 ⁷²	Yes	Yes	Yes	Yes	Yes	5
Inukai, 2005 ¹¹¹	Yes	Not described	No	No	No	1
Langenfeld, 2005 ¹⁴⁶	Yes	Inappropriate	No	No	Yes	1
Feinglos, 2005 ¹⁰⁴	Yes	Not described	Yes	Not described	Yes	3
Mari, 2005 ²⁶²	Yes	Not described	Yes	Not described	No	2
Goke, 2002 ⁷⁵	Yes	Not described	No	No	Yes	2
Charbonnel, 2005 ⁶³	Yes	Not described	Yes	Yes	No	3
Tan, 2005 ⁶¹	Yes	Not described	Yes	Yes	Yes	4
McCluskey, 2004 ⁷⁶	Yes	Not described	Yes	Not described	Yes	3
Kim, 2005 ¹⁵²	Yes	Not described	No	No	Yes	2
Scherthaner, 2004 ⁵⁶	Yes	Yes	Yes	Yes	Yes	5
Smith, 2005 ¹⁶¹	Yes	Not described	Yes	Yes	No	3
Choi, 2004 ⁷⁷	Yes	Not described	No	No	Yes	2
Matthews, 2005 ⁷⁰	Yes	Not described	Yes	Yes	Yes	4
Derosa, 2004 ⁹⁰	Yes	Not described	No	No	Yes	2

Appendix F: Evidence Table 14. Quality of randomized controlled trials evaluating comparative effectiveness of oral diabetes medications on proximal clinical outcomes

Author, year	Randomized	Randomization scheme described	Double blinded	Blinding described	Withdrawals described	Quality score
Schernthaner, 2004 ¹⁰⁶	Yes	Yes	Nr	Not described	Yes	3
Tan, 2004 ⁶⁵	Yes	Not described	Nr	Not described	Yes	2
Baksi, 2004 ¹²⁶	Yes	Not described	Yes	Not described	Yes	3
Tan, 2004 ⁶⁹	Yes	Not described	Yes	Not described	Yes	3
Natali, 2004 ¹⁴⁴	Yes	Not described	Yes	Yes	Yes	4
Saad, 2004 ¹⁶⁴	Yes	Not described	No	No	Yes	2
Rosenstock, 2004 ¹³¹	Yes	Not described	No	No	Yes	2
Raskin, 2004 ⁷⁴	Yes	Not described	Nr	No	Yes	2
Yanagawa, 2004 ⁶²	Yes	Not described	Nr	No	No	1
Manzella, 2004 ¹⁴⁸	Yes	Not described	No	No	Yes	2
Feinbock, 2003 ¹³⁰	Yes	Not described	No	No	Yes	2
Kerenyi, 2004 ¹²⁵	Yes	Not described	Yes	Yes	Yes	4
Jovanovic, 2004 ⁷³	Yes	Not described	No	No	Yes	2
Hanefeld, 2004 ⁶⁰	Yes	Not described	Yes	Yes	No	3
Lawrence, 2004 ⁵⁴	Yes	Not described	No	No	Yes	2
Garber, 2003 ⁸⁰	Yes	Yes	Yes	Yes	Yes	5
Takagi, 2003 ⁷⁸	Yes	Not described	No	No	No	1
Tosi, 2003 ⁹⁵	Yes	Not described	Yes	Yes	Yes	4
Goldstein, 2003 ⁸²	Yes	Yes	No	No	Yes	3
Herz, 2003 ¹⁶³	Yes	Not described	Yes	Not described	Yes	3
Bech, 2003 ¹⁹⁷	Yes	Not described	Yes	Not described	No	2
Derosa, 2003 ⁹⁷	Yes	Not described	No	No	Yes	2
Barnett, 2003 ¹⁷²	Yes	Not described	Yes	Yes	Yes	4
Fujioka, 2003 ¹⁰⁵	Yes	Not described	Yes	Yes	Yes	4
Del Prato, 2003 ¹⁴⁹	Yes	Not described	Yes	Yes	Yes	4
Pavo, 2003 ⁵⁹	Yes	Not described	Yes	Not described	Yes	3
Luis Bautista, 2003 ¹⁹³	Yes	Not described	Yes	Yes	Yes	4
Vongthavaravat, 2002 ¹⁷⁰	Yes	Yes	No	No	No	2
Virtanen, 2003 ¹⁴³	Yes	Not described	Nr	Not described	Yes	2

Appendix F: Evidence Table 14. Quality of randomized controlled trials evaluating comparative effectiveness of oral diabetes medications on proximal clinical outcomes

Author, year	Randomized	Randomization scheme described	Double blinded	Blinding described	Withdrawals described	Quality score
Vakkilainen, 2002 ¹²²	Yes	Not described	Yes	Yes	Yes	4
Hallsten, 2002 ⁵⁸	Yes	Not described	No	No	Yes	2
Scherbaum, 2002 ¹⁴¹	Yes	Not described	Yes	Not described	Yes	3
Blonde, 2002 ⁸¹	Yes	Not described	Yes	Not described	Yes	3
St John Sutto, 2002 ⁶⁷	Yes	Not described	No	No	Yes	2
Rachmani, 2002 ¹⁵⁰	Yes	Yes	No	No	Yes	3
Saloranta, 2002 ²⁴¹	Yes	Not described	Yes	Yes	Yes	4
Marre, 2002 ⁸⁴	Yes	Not described	Yes	Not described	Yes	3
Garber, 2002 ⁷⁹	Yes	Not described	Yes	Yes	Yes	4
Gomez-Perez, 2002 ¹⁰²	Yes	Not described	Yes	Not described	Yes	3
Khan, 2002 ⁵¹	Yes	Not described	No	No	Yes	2
Charpentier, 2001 ⁸⁹	Yes	Not described	Yes	Not described	Yes	3
Rosenblatt, 2001 ¹⁶²	Yes	Yes	Yes	Not described	Yes	4
Madsbad, 2001 ¹¹⁹	Yes	Not described	Yes	Not described	Yes	3
Kipnes, 2001 ¹⁶⁶	Yes	Not described	Yes	Not described	Yes	3
Amador-Licona, 2000 ⁸⁵	Yes	Not described	No	No	Yes	2
Lebovitz, 2001 ¹⁶⁹	Yes	Not described	No	No	No	1
Patel, 1999 ¹⁶⁷	Yes	Inappropriate	Yes	Not described	Yes	2
Phillips, 2001 ¹⁶⁸	Yes	Not described	Yes	Not described	Yes	3
Moses, 2001 ²¹⁸	Yes	Not described	Yes	Not described	Yes	3
Einhorn, 2000 ¹⁶⁰	Yes	Not described	Yes	Not described	Yes	3
Fonseca, 2000 ¹⁰³	Yes	Yes	Yes	Yes	Yes	5
Nakamura, 2000 ⁶⁴	Yes	Not described	No	No	No	1
Horton, 2000 ⁹⁶	Yes	Not described	Yes	Yes	Yes	4
Aronoff, 2000 ¹⁶⁵	Yes	Not described	Yes	Not described	No	2
Hanefeld, 2000 ¹⁹⁰	Yes	Not described	Yes	Yes	No	3
Hasche, 1999 ¹³⁸	Yes	Not described	Yes	Not described	Yes	3
Wolffenbuttel, 2000 ¹⁷¹	Yes	Not described	Yes	Not described	No	2

Appendix F: Evidence Table 14. Quality of randomized controlled trials evaluating comparative effectiveness of oral diabetes medications on proximal clinical outcomes

Author, year	Randomized	Randomization scheme described	Double blinded	Blinding described	Withdrawals described	Quality score
Gregorio, 1999 ¹²⁹	Yes	Yes	No	No	Yes	3
Jovanovic, 2000 ¹⁹⁴	Yes	Yes	Yes	Yes	Yes	5
Willms, 1999 ⁹⁹	Yes	Not described	Yes	Yes	Yes	4
Erle, 1999 ¹²⁷	Yes	Not described	Yes	Not described	Yes	3
Landgraf, 1999 ¹²¹	Yes	Not described	Yes	Yes	Yes	4
Marbury, 1999 ¹¹⁶	Yes	Not described	Yes	Not described	Yes	3
Wolffenbuttel, 1999 ¹¹⁷	Yes	Not described	Yes	Yes	Yes	4
Testa, 1998 ¹⁹⁸	Yes	Not described	Yes	Not described	Yes	3
Goldberg, 1998 ¹³⁹	Yes	Not described	Yes	Not described	Yes	3
1998, ¹⁶	Yes	Yes	No	No	No	2
Schade, 1998 ¹³⁵	Yes	Not described	Yes	Not described	Yes	3
1998, ¹²⁸	Yes	Not described	No	No	No	1
Lee, 1998 ²⁵⁹	Yes	Not described	Yes	Yes	Yes	4
Simonson, 1997 ¹³⁶	Yes	Not described	Yes	Not described	Yes	3
Rosenstock, 1996 ¹⁸⁹	Yes	Not described	Yes	Not described	Yes	3
Dills, 1996 ¹⁰⁷	Yes	Not described	Yes	Not described	Yes	3
Goldberg, 1996 ¹³⁴	Yes	Not described	Yes	Not described	Yes	3
Grant, 1996 ¹⁵⁴	Yes	Not described	Yes	Not described	No	2
Vray, 1995 ¹³⁷	Yes	Not described	Yes	Not described	Yes	3
DeFronzo, 1995 ⁸⁸	Yes	Not described	Yes	Yes	Yes	4
1995, ⁹²	Yes	Not described	No	No	No	1
Hermann, 1994 ⁸⁷	Yes	Yes	Yes	Yes	No	4
Campbell, 1994 ⁸³	Yes	Yes	No	No	Yes	3
Birkeland, 1994 ¹¹⁰	Yes	Not described	Yes	Yes	Yes	4
Rosenstock, 1993 ¹⁰⁹	Yes	Not described	No	No	Yes	2
Carlson, 1993 ¹⁰⁸	Yes	Not described	Yes	Not described	Yes	3
Wolffenbuttel, 1993 ¹²⁰	Yes	Yes	No	No	Yes	3
Leonhardt, 1991 ²⁶³	Yes	Yes	No	No	Yes	3
Teupe, 1991 ¹⁵⁵	Yes	Not described	No	No	Yes	2
Noury, 1991 ⁸⁶	Yes	Not described	Nr	No	Yes	2

Appendix F: Evidence Table 14. Quality of randomized controlled trials evaluating comparative effectiveness of oral diabetes medications on proximal clinical outcomes

Author, year	Randomized	Randomization scheme described	Double blinded	Blinding described	Withdrawals described	Quality score
Hermann, 1991 ⁹⁴	Yes	Yes	Yes	Yes	No	4
Schneider, 1991 ¹⁷³	Yes	Inappropriate	Yes	Not described	Yes	2
Hermann, 1991 ¹⁵⁹	Yes	Not described	Yes	Not described	Yes	3
Doman, 1991 ²⁶⁰	Yes	Not described	Yes	Not described	No	2
Kilo, 1988 ¹⁴⁷	Yes	Not described	No	No	No	1
1985, ⁹¹	Yes	Not described	No	No	No	1
Harrower, 1985 ¹¹³	Yes	Not described	No	No	Yes	2
Baba, 1983 ¹³³	Yes	Not described	Yes	Not described	Yes	3
Tseng, 2005 ¹⁴⁰	Yes	Not described	Yes	Not described	No	2
Wolever, 2000 ⁹⁸	Yes	Not described	No	No	No	1
Cefalu, 1998 ²⁶¹	Yes	Not described	Yes	Not described	No	2
Turner, 1998 ⁹³	Yes	Not described	No	No	Yes	2
Garber, 2006 ⁷¹	Yes	Not described	Yes	Yes	Yes	4
Zhu, 2003 ¹⁸⁸	Yes	Yes	Yes	Yes	Yes	5
Bakris, 2003 ⁶⁶	Yes	Not described	No	No	No	1
Draeger, 1996 ¹¹²	Yes	Not described	Yes	Yes	Yes	4
Derosa, 2003 ¹¹⁸	Yes	Yes	Yes	Yes	Yes	5
Garber, 1997 ²¹⁷	Yes	Not described	Yes	Yes	Yes	4

Appendix F: Evidence Table 15. Study Design Characteristics Table for Studies Reporting on Distal-Diabetes Related Complications (Key Question 2)

Author, year			Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Study group	Study design	Country			
Simpson, 2006 ¹⁴	Cohort	Canada	No	4.6 years (mean followup)	Age <30, other
Nishio, 2006 ¹⁵¹	RCT	Japan	No	6 months (planned duration)	Any liver disease, any kidney disease, no type 2 diabetes, other
Weissman, 2005 ¹⁰⁰	RCT	US	Yes	24 weeks (planned duration)	Age <18 and >75, any liver disease, any kidney disease, history of CVD, HbA1c <6.5 or >8.5 for patients having received prior combination treatment; <7 or >10 prior monotherapy or drug naive patients, no type 2 diabetes, other
Rosenstock, 2006 ¹²⁴	RCT	US, Canada	No	NR	Age <60, history of CVD, no type 2 diabetes, other
Bailey, 2005 ¹⁰¹	RCT	UK, 14 European countries	Yes	24 weeks (planned duration)	Age <18 or >70, history of CVD, no type 2 diabetes, other
Dormandy, 2005 ¹⁸⁵	RCT	19 European countries	Yes	NR	Age <35 or >75, any liver disease, HbA1c <6.5% for assay or lab equivalent DCCT, no type 2 diabetes, other
PROactive Eurich, 2005 ¹⁷⁹	Cohort	Canada	No	2.1 years (mean followup)	History of CVD, treatment experienced, other
Saskatchewan Health database Johnson, 2005 ¹³	Cohort	Canada	No	Median followup periods for each group ranged from 4.6 to 5.6 years	Age <30, no type 2 diabetes, other
Saskatchewan health database Cryer, 2005 ¹⁷⁶	RCT	US	Yes	12 months (planned duration)	Age <18, any liver disease, any kidney disease, no type 2 diabetes, other
COSMIC Approach Study					
Schernthaner, 2004 ⁵⁶	RCT	Europe	No	12 months (planned duration)	Age <35 or >75, treatment experienced, HbA1c <7.5% or >11%, no type 2 diabetes
Choi, 2004 ⁷⁷	RCT	Korea	No	6 months (planned duration)	Any liver disease, any kidney disease, other
Baksi, 2004 ¹²⁶	RCT	7 European countries	Yes	26 weeks (planned duration)	Age <35 or >80, any liver disease, history of CVD, treatment experienced, neuropathy, no type 2 diabetes, other
Gulliford, 2004 ¹⁷⁷	Cohort	UK, Wales, Scotland, and Ireland	No	Median followup for each group ranged from 1.67 to 3.49 years	Treatment experienced, no type 2 diabetes, other
UK General Practice Research Database Yanagawa, 2004 ⁶²	RCT	Japan	No	12 weeks (planned duration)	Age <40 or >80, any liver disease, HbA1c <7 or >10, no type 2 diabetes, other
Manzella, 2004 ¹⁴⁸	RCT	Italy	No	4 months (planned duration)	History of CVD, treatment experienced, neuropathy, no type 2 diabetes, other

Appendix F: Evidence Table 15. Study Design Characteristics Table for Studies Reporting on Distal-Diabetes Related Complications (Key Question 2)

Author, year					
Study group	Study design	Country	Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Mannucci, 2004 ¹⁸¹	Cohort	Italy	No	220.4 (mean followup)	No type 2 diabetes, other
Hanefeld, 2004 ⁶⁰	RCT	Canada, UK, Hungary, Finland, Slovak Republic, Belgium, Estonia, Lithuania, Denmark, Italy, Greece, Sweden, and Netherlands	Yes	NR	Age <35 or >75, history of CVD, HbA1c <7.5 or >11, no type 2 diabetes, other
QUARTET study group					
Lawrence, 2004 ⁵⁴	RCT	UK	Yes	12 titration, 12 week maintenance (planned duration)	Age <45 or >80, any liver disease, any kidney disease, history of CVD, HbA1c for diet treated diabetes: <7% or >10% for low-dose oral hypoglycemic therapy: >7.5%, no type 2 diabetes, other
Meier, 2003 ¹⁸²	Cohort	Germany	No	NR	Hba1c < 6.2%, no type 2 diabetes, other
The Langendreer Myocardial Infarction and Blood Glucose in Diabetic Patients Assessment (LAMBDA)					
Garber, 2003 ⁸⁰	RCT	US	Yes	16 weeks (planned duration)	Age < 20 and age>79, any liver disease, any kidney disease, treatment experienced, HbA1c > 7 and <12%, no type 2 diabetes, other
Takagi, 2003 ⁷⁸	RCT	Japan	No	NR	Any liver disease, any kidney disease, no type 2 diabetes, other
Goldstein, 2003 ⁸²	RCT	US	Yes	18 weeks (planned duration)	Any liver disease, any kidney disease, history of CVD, HbA1c <7.5 and >12.0, other
Herz, 2003 ¹⁶³	RCT	Canada and Spain	Yes	16 weeks (planned duration)	Any liver disease, any kidney disease, treatment experienced, HbA1c < 6.5% or HbA1c>9.8%, no type 2 diabetes, other
Barnett, 2003 ¹⁷²	RCT	UK	No	26 weeks (planned duration)	Age <30 or age > 80, any liver disease, HbA1c <7.5%, no type 2 diabetes, other
Fujioka, 2003 ¹⁰⁵	RCT	US	Yes	24 weeks (planned duration)	Any liver disease, any kidney disease, history of CVD, HbA1c >8.5% and FPG>200 mg/dl while on MIR for >=8 weeks, no type 2 diabetes, other
Zhu, 2003 ¹⁸⁸	RCT	China	Yes	24 weeks (planned duration)	Age <40 or age>70, any liver disease, any kidney disease, history of CVD, neuropathy, retinopathy, HbA1c <7.5%, no type 2 diabetes, other
Luis Bautista, 2003 ¹⁹³	RCT	US	Yes	NR	Age <35 or >80, HbA1c <8.0% or >10.5%, no type 2 diabetes, other
Bakris, 2003 ⁶⁶	RCT	likely US and UK	Yes	52 weeks (planned duration)	NR

Appendix F: Evidence Table 15. Study Design Characteristics Table for Studies Reporting on Distal-Diabetes Related Complications (Key Question 2)

Author, year					
Study group	Study design	Country	Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Vongthavaravat, 2002 ¹⁷⁰	RCT	India, Thailand, Philippines, Tunisia, Argentina, and Brazil	Yes	26 weeks (planned duration)	Age <40 or >80, any liver disease, any kidney disease, history of CVD, treatment experienced, neuropathy, retinopathy, no type 2 diabetes, other
Virtanen, 2003 ¹⁴³	RCT	Finland	Yes	26 weeks (planned duration)	Age <45 or >75, any liver disease, any kidney disease, history of CVD, treatment experienced, neuropathy, retinopathy, no type 2 diabetes, other
Johnson, 2002 ¹²	Cohort	Canada	No	5.1 years (mean followup)	Age <30, other
Saskatchewan health database Hallsten, 2002 ⁵³	RCT	Finland	Yes	26 weeks (planned duration)	Any liver disease, any kidney disease, history of CVD, no type 2 diabetes, other
St John Sutto, 2002 ⁶⁷	RCT	US	Yes	52 weeks (planned duration)	Age <40 or age >80, any liver disease, any kidney disease, history of CVD, no type 2 diabetes, other
Rachmani, 2002 ¹⁵⁰	RCT	Israel	No	4 years (planned duration)	Age < 40 or > 75, no type 2 diabetes, other
Gomez-Perez, 2002 ¹⁰²	RCT	Mexico	Yes	26 weeks (planned duration)	Age <40 or >80, any liver disease, any kidney disease, history of CVD, treatment experienced, no type 2 diabetes, other
Fisman, 2001 ¹⁸⁶	Cohort	Israel	No	7.7 years (mean followup)	Age < 45 or >74, any liver disease, any kidney disease, other
Kipnes, 2001 ¹⁶⁶	RCT	US	Yes	NR	Age <30 or >75, any liver disease, any kidney disease, history of CVD, neuropathy, retinopathy, HbA1c <8, no type 2 diabetes, other
Gegick, 2001 ¹⁹²	Cohort	US	Yes	12.8 (mean followup)	Hba1c had not had at least two baseline determinations while receiving maintenance troglitazone therapy, no type 2 diabetes, other
Amador-Licona, 2000 ⁸⁵	RCT	Mexico	No	12 weeks (planned duration)	Age >65, any liver disease, history of CVD, other
Lebovitz, 2001 ¹⁶⁹	RCT	US	No	26 weeks (planned duration)	Age < 36 or >81, any liver disease, any kidney disease, history of CVD, no type 2 diabetes, other
Fonseca, 2000 ¹⁰³	RCT	US	No	26 weeks (planned duration)	Age <40 or >80, any liver disease, any kidney disease, history of CVD, treatment experienced, neuropathy, no type 2 diabetes, other
Nakamura, 2000 ⁶⁴	RCT	Japan	No	3 months (planned duration)	Any liver disease, history of CVD, treatment experienced, HbA1c <6.5%, no type 2 diabetes, other
Horton, 2000 ⁹⁶	RCT	US	Yes	24 weeks (planned duration)	Age <30, any kidney disease, HbA1c <6.8% or >11%, no type 2 diabetes, other
Aronoff, 2000 ¹⁶⁵	RCT	US	Yes	26 weeks (planned duration)	Any liver disease, any kidney disease, history of CVD, neuropathy, retinopathy, HbA1c <7%, no type 2 diabetes, other

Appendix F: Evidence Table 15. Study Design Characteristics Table for Studies Reporting on Distal-Diabetes Related Complications (Key Question 2)

Author, year					
Study group	Study design	Country	Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Hanefeld, 2000 ¹⁹⁰	RCT	Europe	Yes	12 weeks (planned duration)	Age <30 or >75, any kidney disease, history of CVD, neuropathy, retinopathy, HbA1c mean level of two tests <6.8 or >10.5, no type 2 diabetes, other
Olsson, 2000 ¹⁷⁸	Cohort	Sweden	No	6.1 (0.1-13.0) years (mean followup)	No type 2 diabetes
Hasche, 1999 ¹³⁸	RCT	Germany	No	104 weeks (planned duration)	Age < 40 or >80, any liver disease, any kidney disease, history of CVD, treatment experienced, retinopathy, HbA1c <7.5 or >9.5%, no type 2 diabetes, other
Klamann, 2000 ¹⁸³ Jovanovic, 2000 ¹⁹⁴	Cohort RCT	Germany US	No Yes	NR 24 weeks (planned duration)	No type 2 diabetes, other Age <40 or > 75, any liver disease, any kidney disease, history of CVD, HbA1c with ODM (naive): <6.5%; with ODM-treatment: > 12%, no type 2 diabetes, other
Marbury, 1999 ¹¹⁶	RCT	US and Canada	Yes	12 months (planned duration)	Age >37 or <75, any liver disease, any kidney disease, history of CVD, treatment experienced, retinopathy, HbA1c <6.5% or 14.6%, no type 2 diabetes, other
Wolffenbuttel, 1999 ¹¹⁷	RCT	Germany, Austria, and Netherlands	No	12 months (planned duration)	Age <40 or >75, any liver disease, any kidney disease, history of CVD, treatment experienced, HbA1c <6.5 if treated with diet only; >12% if treated with diet plus oral, other
Garratt, 1999 ¹⁰	Cohort	US	No	Mean followup for each group ranged from 2.3 to 3.8 years (mean followup)	No type 2 diabetes, other
Goldberg, 1998 ¹³⁹	RCT	US	Yes	18 weeks (planned duration)	Age <40 and >75, no type 2 diabetes, other
1998, ¹⁵	RCT	UK	Yes	NR	Age <25 or >65, treatment experienced, no type 2 diabetes, other
UKPDS 1998, ¹⁶	RCT	UK	Yes	NR	Age <25 or >65, any kidney disease, history of CVD, treatment experienced, retinopathy, no type 2 diabetes, other
UKPDS Sonnenberg, 1997 ¹⁹¹	RCT, cross-over	US	Yes	4 weeks (planned duration)	Age <40 or >80, any liver disease, any kidney disease, treatment experienced, no type 2 diabetes, other
Rosenstock, 1996 ¹⁸⁹	NR	NR	No	NR	No type 2 diabetes, other
Draeger, 1996 ¹¹²	RCT	UK, Europe, Asia, South Africa, and South America	No	12 months (planned duration)	Age < 40 or > 80, any liver disease, any kidney disease, treatment experienced, no type 2 diabetes, other

Appendix F: Evidence Table 15. Study Design Characteristics Table for Studies Reporting on Distal-Diabetes Related Complications (Key Question 2)

Author, year					
Study group	Study design	Country	Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Lomuscio, 1996 ¹¹	unable to tell - may be cohort or case-control	Italy	No	NR	Other
DeFronzo, 1995 ⁸⁸	RCT	US	No	29 weeks (planned duration)	Age <40 or >70, any liver disease, any kidney disease, history of CVD, treatment experienced, no type 2 diabetes, other
Ikeda, 1994 ¹⁹⁵	Cohort	Japan	No	NR	Age <50 or >70, no type 2 diabetes, other
Hermann, 1994 ⁸⁷	RCT	Sweden	Yes	6 months (planned duration)	No type 2 diabetes, other
Carlson, 1993 ¹⁰⁸	RCT	US	Yes	12 weeks (planned duration)	Age <30 or >75, any liver disease, any kidney disease, no type 2 diabetes, other
Teupe, 1991 ¹⁵⁵	RCT	Germany	No	2 years (planned duration)	Age >70, any liver disease, any kidney disease, history of CVD, no type 2 diabetes, other
Akanuma, 1988 ¹⁹⁶	RCT	Japan	No	5 years (planned duration)	No type 2 diabetes, other
Diabetic Retinopathy Program					
Baba, 1983 ¹³³	RCT	Japan	No	24 weeks (planned duration)	No type 2 diabetes, other
Inzucchi, 2005 ¹⁸⁴	Cohort	US	No	NR	Age <65, no type 2 diabetes, other
Florkowski, 2001 ¹⁸⁷	Cohort	New Zealand	No	NR	Diagnosed diabetes before age 30, no type 2 diabetes, other

RCT = Randomized controlled trial; CVD = cardiovascular disease; HbA1c = Hemoglobin A1c; MIR = Metformin Immediate Release; US = United States; UK = United Kingdom; DCCT = Diabetes Control and Complications Trial-traceable assay; FPG = fasting plasma glucose; ODM = oral diabetes medication

Author, year								
Study group	Group, N	Mean age (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight (other measure)	Mean HbA1c	Mean duration of diabetes
Simpson,	Metformin, N=769	63.2	419 (54)	NR	NR	NR	NR	NR

Appendix F: Evidence Table 16. Study Population Table for Studies Reporting on Distal Diabetes-Related Complications (Key Question 2)

Author, year								
Study group	Group, N	Mean age (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight (other measure)	Mean HbA1c	Mean duration of diabetes
2006 ¹⁴	Metformin, N=768	64.6	409 (53)	NR	NR	NR	NR	NR
	Glyburide, N=2071	66.4	1148 (55)	NR	NR	NR	NR	NR
	Glyburide, N=2067	67.8	1239 (60)	NR	NR	NR	NR	NR
Nishio, 2006 ¹⁵¹	Control group (no placebo), N=28	67.5	20 (71.4)	AA: 0; C: 0; Asian: 0; H: 0; O: (100)	24.6	NR	6.9	NR
	Pioglitazone, N=26	66.2	19 (73.1)	AA: 0; C: 0; Asian: 0; H: 0; O: (100)	24.6	NR	7.7	NR
Weissman, 2005 ¹⁰⁰	Metformin + rosiglitazone, N=382	55.5	NR	NR	34.4	98.2	8.05	NR
	Metformin, N=384	55.7	NR	NR	33.8	96.7	7.97	NR
Rosenstock, 2006 ¹²⁴	Glipizide + rosiglitazone, N=116	68.7	(74.8)	NR	30.2	NR	7.72	6.8
	Placebo + glipizide, N=111	68.2	(71.8)	NR	30.5	NR	7.65	6.6
Bailey, 2005 ¹⁰¹	Metformin + rosiglitazone, N=288	58.1	168 (58)	AA: 2 (1); C: 280 (97); Asian: 3 (1); H: 0; O: 3 (1)	32.2	90.9	7.4	6
	Metformin, N=280	57.6	159 (57)	AA: 1 (<1); C: 273 (98); Asian: 3 (1); H: 0; O: 3 (1)	32.1	89.5	7.5	6.1
Dormandy, 2005 ¹⁸⁵	Pioglitazone, N=2605	61.9 (54.3 - 69.5)	1735 (67)	AA: 0; C: 2564 (98); Asian: 0; H: 0; O: 0	30.7	NR	Median 7.8	Median 8
	Placebo, N=2633	61.6 (53.8 - 69.4)	1728 (66)	AA: 0; C: 2600 (99); Asian: 0; H: 0; O: 0	31	NR	Median 7.9	Median 8
PROactive								
Eurich, 2005 ¹⁷⁹	Unspecified sulfonylurea, N=773	74.8	451 (58)	NR	NR	NR	NR	NR
Saskatchewan Health database	Metformin, N=208	72.5	123 (59)	NR	NR	NR	NR	NR
	Metformin + unspecified sulfonylurea, N=852	70	472 (55)	NR	NR	NR	NR	NR
Johnson, 2005 ¹³	Unspecified sulfonylurea, N=2138	67.8 (55.4 - 80.2)	(59)	NR	NR	NR	NR	NR
	Metformin, N=923	64.3 (51.9 - 76.7)	(52)	NR	NR	NR	NR	NR
Saskatchewan health database	Metformin + unspecified sulfonylurea, N=1081	62 (49.7 - 74.3)	(54)	NR	NR	NR	NR	NR
Cryer, 2005 ¹⁷⁶	Diet + metformin + existing metformin, N=7227	58.3	(49.3)	AA: (16.2); C: (78); Asian: (2.9); H: 0; O: (2.8)	92.5	NR	4.9	NR
COSMIC								

Appendix F: Evidence Table 16. Study Population Table for Studies Reporting on Distal Diabetes-Related Complications (Key Question 2)

Author, year								
Study group	Group, N	Mean age (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight (other measure)	Mean HbA1c	Mean duration of diabetes
Approach Study	Diet + usual care, N=1505	58.8	(49.5)	AA: (17.5); C: (76.2); Asian: (2.7); H: 0; O: (3.6)	92.2	NR	4.7	NR
Schemthaner, 2004 ⁵⁶	Placebo + diet + pioglitazone, N=597	57	314 (52.6)	31.2	88.2	8.7	3.4	NR
	Placebo + diet + metformin, N=597	56	345 (57.8)	31.4	89.7	8.7	3.1	NR
Choi, 2004 ⁷⁷	Rosiglitazone + diet, 38	60.9	24	NR	24.9	67.6	7.79	7.5
	Uptitration of existing medications, 45	59.9	34	NR	24.8	68.1	7.72	7.2
Baksi, 2004 ¹²⁶	Glyclazide, N=241	61.9	151 (62.7)	AA: 1 (0.4); C: 235 (97.5); Asian: 1 (0.4); H: 0; O: 4 (1.7)	29.7	NR	8.6	6.9
	Glyclazide + rosiglitazone, N=225	61.1	129 (57.3)	AA: 1 (0.4); C: 219 (97.3); Asian: 3 (1.3); H: 0; O: 2 (0.9)	30.2	NR	8.5	6.5
Gulliford, 2004 ¹⁷⁷	Unspecified sulfonylurea, N=6620	67	3644 (55)	NR	NR	NR	NR	NR
	Metformin + unspecified sulfonylurea, N=1868	61	945 (51)	NR	NR	NR	NR	NR
UK General Practice Research Database	Metformin, N=2232	61	1120 (50)	NR	NR	NR	NR	NR
	Metformin + unspecified sulfonylurea, N=867	58	389 (45)	NR	NR	NR	NR	NR
Yanagawa, 2004 ⁶²	Glyclazide, N=21	54	15	NR	24	NR	8.3	6
	Pioglitazone, N=19	54	13	NR	24.6	NR	8.3	6.7
Manzella, 2004 ¹⁴⁸	Placebo + diet, N=60	57 (all patients)	33	NR	29.2	NR	8.1	NR
	Diet + metformin, N=60	57 (all patients)	31	NR	29.5	NR	8	NR
Mannucci, 2004 ¹⁸¹	Metformin + unspecified sulfonylurea (women), N=197	67.6	(0)	NR	28.8	NR	8.9	14.5
	SU or biguanide or insulin (women), N=237	68.7	(0)	NR	27.2	NR	8.1	13.5
	Metformin + unspecified sulfonylurea (men), N=179	64.2	(100)	NR	27.8	NR	8.6	14
	SU or biguanide or insulin (men), N=314	62.8	(100)	NR	26.7	NR	8	10.5

Appendix F: Evidence Table 16. Study Population Table for Studies Reporting on Distal Diabetes-Related Complications (Key Question 2)

Author, year		Mean age (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight (other measure)	Mean HbA1c	Mean duration of diabetes
Study group	Group, N							
Hanefeld, 2004 ⁶⁰	Placebo + unspecified sulfonylurea + pioglitazone, N=31	60	171 (53.6)	AA: 2 (0.6); C: 317 (99.4); Asian: 0; H: 0; O: 0 (0)	30.2	85.3	8.82	7
QUARTET study group	Placebo + metformin + unspecified sulfonylurea, N=320	60	175 (54.7)	AA: 3 (0.9); C: 315 (98.4); Asian: 0; H: 0; O: 2 (0.6)	30	84.9	8.8	7.1
Lawrence, 2004 ⁵⁴	Metformin, N=20	59.5	12	NR	median 29.2	8.04	NR	NR
	Glyclazide, N=20	63.5	13	NR	median 28.7	7.85	NR	NR
	Pioglitazone, N=20	60.4	14	NR	median 30.6	7.43	NR	NR
Meier, 2003 ¹⁸²	Glibenclamide, N=77	73	33	NR	26	71	8.4	10
The Langendreer Myocardial Infarction and Blood Glucose in Diabetic Patients Assessment (LAMBDA)	Not glibenclamide (other diabetes medica-tions), N=75	NR	NR	NR	NR	NR	NR	NR
Garber, 2003 ⁸⁰	Metformin + glyburide, N=171	55.6	76 (44)	AA: 18 (10.5); C: 132 (77.2); Asian: 0; H: 15 (8.8); O: 6 (3.5)	31.4	91.9	8.8	3
	Metformin, N=164	54.7	71 (43.3)	AA: 11 (6.7); C: 132 (80.5); Asian: 0; H: 15 (9.1); O: 6 (3.7)	31.4	92.8	8.5	2.6
	Glyburide, N=151	55.3	66 (43.7)	AA: 11 (7.3); C: 123 (81.5); Asian: 0; H: 12 (7.9); O: 5 (3.3)	31.1	91	8.7	3
Takagi, 2003 ⁷⁸	Pioglitazone, N=23	64	20	NR	25.6	NR	6.8	NR
	Control group (conventional antidiabetic therapy), N=21	65	14	NR	24.5		6.7	
Goldstein, 2003 ⁸²	Metformin + glipizide, N=87	54.6	(58.6)	AA: (11.5); C: (72.4); Asian: (0); H: (16.1); O: 0	31.7	94	8.7	5.9
	Glipizide, N=84	57.4	(64.3)	AA: (11.9); C: (71.4); Asian: (2.4); H: (14.3);	30.6	89.9	8.9	6.5

Appendix F: Evidence Table 16. Study Population Table for Studies Reporting on Distal Diabetes-Related Complications (Key Question 2)

Author, year	Study group	Group, N	Mean age (age range)	Male, n (%)	Race, n (%) O: 0	Mean BMI in kg/m ² (other measure)	Mean weight (other measure)	Mean HbA1c	Mean duration of diabetes
		Metformin, N=76	56.6	(61.8)	AA: (15.8); C: (65.8); Asian: (1.3); H: (17.1); O: 0	31.6	93.8	8.7	7.3
Herz, 2003 ¹⁶³		Placebo, N=99	58 (33-85)	49 (49.5)	AA: 0 (0); C: 96 (97); Asian: 3 (3); H: 0 (0); O: 0	31.7	86.3	7.5	NR
		Pioglitazone, N=99	59 (24-79)	59 (59.6)	AA: 0 (0); C: 97 (98); Asian: 1 (1); H: 1 (1); O: 0	31.7	86.6	7.5	NR
		Pioglitazone, N=99	58.1 (24-84)	52 (52.5)	AA: 0 (0); C: 93 (93.9); Asian: 1 (3); H: 3 (3); O: 0	30.8	84.1	7.6	NR
Barnett, 2003 ¹⁷²		Placebo + unspecified sulfonylurea, N=87	54.1 (32-78)	(75)	AA: 0 (0); C: 0 (0); Asian: 0 (0); H: 0 (0); O: 100	26.4	NR	9.06	6.5
		Unspecified sulfonylurea + rosiglitazone, N=84	54.3 (28-76)	(80)	AA: 0 (0); C: 0 (0); Asian: 0 (0); H: 0 (0); O: 100	26.8	NR	9.21	6.5
Fujioka, 2003 ¹⁶⁵		Placebo + diet + metformin XR, N=75	54	34	NR	32	92	7	3
		Placebo + diet + metformin XR, N=71	55	28	NR	31	88	7	3
		Placebo + Diet + metformin, N=71	54	31	NR	33	96	7.1	3
Zhu, 2003 ¹⁸⁸		Placebo + unspecified sulfonylurea, N=105	58.8	(46)	AA: 0; C: 0; Asian: 100; H: 0; O: 0	25.1	NR	9.8	7.6
		Unspecified sulfonylurea + rosiglitazone, N=215	59	(41)	AA: 0; C: 0; Asian: 100; H: 0; O: 0	24.8	NR	9.8	7.2
		Unspecified sulfonylurea + rosiglitazone, N=210	58.9	(48)	AA: 0; C: 0; Asian: 100; H: 0; O: 0	24.9	NR	9.9	7.9
Luis Bautista, 2003 ¹⁹³		Diet + exercise + glimepiride, N=48	48.4	27 (56.3)	AA: 0; C: 0; Asian: 0; H: (100); O: 0	83.3	10	4.2	NR
		Placebo + diet + exercise, N=22	50.7	11 (50)	AA: 0; C: 0; Asian: 0; H: (100); O: 0	76.3	10.5	5.7	NR
Bakris, 2003 ⁸⁶		Glyburide, N=99	56.1	71	NR	NR	NR	9.5	NR
		Rosiglitazone, N=104	55.1	75	NR	NR	NR	9.1	NR
Vongthavaravat,		Diet + unspecified	54.6 (30-76)	75 (45.7)	AA: 6 (3.7); C: 66	27.1	69	9.1	5

Appendix F: Evidence Table 16. Study Population Table for Studies Reporting on Distal Diabetes-Related Complications (Key Question 2)

Author, year					Mean BMI in kg/m ² (other measure)	Mean weight (other measure)	Mean HbA1c	Mean duration of diabetes
Study group	Group, N	Mean age (age range)	Male, n (%)	Race, n (%)				
2002 ¹⁷⁰	sulfonylurea + rosiglitazone, N=164 Diet + unspecified sulfonylurea, N=170	57.3 (37-77)	72 (42.4)	(40.2); Asian: 91 (55.5); H: 0; O: 1 (0.6) AA: 4 (2.4); C: 62 (36.5); Asian: 101 (59.4); H: 0; O: 3 (1.8)	27.1	68.8	8.9	6
Virtanen, 2003 ¹⁴³	Placebo + diet, N=14 Diet + rosiglitazone, N=14 Diet + metformin, N=13	58 58 58	10 10 8	NR NR NR	30.3 29.1 29.9	88.3 83.7 88.8	6.3 6.8 6.9	NR NR NR
Johnson, 2002 ¹²	Unspecified sulfonylurea, N=3033 Metformin, N=1150	67.2 63.8	1789 (59) 621 (54)	NR NR	NR NR	NR NR	NR NR	NR NR
Saskatchewan health database	Metformin + unspecified sulfonylurea, N=4683	62.1	2543 (54.3)	NR	NR	NR	NR	NR
Hallsten, 2002 ³⁸	Placebo + diet, N=14 Diet + metformin, N=13 Diet + rosiglitazone, N=14	57.7 57.8 58.6	10 8 10	NR NR NR	30.3 29.9 29.3	NR NR NR	6.3 6.9 6.8	NR NR NR
St John Sutton, 2002 ⁶⁷	Glyburide, N=99 Rosiglitazone, N=104	56.1 (40-76) 55.1 (40-77)	(71) (75)	AA: (3); C: (76); Asian: 0; H: 0; O: (21) AA: (5); C: (73); Asian: 0; H: 0; O: (22)	65.7% >=27 67.3% >=27	9.5 9.1	6.2 5.3	NR NR
Rachmani, 2002 ¹⁵⁰	Metformin stopped + diet, N=198 Metformin continued + diet, N=195	64 65	102 103	NR NR	28.4 28.7	NR NR	8.6 8.6	14 15
Gomez-Perez, 2002 ¹⁰²	Placebo + metformin, N=34 Metformin + rosiglitazone, N=35 Metformin + rosiglitazone, N=36	53.4 (40-68) 51.7 (40-73) 54.2 (42-76)	10 10 7	AA: 0; C: 1; Asian: 0; H: 26; O: 7 AA: 0; C: 0; Asian: 0; H: 28; O: 7 AA: 0; C: 4; Asian: 0; H: 26; O: 6	28.5 28 27.6	NR NR NR	NR NR NR	9.1 11.1 10.7
Fisman, 2001 ¹⁸⁶	Diet, N=990 Glyburide, N=953 Metformin, N=79 Metformin + glyburide, N=253	60.3 59.8 59.5 60.7	(76) (76) (66) (66)	NR NR NR NR	27 27 29 27	76 77 81 75	NR NR NR NR	NR NR NR NR
Kipnes, 2001 ¹⁶⁶	Placebo + unspecified	56.9	109	AA: 25; C: 141; Asian:	32	NR	9.9	19

Appendix F: Evidence Table 16. Study Population Table for Studies Reporting on Distal Diabetes-Related Complications (Key Question 2)

Author, year					Mean BMI in kg/m ² (other measure)	Mean weight (other measure)	Mean HbA1c	Mean duration of diabetes
Study group	Group, N	Mean age (age range)	Male, n (%)	Race, n (%)				
	sulfonylurea, N=187			3; H: 18; O: 0				
	Unspecified sulfonylurea + pioglitazone, N=184	56.5	109	AA: 20; C: 146; Asian: 3; H: 15; O: 0	31.4	NR	10	29
	Unspecified sulfonylurea + pioglitazone, N=189	56.6	113	AA: 17; C: 156; Asian: 3; H: 13; O: 0	32.4	NR	9.9	26
Gegick, 2001 ¹⁹²	Pioglitazone, N=67	66 (57 - 75)	NR	NR	98.3	7.1	14	NR
	Rosiglitazone, N=77	59 (48.6 - 69.4)	NR	NR	103	6.97	12	NR
Amador-Licona, 2000 ⁸⁵	Glibenclamide, N=23	48.2	7	NR	30.4	73.2	8.4	4
	Metformin, N=28	49.3	11	NR	26.8	70.7	8.5	4.5
Lebovitz, 2001 ¹⁶⁹	Placebo, N=158	59	104	NR	29.9	NR	9.0	4.6
	Rosiglitazone, N=166	60	107	NR	30.2	NR	9.0	4.8
	Rosiglitazone, N=169	61	113	NR	29.1	NR	8.8	5.4
Fonseca, 2000 ¹⁰³	Placebo + metformin, N=113	58.8	74.3	AA: (3.5); C: (81.4); Asian: 0; H: 0; O: (15)	30.3	NR	8.6	7.3
	Metformin + rosiglitazone, N=116	57.5	62.1	AA: (6.9); C: (80.2); Asian: 0; H: 0; O: (12.9)	30.2	NR	8.9	7.5
	Metformin + rosiglitazone, N=110	58.3	68.2	AA: (10); C: (77.3); Asian: 0; H: 0; O: (12.7)	29.8	NR	8.9	8.3
Nakamura, 2000 ⁶⁴	Pioglitazone, N=15	60	7	NR	NR	NR	7.7	16
	Glibenclamide, N=15	61	8	NR	NR	NR	7.8	14
	Voglibose, N=15	56	8	NR	NR	NR	7.6	15
Horton, 2000 ⁹⁶	Nateglinide, N=179	58.6	110	AA: (9.5); C: (82.1); Asian: (2.8); H: 0; O: 5.6	29.6	NR	8.3	4.7
	Metformin, N=178	56.8	121	AA: (9.6); C: (79.2); Asian: (2.2); H: 0; O: 9	29.6	NR	8.4	7.5
	Metformin + nateglinide, N=172	58.4	101	AA: (11.6); C: (82.6); Asian: (0.6); H: 0; O: 5.2	30	NR	8.4	4.5
	Placebo, N=172	59.6	104	AA: (16.9); C: (78.5); Asian: (0.6); H: 0; O: 4.1	29.2	NR	8.3	4.6
Aronoff, 2000 ¹⁶⁵	Placebo, N=79	53.7 overall mean (29-75 overall age)	(58 overall)	AA: overall (8); C: overall (78); Asian: overall (2); H: overall	90.4	10.4	NR	NR

Appendix F: Evidence Table 16. Study Population Table for Studies Reporting on Distal Diabetes-Related Complications (Key Question 2)

Author, year					Mean BMI in kg/m ² (other measure)	Mean weight (other measure)	Mean HbA1c	Mean duration of diabetes
Study group	Group, N	Mean age (age range)	Male, n (%)	Race, n (%)				
	Pioglitazone, N=81	53.7 overall mean (29-75 overall age)	(58overall)	(12); O: (1) AA: overall (8); C: overall (78); Asian: overall (2); H: overall (12); O: (1)	93.5	10	NR	NR
	Pioglitazone, N=81	53.7 overall mean (29-75 overall age)	(58overall)	AA: overall (8); C: overall (78); Asian: overall (2); H: overall (12); O: (1)	91.2	10.2	NR	NR
	Pioglitazone, N=87	53.7 overall mean (29-75 overall age)	(58overall)	AA: overall (8); C: overall (78); Asian: overall (2); H: overall (12); O: (1)	90.3	10.2	NR	NR
	Pioglitazone, N=80	53.7 overall mean (29-75 overall age)	(58overall)	AA: overall (8); C: overall (78); Asian: overall (2); H: overall (12); O: (1)	90.8	10.3	NR	NR
Hanefeld, 2000 ¹⁹⁰	Placebo, N=60	57.4	36	NR	28.3	NR	8.5	5.4
	Nateglinide, N=51	58	36	NR	29	NR	8.4	4.5
	Nateglinide, N=58	56.1	41	NR	28.1	NR	8.3	6.2
	Nateglinide, N=63	54.4	44	NR	28.6	NR	8.3	4.4
	Nateglinide, N=57	56.5	36	NR	28.8	NR	8.5	3.7
Olsson, 2000 ¹⁷⁸	Unspecified sulfonylurea, N=741	NR	26.3	NR	7.3	NR	NR	NR
	Metformin + unspecified sulfonylurea, N=169	3.6 yr younger than group 1	28.8	NR	8.3	NR	NR	NR
Hasche, 1999 ¹³⁸	Diet + acarbose, N=36	63.8	17	NR	26.1	74.3	8.5	1
	Placebo + diet, N=38	63.1	19	NR	26.7	75.5	8.3	1
Klamann, 2000 ¹⁸³	Glibenclamide, N=76	72	37	NR	26.8	73	8.4	10
	Not glibenclamide (other diabetes medica-tions, diet or no treatment), N=89	73	54	NR	26.8	71	7.7	8
Jovanovic, 2000 ¹⁹⁴	Placebo, N=75	58.5	49 (65)	AA: 11 (15); C: 51 (68); Asian: 1 (1); H: 0; O: 12 (16)	29.8	NR	8.6	6.8
	Repaglinide, N=140	57.9	96 (69)	AA: 14 (10); C: 107	29.4	NR	8.9	6.6

Appendix F: Evidence Table 16. Study Population Table for Studies Reporting on Distal Diabetes-Related Complications (Key Question 2)

Author, year					Mean BMI in kg/m ² (other measure)	Mean weight (other measure)	Mean HbA1c	Mean duration of diabetes
Study group	Group, N	Mean age (age range)	Male, n (%)	Race, n (%) (76); Asian: 0 (0); H: 0; O: 19 (14) AA: 18 (12); C: 110 (75); Asian: 2 (1); H: 0; O: 16 (11)				
	Repaglinide, N=146	57.6	87 (60)		29.5	NR	8.7	6.3
Marbury, 1999 ¹¹⁶	Repaglinide, N=362	58.3	242 (67)	AA: 33 (9); C: 279 (77); Asian: 0; H: 0; O: 50 (14)	29.4	NR	8.7	7.2
	Placebo + glyburide, N=182	58.7	120 (66)	AA: 16 (9); C: 144 (79); Asian: 0; H: 0; O: 22 (12)	29.1	NR	8.9	8.3
Wolffenbuttel, 1999 ¹¹⁷	Repaglinide, N=286	61 years	(62)	NR	28.4	81.5	7.1	Median 6
	Placebo + glyburide, N=139	61 years	(68)	NR	28	81.3	7	Median 6
Garratt, 1999 ¹⁰	Unspecified sulfonylurea, N=67	68.4 years	40 (59.7)	NR	NR	NR	NR	NR
	Diet, insulin, or other oral diabetes medication, N=118	63.2 years	73 (61.9)	NR	NR	NR	NR	NR
Goldberg, 1998 ¹³⁹	Placebo, N=33	56.4	25 (76)	AA: 0; C: 29 (88); Asian: 0; H: 0; O: 4 (12)	30	NR	8.1	5.1
	Repaglinide, N=67	58.7	49 (74)	AA: 0; C: 58 (88); Asian: 0; H: 0; O: 8 (12)	30.6	NR	8.3	5.6
UKPDS, 1998 ¹⁵	Diet, N=411	53	193 (47)	AA: 0; C: (86); Asian: (6); H: 0; O: (8)	31.8	87	7.1	NR
	Diet + metformin, N=342	53	157 (46)	AA: 0; C: (85); Asian: (4); H: 0; O: (11)	31.6	87	7.3	NR
	Diet + glibenclamide, N=277	53	127 (46)	AA: 0; C: (87); Asian: (4); H: 0; O: (9)	31.5	86	7.2	NR
	Diet + unspecified sulfonylurea, N=269	58	164 (61)	AA: 0; C: (77); Asian: (13); H: 0; O: (10)	29.4	82	7.6	NR
	Diet + metformin + unspecified sulfonylurea, N=268	59	158 (59)	AA: 0; C: (77); Asian: (11); H: 0; O: (12)	29.7	83	7.5	NR
UKPDS, 1998 ¹⁶	Diet, N=896	54	555	AA: 0; C: (83); Asian: 0; H: 0; O: (16)	27.5	77	6.2	NR
	Diet + chlorpropamide, N=619	54	359	AA: 0; C: (79); Asian: 0; H: 0; O: (21)	27	75	6.3	NR
	Diet + glibenclamide,	54	381	AA: 0; C: (84); Asian: 0;	27.4	77	6.3	NR

Appendix F: Evidence Table 16. Study Population Table for Studies Reporting on Distal Diabetes-Related Complications (Key Question 2)

Author, year								
Study group	Group, N	Mean age (age range)	Male, n (%)	Race, n (%) H: 0; O: (15)	Mean BMI in kg/m ² (other measure)	Mean weight (other measure)	Mean HbA1c	Mean duration of diabetes
Sonnenberg, 1997 ¹⁹¹	Glimepiride, N=53	61	(70)	NR	NR	86	NR	7.2
	Glimepiride, N=53	NR	NR	NR	NR	NR	NR	NR
	Glimepiride, N=48	NR	NR	NR	NR	NR	NR	NR
	Glimepiride, N=46	NR	NR	NR	NR	NR	NR	NR
Rosenstock, 1996 ¹⁸⁹	Placebo, N=79	61.1	(67)	NR	NR	85.9	8	Median 6
	Glimepiride, N=88	61.8	(74)	NR	NR	82.9	8.1	Median 7
	Glimepiride, N=81	58.8	(70)	NR	NR	86.3	8.1	Median 6
	Glimepiride, N=83	59.6	(66)	NR	NR	84.2	8	Median 5
	Glimepiride, N=85	61.7	(72)	NR	NR	86.8	8.3	Median 7
Draeger, 1996 ¹¹²	Glibenclamide, N=520	60.7 (26-81)	340	AA: 0; C: 0; Asian: 74; H: 0; O: (26)	26.5	NR	8.1	5
	Glimepiride, N=524	59.7 (27-81)	325	NR	26.5	NR	8.1	5
DeFronzo, 1995 ⁸⁸	Metformin, N=143	53	62	NR	29.9	94.4	8.4	6
	Placebo, N=53	53	62	NR	29.2	92.2	8.2	6
	Placebo + metformin, N=210	55	96	NR	29.4	92.6	8.9	8.4
	Placebo + glyburide, N=209	56	103	NR	29.1	92.6	8.5	8.7
	Metformin + glyburide, N=213	55	98	NR	29	92.1	8.8	7.8
Ikeda, 1994 ¹⁹⁵	Diet, N=20	63.6	10	NR	NR	NR	7.3	13.2
	Glibenclamide, N=20	62.6	10	NR	NR	NR	7.7	13.5
Hermann, 1994 ⁸⁷	Diet + metformin, N=25	60 (34-74)	(63)	NR	NR	78.6	6.9	4
	Diet + glibenclamide, N=21	NR	NR	82.6	6.7	NR	NR	NR
	Diet + metformin + glibenclamide + other A, N=54	NR	80.2	6.8	NR	NR	NR	NR
Carlson, 1993 ¹⁰⁸	Glyburide, N=104	59.2 (33-80)	61	AA: 11; C: 81; Asian: 0; H: 7; O: 5	7.6	N=15/32/57 for <1/1-5/>5 yrs	NR	NR
	Glyburide, N=102	60.3 (38-78)	62	AA: 13; C: 81; Asian: 0; H: 4; O: 4	7.6	N=6/42/54 for <1/1-5/>5 yrs	NR	NR
Teupe, 1991 ¹⁵⁵	Diet, N=50	56	20	NR	NR	86.1	9.6	6.4
	Diet + metformin, N=50	51.5	20	NR	NR	89.1	10	8.1

Appendix F: Evidence Table 16. Study Population Table for Studies Reporting on Distal Diabetes-Related Complications (Key Question 2)

Author, year		Mean age (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight (other measure)	Mean HbA1c	Mean duration of diabetes
Study group	Group, N							
Akanuma, 1988 ¹⁹⁶ Diabetic Retinopathy Program	Glipizide, N=21	57	10 (47.6)	NR	Relative Wt at 1st Visit: 115%	131 months	NR	NR
	Unspecified sulfonylurea, N=19	58	10 (52.6)	NR	Relative Wt at 1st Visit: 115%	115 months	NR	NR
	Diet, N=20	57	16 (80)	NR	Relative Wt at 1st Visit: 114%	120 months	NR	NR
Baba, 1983 ¹³³	Glyclazide, N=146	(<39 - >70)	78 (53.42)	Obesity Index: <119: 71.9; >120: 28.1	N=35/25/39/47 for <1/1-4/5-9/>=10 yrs	NR	NR	NR
	Glibenclamide, N=131	(<39 - >70)	55 (41.98)	Obesity Index: <119: 71; >120: 29	N=30/35/31/35 for <1/1-4/5-9/>=10 yrs	NR	NR	NR
Inzucchi, 2005 ¹⁸⁴	Non- insulin-sensitizing antihyperglycemic, N=6641	76.8 +/- 7.1	3108 (46.8)	AA: 0; C: 5811 (87.5); Asian: 0; H: 0; O: 0	NR	NR	NR	NR
	Metformin, N=1273	75.2 +/- 7.0	659 (51.8)	AA: 0; C: 1164 (91.4); Asian: 0; H: 0; O: 0	NR	NR	NR	NR
	Unspecified TZD, N=819	75.8 +/- 6.9	385 (47)	AA: 0; C: 731 (89.3); Asian: 0; H: 0; O: 0	NR	NR	NR	NR
	Metformin + unspecified TZD, N=139	73.6 +/- 6.8	74 (53.2)	AA: 0; C: 123 (88.5); Asian: 0; H: 0; O: 0	NR	NR	NR	NR
Florkowski, 2001 ¹⁸⁷	Metformin, N=447 baseline for entire group	62.2 (30-82)	208	NR	overall 28.4	6.3 (glycated hemoglobin)	overall 9.6	NR

AA = African American; C = Caucasian; H = Hispanic; O = Other; XR = extended release; HbA1c = hemoglobin A1c; BMI = body-mass index; TZD = thiazolidinedione

Grading of the quality of evidence of the efficacy/effectiveness of oral diabetes medications: Thiazolidinedione vs. Metformin

	Key Question 2 Comparative Effectiveness of Distal Complications
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Appendix F: Evidence Table 17. Grading of the Body of Evidence for Distal Diabetes-Related Complications

	All Cause Mortality	CVD Mortality/ Morbidity	Microvascular outcomes (retinopathy, neuropathy, nephropathy)	Peripheral vascular disease
Quantity of Evidence:	2	3	2	3 (indirect)
Number of studies				
Total number of patients studied	1833	96	1838	6545
Quality and Consistency of Evidence:	high	high	high	high
Were study designs mostly randomized trials (high quality), non-randomized controlled trials (medium quality), observational studies (low quality), or about a 50:50 mix of experimental and observational (medium quality) ?				
Did the studies have serious (-1) or very serious (-2) limitations in quality? (Enter 0 if none)	-0.5	-1	0	-0.5
Did the studies have important inconsistency? (-1)	0	0	0	NA
Was there some (-1) or major (-2) uncertainty about the directness (i.e. extent to which the people, interventions and outcomes are similar to those of interest?) <u>Reminder: we're looking for head to head comparisons of different diabetes meds to get full credit for directness in addressing our question.</u>	-1	-1	-1	-2
Were data imprecise or sparse? (-1) (i.e. lack of data or very wide confidence intervals that may change conclusions)	-1	-1	-1	-1
Did the studies have high probability of reporting bias? (-1)	0	0	0	0
Did the studies show strong evidence of association between intervention and recruitment outcome? ("strong" if significant relative risk or odds ratio > 2 based on consistent evidence from 2 or more studies with no plausible confounders (+1); "very strong" if significant relative risk or odds ratio > 5 based on direct evidence with no major threats to validity (+2)	0	0	0	0
Did the studies have evidence of a dose-response gradient? (+1)	0	0	0	0
Did the studies have unmeasured plausible confounders that most likely reduced the magnitude of the observed association? (+1)	0	0	0	0
Overall grade of evidence (high, moderate, low, very low)	Very low	Very low	Very low	Very low

High = further research is very unlikely to change our confidence in the estimates; moderate = further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low = further research is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; very low = any estimate of effect is very uncertain.

Grading of the quality of evidence of the efficacy/effectiveness of oral diabetes medications: Thiazolidinediones vs Second Generation Sulfonylureas

	<p>Key Question 2</p> <p>Comparative Effectiveness of Distal Complications</p>
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Appendix F: Evidence Table 17. Grading of the Body of Evidence for Distal Diabetes-Related Complications

	All Cause Mortality	CVD Mortality/ Morbidity	Microvascular outcomes (retinopathy, neuropathy, nephropathy)	Peripheral vascular disease
Quantity of Evidence:	0 (direct)	2	3	3 (indirect)
Number of studies	7 (indirect)			
Total number of patients studied	10,548	246	191	7303
Quality and Consistency of Evidence:	low	high	high	high
Were study designs mostly randomized trials (high quality), non-randomized controlled trials (medium quality), observational studies (low quality), or about a 50:50 mix of experimental and observational (medium quality) ?				
Did the studies have serious (-1) or very serious (-2) limitations in quality? (Enter 0 if none)	-1	-1	-1	-0.5
Did the studies have important inconsistency? (-1)	-0.5	0	0	NA
Was there some (-1) or major (-2) uncertainty about the directness (i.e. extent to which the people, interventions and outcomes are similar to those of interest?) <u>Reminder: we're looking for head to head comparisons of different diabetes meds to get full credit for directness in addressing our question.</u>	-1	-2	-1	-2
Were data imprecise or sparse? (-1) (i.e. lack of data or very wide confidence intervals that may change conclusions)	-1	-1	-1	-1
Did the studies have high probability of reporting bias? (-1)	0	0	0	0
Did the studies show strong evidence of association between intervention and recruitment outcome? ("strong" if significant relative risk or odds ratio > 2 based on consistent evidence from 2 or more studies with no plausible confounders (+1); "very strong" if significant relative risk or odds ratio > 5 based on direct evidence with no major threats to validity (+2)	0	0	0	0
Did the studies have evidence of a dose-response gradient? (+1)	0	0	0	0
Did the studies have unmeasured plausible confounders that most likely reduced the magnitude of the observed association? (+1)	0	0	0	0
Overall grade of evidence (high, moderate, low, very low)	Very low	Very low	low	Very low

High = further research is very unlikely to change our confidence in the estimates; moderate = further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low = further research is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; very low = any estimate of effect is very uncertain.

Grading of the quality of evidence of the efficacy/effectiveness of oral diabetes medications: Metformin vs Second Generation Sulfonylureas

	Key Question 2
	Comparative Effectiveness of Distal Complications

Appendix F: Evidence Table 17. Grading of the Body of Evidence for Distal Diabetes-Related Complications

	All Cause Mortality	CVD Mortality/ Morbidity	Microvascular outcomes (retinopathy, neuropathy, nephropathy)	Peripheral vascular disease
Quantity of Evidence:				
Number of studies	4 (direct) 5 (indirect)	5	1 (direct); 1 (indirect)	1 (indirect)
Total number of patients studied	7072 (direct)	9,212	51 (direct); 2264 (indirect)	2264
Quality and Consistency of Evidence:				
Were study designs mostly randomized trials (high quality), non-randomized controlled trials (medium quality), observational studies (low quality), or about a 50:50 mix of experimental and observational (medium quality) ?	low	medium	high	high
Did the studies have serious (-1) or very serious (-2) limitations in quality? (Enter 0 if none)	-2	-1	-2	-1
Did the studies have important inconsistency? (-1)	0	0	0	NA
Was there some (-1) or major (-2) uncertainty about the directness (i.e. extent to which the people, interventions and outcomes are similar to those of interest?) <u>Reminder: we're looking for head to head comparisons of different diabetes meds to get full credit for directness in addressing our question.</u>	-1	-1	0	-2
Were data imprecise or sparse? (-1) (i.e. lack of data or very wide confidence intervals that may change conclusions)	-1	-1	-1	-1
Did the studies have high probability of reporting bias? (-1)	-1	0	0	0
Did the studies show strong evidence of association between intervention and recruitment outcome? ("strong" if significant relative risk or odds ratio > 2 based on consistent evidence from 2 or more studies with no plausible confounders (+1); "very strong" if significant relative risk or odds ratio > 5 based on direct evidence with no major threats to validity (+2))	0	0	0	0
Did the studies have evidence of a dose-response gradient? (+1)	0	+0.5	0	0
Did the studies have unmeasured plausible confounders that most likely reduced the magnitude of the observed association? (+1)	0	0	0	0
Overall grade of evidence (high, moderate, low, very low)	Very low to low	Very low to low	Very low	Very low

High = further research is very unlikely to change our confidence in the estimates; moderate = further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low = further research is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; very low = any estimate of effect is very uncertain.

Appendix F: Evidence Table 17. Grading of the Body of Evidence for Distal Diabetes-Related Complications

Grading of the quality of evidence of the efficacy/effectiveness of oral diabetes medications: Second Generation Sulfonylureas vs Meglitinides

	Key Question 2 Comparative Effectiveness of Distal Complications			
	All Cause Mortality	CVD Mortality/ Morbidity	Microvascular outcomes (retinopathy, neuropathy, nephropathy)	Peripheral vascular disease
Quantity of Evidence:				
Number of studies	1	2	0	0
Total number of patients studied	576	1001	0	0
Quality and Consistency of Evidence:				
Were study designs mostly randomized trials (high quality), non-randomized controlled trials (medium quality), observational studies (low quality), or about a 50:50 mix of experimental and observational (medium quality) ?	high	high		
Did the studies have serious (-1) or very serious (-2) limitations in quality? (Enter 0 if none)	-1	-1		
Did the studies have important inconsistency? (-1)	NA	0		
Was there some (-1) or major (-2) uncertainty about the directness (i.e. extent to which the people, interventions and outcomes are similar to those of interest?) <u>Reminder: we're looking for head to head comparisons of different diabetes meds to get full credit for directness in addressing our question.</u>	-2	-1		
Were data imprecise or sparse? (-1) (i.e. lack of data or very wide confidence intervals that may change conclusions)	-1	-1		
Did the studies have high probability of reporting bias? (-1)	0	0		
Did the studies show strong evidence of association between intervention and recruitment outcome? ("strong" if significant relative risk or odds ratio > 2 based on consistent evidence from 2 or more studies with no plausible confounders (+1); "very strong" if significant relative risk or odds ratio > 5 based on direct evidence with no major threats to validity (+2))	0	0		
Did the studies have evidence of a dose-response gradient? (+1)	0	0		
Did the studies have unmeasured plausible confounders that most likely reduced the magnitude of the observed association? (+1)	0	0		
Overall grade of evidence (high, moderate, low, very low)	Very low	Very low		

High = further research is very unlikely to change our confidence in the estimates; moderate = further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low = further research is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; very low = any estimate of effect is very uncertain.

Appendix F: Evidence Table 17. Grading of the Body of Evidence for Distal Diabetes-Related Complications

Grading of the quality of evidence of the efficacy/effectiveness of oral diabetes medications: Metformin vs Metformin + Second Generation Sulfonylureas

	Key Question 2 Comparative Effectiveness of Distal Complications			
	All Cause Mortality	CVD Mortality/ Morbidity	Microvascular outcomes (retinopathy, neuropathy, nephropathy)	Peripheral vascular disease
Quantity of Evidence: Number of studies	4 (direct) 3 (indirect)	4	0	0
Total number of patients studied	5267 (direct)	4026	0	0
Quality and Consistency of Evidence: Were study designs mostly randomized trials (high quality), non-randomized controlled trials (medium quality), observational studies (low quality), or about a 50:50 mix of experimental and observational (medium quality) ?	medium	low		
Did the studies have serious (-1) or very serious (-2) limitations in quality? (Enter 0 if none)	-1	-1		
Did the studies have important inconsistency? (-1)	-0.5	-1		
Was there some (-1) or major (-2) uncertainty about the directness (i.e. extent to which the people, interventions and outcomes are similar to those of interest?) <u>Reminder: we're looking for head to head comparisons of different diabetes meds to get full credit for directness in addressing our question.</u>	-2	-1		
Were data imprecise or sparse? (-1) (i.e. lack of data or very wide confidence intervals that may change conclusions)	-1	-1		
Did the studies have high probability of reporting bias? (-1)	0	0		
Did the studies show strong evidence of association between intervention and recruitment outcome? ("strong" if significant relative risk or odds ratio > 2 based on consistent evidence from 2 or more studies with no plausible confounders (+1); "very strong" if significant relative risk or odds ratio > 5 based on direct evidence with no major threats to validity (+2)	0	0		
Did the studies have evidence of a dose-response gradient? (+1)	0	0		
Did the studies have unmeasured plausible confounders that most likely reduced the magnitude of the observed association? (+1)	0	0		
Overall grade of evidence (high, moderate, low, very low)	Very low to low	Very low		

High = further research is very unlikely to change our confidence in the estimates; moderate = further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low = further research is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; very low = any estimate of effect is very uncertain.

Appendix F: Evidence Table 17. Grading of the Body of Evidence for Distal Diabetes-Related Complications

Grading of the quality of evidence of the efficacy/effectiveness of oral diabetes medications: Second generation Sulfonylurea vs Metformin + Second Generation Sulfonylureas

	Key Question 2 Comparative Effectiveness of Distal Complications			
	All Cause Mortality	CVD Mortality/ Morbidity	Microvascular outcomes (retinopathy, neuropathy, nephropathy)	Peripheral vascular disease
Quantity of Evidence: Number of studies	5(direct) 3(indirect)	6	1	1
Total number of patients studied	21,218	14,010	45	545
Quality and Consistency of Evidence: Were study designs mostly randomized trials (high quality), non-randomized controlled trials (medium quality), observational studies (low quality), or about a 50:50 mix of experimental and observational (medium quality)?	low	medium	high	high
Did the studies have serious (-1) or very serious (-2) limitations in quality? (Enter 0 if none)	-2	-1	-2	-1
Did the studies have important inconsistency? (-1)	-0.5	-0.5	0	NA
Was there some (-1) or major (-2) uncertainty about the directness (i.e. extent to which the people, interventions and outcomes are similar to those of interest?) <u>Reminder: we're looking for head to head comparisons of different diabetes meds to get full credit for directness in addressing our question.</u>	-1	-1	0	-1
Were data imprecise or sparse? (-1) (i.e. lack of data or very wide confidence intervals that may change conclusions)	-1	-1	-1	-1
Did the studies have high probability of reporting bias? (-1)	0	0	0	0
Did the studies show strong evidence of association between intervention and recruitment outcome? ("strong" if significant relative risk or odds ratio > 2 based on consistent evidence from 2 or more studies with no plausible confounders (+1); "very strong" if significant relative risk or odds ratio > 5 based on direct evidence with no major threats to validity (+2))	0	0	0	0
Did the studies have evidence of a dose-response gradient? (+1)	0	0	0	0
Did the studies have unmeasured plausible confounders that most likely reduced the magnitude of the observed association? (+1)	0	0	0	0
Overall grade of evidence (high, moderate, low, very low)	Very low	Very low to Low	Very low	Very low

High = further research is very unlikely to change our confidence in the estimates; moderate = further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low = further research is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; very low = any estimate of effect is very uncertain.

Appendix F: Evidence Table 18. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications in randomized controlled trials: all cause mortality

Author, year Study group	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP1, initial dose in mg (fixed or esc) max dose	GP2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) p-value GP1	GP2 "X"R (95% CI) p-value GP2
Second Generation Sulfonylurea vs. Metformin + Second Generation Sulfonylurea										
UKPDS, 1998 ¹⁵	RCT	All cause mortality/unclear mortality	Un-specified SU + diet, 269	Metformin + un-specified SU + diet, 268	NR (NR)	NR (NR)	31	47	IR 19.1	IR 30.3 HR 1.6 (1.02-2.52)
Other Direct Comparisons										
Weissman, 2005 ¹⁰⁰	RCT	All cause mortality/unclear mortality	Metformin, 384	Rosiglitazone + metformin, 382	1000 (esc) 2000	4 (esc) 8 1000 (fixed)	0	1	NR	NR
Schermer-thaner, 2004 ⁵⁶	RCT	All cause mortality/unclear mortality	Pioglitazone + placebo + diet, 597	Metformin + placebo + diet, 597	30 (esc) 45	850 up to 3 times/day (esc) 2550	3	2	NR	NR
Hanefeld, 2004 ⁸⁰ QUARTET study group	RCT	All cause mortality/unclear mortality	Pioglitazone + un-specified SU + placebo, 319	Metformin + un-specified SU + placebo, 320	15 (esc) 45 NR	850 (esc) 850 tid NR	1	2	NR	NR
Garber, 2003 ⁸⁰	RCT	All cause mortality/unclear mortality	Metformin, 164	Glyburide (no trade drug specified), 151	500 (esc) 2000	2.5 (esc) 10	0	0	NR	NR
Garber, 2003 ⁸⁰	RCT	All cause mortality/unclear mortality	Metformin, 164	Metformin + glyburide (no trade drug specified), 171	500 (esc) 2000	250 (esc) 1000 1.25 (esc) 5	0	2	NR	NR
Garber, 2003 ⁸⁰	RCT	All cause mortality/unclear mortality	Glyburide (no trade drug specified), 151	Metformin + glyburide (no trade drug specified), 171	2.5 (esc) 10	250 (esc) 1000 1.25 (esc) 5	0	2	NR	NR

Appendix F: Evidence Table 18. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications in randomized controlled trials: all cause mortality

Author, year Study group	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP1, initial dose in mg (fixed or esc) max dose	GP2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) p-value GP1	GP2 "X"R (95% CI) p-value GP2
Goldstein, 2003 ⁸²	RCT	All cause mortality/unclear mortality	Metformin, 75	Glipizide, 84	500 (esc) 2000	15 bid (fixed)	0	0	NR	NR
Goldstein, 2003 ⁸²	RCT	All cause mortality/unclear mortality	Metformin, 75	Metformin + glipizide, 87	500 (esc) 2000	500 (esc) 2000 5 (esc) 20	0	0	NR	NR
Goldstein, 2003 ⁸²	RCT	All cause mortality/unclear mortality	Glipizide, 84	Metformin + glipizide, 87	30 (fixed)	500 (esc) 2000 5 (esc) 20	0	0	NR	NR
Fujioka, 2003 ¹⁰⁵	RCT	All cause mortality/unclear mortality	Metformin + placebo + diet, 71	Metformin XR + placebo + diet, 71	1000 (esc) 1500	1000 (esc) 2000	0	1	NR	NR
Fujioka, 2003 ¹⁰⁵	RCT	All cause mortality/unclear mortality	Metformin + placebo + diet, 71	Metformin XR + placebo + diet, 75	1000 (esc) 1500	1000 (esc) 1500	0	0	NR	NR
Marbury, 1999 ¹¹⁶	RCT	All cause mortality/not specified	Glyburide (no trade drug specified) + placebo, 193	Repaglinide, 383	2.5 (esc) 15	0.5 (esc) 12	1	3	NR	NR
Draeger, 1996 ¹¹²	RCT	All cause mortality/not specified	Glimepiride, 524	Glibenclamide, 520	1 (esc) 8	2.5 (esc) 20	11	5	NR	NR
Cryer, 2005 ¹⁷⁶ COSMIC Approach Study	RCT	All cause mortality/unclear mortality	Metformin + existing medications + diet, 7227	Diet + usual care, 1505	500 (esc) 2500	NR (NR)	(1.1)	(1.3)	NR	NR
Choi, 2004 ⁷⁷	RCT	Mortality	Rosiglitazone + existing oral diabetes medications, 38	Uptitration of usual care, 45	8 (other) 4	NR (esc)	0	0	NR	NR

Appendix F: Evidence Table 18. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications in randomized controlled trials: all cause mortality

Author, year Study group	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP1, initial dose in mg (fixed or esc) max dose	GP2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) p-value GP1	GP2 "X"R (95% CI) p-value GP2
Metformin Or Second Generation Sulfonylurea vs. Placebo										
UKPDS, 1998 ¹⁵	RCT	All cause mortality/unclear mortality	Metformin + diet, 342	Diet, 411	850 (esc) 2550	NA	50	89	IR 13.5 HR 0.64 (0.45-0.91)	IR 20.6, reference group
UKPDS, 1998 ¹⁶	RCT	All cause mortality/unclear mortality	Glibenclamide + diet, 615	Diet, 896	2.5 (esc) 20	NA	18.2	19.9	RR 0.91 (0.73-1.15)	Reference group
Rachmani, 2002 ¹⁵⁰	RCT	All cause mortality/unclear mortality	Metformin continued + diet, 195	Metformin stopped + diet, 198	NR (NR)	NR (NR)	62 (32)	64 (34)	no significant differences between groups	
Pioglitazone vs. Placebo										
Dormandy, 2005 ¹⁸⁵ PROactive	RCT	Primary endpoint (all-cause mortality, non-fatal MI, stroke, acute coronary syndrome, endovascular or surgical intervention in the coronary or leg arteries, and amputation above the ankle)	Pioglitazone + existing diabetes medications, 2605	Placebo + existing diabetes medications, 2633	15 (esc) 45	NR (NR)	514	572	HR 0.90 (0.80-1.02)	Reference group
Dormandy, 2005 ¹⁸⁵ PROactive	RCT	Secondary endpoint: death from any cause, nonfatal MI (excluding silent MI), or stroke	Pioglitazone + existing diabetes medications, 2605	Placebo + existing diabetes medications, 2633	15 (esc) 45	NR (NR)	358	301	Adjusted HR 0.84 (0.72-0.98); 0.03	HR ref
Nishio, 2006 ¹⁵¹	RCT	All cause mortality/unclear mortality	Pioglitazone, 26	Control group (existing medications), 28	30 (fixed)	NR (NR)	0	0	NR	NR

Comp = comparison; GP = group; mg = milligrams; esc = escalated; max = maximum; CI = confidence interval; IR = incidence rate; RR = relative risk; HR = hazard ratio; OR = odds ratio; SU = sulfonylurea; NR = not reported; RCT = randomized controlled trial; ref = reference; MI = myocardial infarction; XR = extended release

Appendix F: Evidence Table 19. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications in non-randomized trials and cohort studies: all cause mortality

Author, year Study group	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP1, initial dose in mg (fixed or esc) max dose	GP2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) p-value GP1	GP2 "X"R (95% CI) p-value GP2
Metformin Or Second Generation Sulfonylurea Monotherapy vs. Metformin + Second Generation Sulfonylurea										
Gulliford, 2004 ¹⁷⁷ UK General Practice Research Database	Cohort	All cause mortality/used research database to identify	Metformin, 3099	Metformin + un-specified SU, 1868	NR (NR)	NR (NR)	144	127	Reference	Adjusted HR 1.06 (0.85-1.31); 0.616
Gulliford, 2004 ¹⁷⁷ UK General Practice Research Database	Cohort	All cause mortality/used research database to identify	Un-specified SU, 8488	Metformin + un-specified SU, 867	NR (NR)	NR (NR)	1030	32	Reference group	Adjusted HR 0.95 (0.64-1.4); 0.801
Eurich, 2005 ¹⁷⁹ Saskatchewan Health database	Cohort	All cause mortality/unclear mortality	Un-specified SU	Metformin + SU	NR (NR)	NR (NR)	NR	NR	Reference group	Adjusted HR 0.61 (0.52-0.72)
Johnson, 2002 ¹² Saskatchewan health database	Cohort	All cause mortality/mortality registry + vital statistics file of Saskatchewan database	Un-specified SU, 3033	Metformin + un-specified SU, 4683	NR (NR)	NR (NR)	750 (24.7)	635 (13.6)	RR 1 OR 1.0 (ref)	Adjusted RR 0.63 (0.58-0.75) Adjusted OR 0.66 (0.58-0.75)
Olsson, 2000 ¹⁷⁸	Cohort	All cause mortality/mortality registry	Un-specified SU, 741	Metformin + un-specified SU, 169	NR (NR)	NR (NR)	NR	NR	OR 1	Adjusted OR 1.63 (1.27-2.09)

Appendix F: Evidence Table 19. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications in non-randomized trials and cohort studies: all cause mortality

Author, year Study group	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP1, initial dose in mg (fixed or esc) max dose	GP2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) p-value GP1	GP2 "X"R (95% CI) p-value GP2
Metformin + Second Generation Sulfonylurea vs. Other Oral Diabetes Medications										
Mannucci, 2004 ¹⁸¹	Cohort	All cause mortality/city of Florence registry office or other registry offices	Metformin + Un-specified SU, 314	SU or biguanide or insulin, 197	Mean dose = 7.3 for glibenclamide; 338 for chlorpropamide; 1100 metformin; 60.1 phenfor-min	NR (NR)	NR	NR	Adjusted HR for women only: 2.08 (1.18-3.67)	Reference group
Mannucci, 2004 ¹⁸¹	Cohort	All cause mortality/city of Florence registry office or other registry offices	Metformin + Un-specified SU, 314	SU or biguanide or insulin, 179	Mean dose = 7.3 for glibenclamide; 338 for chlorpropamide; 1100 metformin; 60.1 phenfor-min	NR (NR)	NR	NR	Adjusted HR for men only: 1.68 (1.01-2.79)	Reference group
Metformin vs. Second Generation Sulfonylurea										
Eurich, 2005 ¹⁷⁹ Saskatchewan Health database	Cohort	All cause mortality/unclear mortality	Metformin	SU	NR (NR)	NR (NR)	NR	NR	Adjusted HR 0.70 (0.54-0.91)	Reference group
Evans*, 2006 ¹⁸⁰	Cohort	All cause mortality/unclear mortality	SU, 3331	Metformin, 2286	NR (NR)	NR (NR)	NR	NR	Adjusted RR 1.43 (1.15-1.77)	Reference group
Second Generation Sulfonylurea vs. Other										

Appendix F: Evidence Table 19. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications in non-randomized trials and cohort studies: all cause mortality

Author, year Study group	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP1, initial dose in mg (fixed or esc) max dose	GP2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) p-value GP1	GP2 "X"R (95% CI) p-value GP2
Garratt, 1999 ¹⁰	Cohort	All cause mortality/mortality registry + medical record review + standardized questionnaire	Glibenclamide, 67	Diet, insulin, or other oral diabetes medication, 118	NR (NR)	NR (NR)	NR	NR	Adjusted OR 2.53 (1.13- 5.67)	Reference group
Lomuscio, 1996 ¹¹	Cohort	All cause mortality/unclear mortality	Glibenclamide, 106	Not glibenclamide, 126	at minimum 10 (NR)	NR (NR)	12 (11)	27 (25)	NR	NR
Meier, 2003 ¹⁸² The LAngendreer Myocardial Infarction and Blood Glucose in Diabetic Patients Assessment (LAMBDA)	Cohort	Mortality post-myocardial infarction	Glibenclamide, 77	Not glibenclamide (other diabetes medications), 75	NR (NR)	NR (NR)	NR	NR	p=0.53 vs. GP2	
Klamann, 2000 ¹⁸³	Cohort	Mortality/fatal myocardial infarction + CVD mortality ICD-9 413 for acute MI + used hospital records to see who died during hospitalization	Glibenclamide, 76	Not glibenclamide (other diabetes medications or diet or no treatment), 89	7.4 mean (NR)	NR (NR)	25 (32.9)	29 (33)	p=0.97 vs. GP2	
Thiazolidinedione Or Metformin vs. Other Diabetes Medications										
Inzucchi, 2005 ¹⁸⁴	Cohort	All cause mortality/Linkage with the Medicare Enrollment Database	Un-specified TZD, 819	Non-insulin-sensitizing antihyperglycemic, 6641	NR (NR)	NR (NR)	237 (28.9)	2014 (30.3)	Adjusted HR 0.92 (0.8-1.05); 0.221	HR 1
Inzucchi, 2005 ¹⁸⁴	Cohort	All cause mortality/Linkage with the Medicare Enrollment Database	Metformin, 1273	Non-insulin-sensitizing antihyperglycemic, 6641	NR (NR)	NR (NR)	246 (19.3)	2014 (30.3)	Adjusted HR 0.92 (0.81-1.06); 0.255	HR 1

Appendix F: Evidence Table 19. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications in non-randomized trials and cohort studies: all cause mortality

Author, year	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP1, initial dose in mg (fixed or esc) max dose	GP2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) p-value GP1	GP2 "X"R (95% CI) p-value GP2
Study group	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP1, initial dose in mg (fixed or esc) max dose	GP2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) p-value GP1	GP2 "X"R (95% CI) p-value GP2
Metformin Or Second Generation Sulfonylurea vs. Placebo/Diet										
Simpson, 2006 ¹⁴	Cohort	All cause mortality/vital statistics files of Saskatchewan Health database	Glyburide high dose	Glyburide low dose	High dose/ above group median (NR)	Low dose/ below group median (NR)	41.5	70.2	HR 1.29 (1.1-1.45)	
Simpson, 2006 ¹⁴	Cohort	All cause mortality/vital statistics files of Saskatchewan Health database	Metformin high dose	Metformin low dose	High dose/ above group median (NR)	Low dose/ below group median (NR)	37.6	53.4	HR 0.84 (0.70-1.1)	
Fisman, 2001 ¹⁸⁶	Cohort	All cause mortality/mortality registry + matched the patients' ID number with their life status in the population registry	Metformin, 79	Diet, 990	NR (NR)	NR (NR)	NR	NR	IR 55.7 Adjusted HR 1.26 (0.81-1.96)	IR 39.5; HR 1 (ref)
Fisman, 2001 ¹⁸⁶	Cohort	All cause mortality/mortality registry + matched the patients' ID number with their life status in the population registry	Glyburide (no trade drug specified), 953	Diet, 990	NR (NR)	NR (NR)	NR	NR	IR 53.6 HR 1.22 (1.02-1.45)	IR 39.5; HR 1 (ref)
Florkowski, 2001 ¹⁸⁷	Cohort	All cause mortality/mortality registry + death certificates + clinic records	Metformin	Diet	NR (NR)	NR (NR)	NR	NR	HR 0.79 (0.4-1.58)	HR 1 (ref)
Florkowski, 2001 ¹⁸⁷	Cohort	All cause mortality/mortality registry + death certificates + clinic records	Un-specified SU	Diet	NR (NR)	NR (NR)	NR	NR	HR 1 (0.56-1.79)	HR 1 (ref)
Metformin + Second Generation Sulfonylurea vs. Placebo										
Fisman, 2001 ¹⁸⁶	Cohort	All cause mortality/mortality registry + matched the patients' ID number with their life status in the population registry	Metformin + glyburide (no trade drug specified), 253	Diet, 990	NR (NR)	NR (NR)	NR	NR	IR 75.8 HR 1.53 (1.2-1.96)	IR 39.5; HR 1 (ref)
Florkowski, 2001 ¹⁸⁷	Cohort	All cause mortality/mortality registry + death certificates + clinic records	SU + metformin	Diet	NR (NR)	NR (NR)	NR	NR	HR 1.3 (0.71-2.38)	HR 1 (ref)

Appendix F: Evidence Table 19. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications in non-randomized trials and cohort studies: all cause mortality

Comp = comparison; GP = group; mg = milligrams; esc = escalated; max = maximum; CI = confidence interval; IR = incidence rate; RR = relative risk; HR = hazard ratio; OR = odds ratio; SU = sulfonylurea; TZD = Thiazolidinedione; NR = not reported; ref = reference; MI = myocardial infarction; CVD = cardiovascular disease; ICD-9 = International Classification of Diseases – 9; ID = identification; UK = United Kingdom; vs = versus

* Study was published after the end date of our search.

Appendix F: Evidence Table 20. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications for randomized controlled trials: cardiovascular mortality

Author, year Study group	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP1, initial dose in mg (fixed or esc) max dose	GP2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) p-value GP1	GP2 "X"R (95% CI) p-value GP2
Thiazolidinedione vs. Other Diabetes Medications										
Lawrence, 2004 ⁵⁴	RCT	Cardiovascular disease mortality/fatal myocardial infarction	Pioglitazone, 21	Metformin, 21	30 (esc) 45	500 bid (esc) 1000 tid	0	1	NR	NR
Lawrence, 2004 ⁵⁴	RCT	Cardiovascular disease mortality/fatal myocardial infarction	Pioglitazone, 21	Gliclazide, 22	30 (esc) 45	80 od (esc) 160 bid	0	0	NR	NR
Choi, 2004 ⁷⁷	RCT	Cardiovascular disease mortality	Rosiglitazone + existing oral diabetes medications, 38	Uptitration of usual care, 45	8 (other) 4	NR (esc)	0	0	NR	NR
Metformin vs. Second Generation Sulfonylurea										
Lawrence, 2004 ⁵⁴	RCT	Cardiovascular disease mortality/fatal myocardial infarction	Metformin, 21	Gliclazide, 22	500 bid (esc) 1000 tid	80 (esc) 160 bid	1	0	NR	NR
DeFronzo, 1995 ⁸⁸	RCT	Cardiovascular disease mortality/fatal myocardial infarction	Metformin + placebo, 210	Glyburide (no trade drug specified) + placebo, 209	500 (esc) 2500	5 bid (esc) 10 bid	1	0	NR	NR
Metformin vs. Meglitinide										
Horton, 2000 ⁹⁶	RCT	Cardiovascular disease mortality/due to arteriosclerotic and hypertensive heart disease + unclear CHD	Metformin, 178	Nateglinide, 179	500 tid (fixed)	120 tid (fixed)	1	0	NR	NR
Metformin vs. Metformin + Thiazolidinedione										
Bailey, 2005 ¹⁰¹	RCT	Cardiovascular disease mortality/sudden cardiac death	Metformin, 280	Rosiglitazone + metformin, 288	2500 (esc) 3000	4 (esc) 8 2000 (fixed)	0	1	NR	NR

Appendix F: Evidence Table 20. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications for randomized controlled trials: cardiovascular mortality

Author, year Study group	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP1, initial dose in mg (fixed or esc) max dose	GP2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) p-value GP1	GP2 "X"R (95% CI) p-value GP2
Fonseca, 2000 ¹⁰³	RCT	Cardiovascular disease mortality/unclear mortality + fatal myocardial infarction	Metformin + placebo, 113	Rosiglitazone + metformin, 116	2500 (fixed)	4 (fixed) 2500 (fixed)	0	1	NR	NR
Fonseca, 2000 ¹⁰³	RCT	Cardiovascular disease mortality/unclear mortality + fatal myocardial infarction	Metformin + placebo, 113	Rosiglitazone + metformin, 110	2500 (fixed)	8 (fixed) 2500 (fixed)	0	0	NR	NR
Metformin vs. Metformin + Second Generation Sulfonylurea										
DeFronzo, 1995 ⁸⁸	RCT	Cardiovascular disease mortality/fatal myocardial infarction	Metformin + placebo, 210	Metformin + glyburide (no trade drug specified), 213	500 (esc) 2500	500 (esc) 2500 10 (esc) 20	1	0	NR	NR
Second Generation Sulfonylurea vs. Metformin + Second Generation Sulfonylurea										
DeFronzo, 1995 ⁸⁸	RCT	Cardiovascular disease mortality/fatal myocardial infarction	Glyburide (no trade drug specified) + placebo, 209	Metformin + glyburide (no trade drug specified), 213	5 bid (esc) 10 bid	500 (esc) 2500 10 (esc) 20	0	0	NR	NR
UKPDS, 1998 ¹⁵	RCT	Fatal myocardial infarction	SU, 269	Metformin + SU, 268	NR (esc) 10 bid	850 (esc) 2550 NR (esc) 10 bid	NR	NR	RR 1 (ref)	RR 1.79 (0.64 – 4.99)
Second Generation Sulfonylurea vs. Second Generation Sulfonylurea										
Draeger, 1996 ¹¹²	RCT	Cardiovascular disease mortality/fatal myocardial infarction + CHF death + myocardial ischemia	Glimepiride, 524	Glibenclamide, 520	1 (esc) 8	2.5 (esc) 20	5	3	NR	NR
Second Generation Sulfonylurea vs. Second Generation Sulfonylurea + Thiazolidinedione										
Rosenstock, 2006 ¹²⁴	RCT	Cardiovascular disease mortality/unclear CVD mortality	Glipizide + placebo, 111	Rosiglitazone + glipizide, 116	10 (esc) 20	4 (fixed) 10 (esc) 20	2	0	NR	NR

Appendix F: Evidence Table 20. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications for randomized controlled trials: cardiovascular mortality

Author, year	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP1, initial dose in mg (fixed or esc) max dose	GP2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) p-value GP1	GP2 "X"R (95% CI) p-value GP2
Baksi, 2004 ¹²⁶	RCT	Cardiovascular disease mortality/fatal myocardial infarction	Gliclazide, 241	Rosiglitazone + gliclazide, 225	160 (esc) 320	160 (fixed) 4 bid (fixed)	0	1	NR	NR
Rosiglitazone vs. Placebo										
Zhu, 2003 ¹⁸⁸	RCT	Cardiovascular disease mortality/fatal myocardial infarction	Rosiglitazone + unspecified SU, 221	Placebo + existing SU, 112	2 bid (fixed) NR (fixed)	NR (fixed)	0	0	NR	NR
Zhu, 2003 ¹⁸⁸	RCT	Cardiovascular disease mortality/fatal myocardial infarction	Rosiglitazone + existing SU, 221	Placebo + existing SU, 112	4 bid (fixed) NR (fixed)	NR (fixed)	1	0	NR	NR
Second Generation Sulfonylurea vs. Placebo										
Rosenstock, 1996 ¹⁸⁹	RCT	Cardiovascular disease mortality/fatal myocardial infarction	Glimp-iride, 88	Placebo, 79	8 od (fixed)	NA	0	0	NR	NR
Rosenstock, 1996 ¹⁸⁹	RCT	Cardiovascular disease mortality/fatal myocardial infarction	Glimp-iride, 85	Placebo, 79	8 bid (fixed)	NA	0	0	NR	NR
Rosenstock, 1996 ¹⁸⁹	RCT	Cardiovascular disease mortality/fatal myocardial infarction	Glimp-iride, 83	Placebo, 79	16 od (fixed)	NA	0	0	NR	NR
Rosenstock, 1996 ¹⁸⁹	RCT	Cardiovascular disease mortality/fatal myocardial infarction	Glimp-iride, 81	Placebo, 79	4 bid (fixed)	NA	1	0	NR	NR
Metformin vs. Placebo										
DeFronzo, 1995 ³⁸	RCT	Cardiovascular disease mortality/fatal myocardial infarction	Metformin, 143	Placebo, 146	850 (esc) 850 tid	NA	0	0	NR	NR
Horton, 2000 ³⁶	RCT	Cardiovascular disease mortality/due to arteriosclerotic and hypertensive heart disease + unclear CHD	Metformin, 178	Placebo, 172	500 tid (fixed)	NA	1	0	NR	NR

Appendix F: Evidence Table 20. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications for randomized controlled trials: cardiovascular mortality

Author, year Study group	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP1, initial dose in mg (fixed or esc) max dose	GP2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) p-value GP1	GP2 "X"R (95% CI) p-value GP2
Rachmani, 2002 ¹⁵⁰	RCT	Cardiovascular disease mortality/unclear CVD mortality	Continued metformin + diet, 195	Stopped metformin + diet, 198	NR (NR)	NR (NR)	50 (26)	52 (26)	NR	NR
Meglitinide vs. Placebo										
Horton, 2000 ⁹⁶	RCT	Cardiovascular disease mortality/due to arteriosclerotic and hypertensive heart disease + unclear CHD	Nateglinide, 179	Placebo, 172	120 (fixed)	NA	0	0	NR	NR
Hanefeld, 2000 ¹⁹⁰	RCT	Cardiovascular disease mortality/fatal myocardial infarction	Nateglinide, 51	Placebo, 60	30 (fixed)	NA	1	0	NR	NR
Hanefeld, 2000 ¹⁹⁰	RCT	Cardiovascular disease mortality/fatal myocardial infarction	Nateglinide, 58	Placebo, 60	60 (fixed)	NA	0	0	NR	NR
Hanefeld, 2000 ¹⁹⁰	RCT	Cardiovascular disease mortality/fatal myocardial infarction	Nateglinide, 63	Placebo, 60	120 (fixed)	NA	0	0	NR	NR
Hanefeld, 2000 ¹⁹⁰	RCT	Cardiovascular disease mortality/fatal myocardial infarction	Nateglinide, 57	Placebo, 60	180 (fixed)	NA	0	0	NR	NR
Goldberg, 1998 ¹³⁹	RCT	Cardiovascular disease mortality/fatal myocardial infarction	Repaglinide, 67	Placebo, 33	0.25 tid (esc) 8.0	NA	1	0	NR	NR

Comp = comparison; GP = group; mg = milligrams; esc = escalated; max = maximum; CI = confidence interval; IR = incidence rate; RR = relative risk; HR = hazard ratio; OR = odds ratio; SU = sulfonylurea; NR = not reported; RCT = randomized controlled trial; ref = reference; CVD = cardiovascular disease; od = once daily; bid = twice daily; tid = three times daily; vs = versus; CAD = coronary artery disease; CHD = coronary heart disease; CHF = congestive heart failure

Appendix F: Evidence Table 21. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications for non-randomized trials and cohort studies: cardiovascular mortality

Author, year Study group	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP1, initial dose in mg (fixed or esc) max dose	GP2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) p-value GP1	GP2 "X"R (95% CI) p-value GP2
Metformin vs. Second Generation Sulfonylurea										
Johnson, 2002 ¹² Saskatchewan health database	Cohort	Cardiovascular disease mortality/fatal myocardial infarction + fatal stroke + CVD mortality + ICD-9 codes 390-398, 401-417, 420-438, 440-444, 446-448, 451-459	Metformin, 1150	Un-specified SU, 3033	NR (NR)	NR (NR)	80 (7)	351 (11.6)	Adjusted RR 0.84 (0.49-0.84) OR 0.64 (0.49-0.84)	OR 1.0 (ref)
Johnson, 2005 ¹³ Saskatchewan health database	Cohort	Cardiovascular disease mortality/CVD mortality registry + CVD mortality + ICD-9 codes 410, 411-414, 420-427, 429, 428, 430-432, 433-434, 436-438, 440	Metformin, 923	Un-specified SU, 2138	250 minimum dose	Various minimum doses	14.4	25.5	Adjusted HR 0.76 (0.58-1)	HR reference
Fisman, 2001 ¹⁸⁶	Cohort	Cardiovascular disease mortality/CVD mortality + ICD-9 codes 410-414 + matched the patients ID number with their life status in the population registry + ischemic heart disease	Metformin, 79	Glyburide (no trade drug specified), 953	NR (NR)	NR (NR)	NR	NR	Age-adjusted IR 30 per 1000 person-years	Age-adjusted IR 24.5 per 1000 person-years
Evans, 2006 ¹⁸⁰	Cohort	Cardiovascular mortality	Metformin, 2286	Un-specified SU, 3331	NR (NR)	NR (NR)	NR	NR	RR 1 (ref)	Adjusted RR 1.7 (1.18-2.45)
Second Generation Sulfonylurea vs. Other Oral Diabetes Medications										
Garratt, 1999 ¹⁰	Cohort	Cardiovascular disease mortality/fatal myocardial infarction + CVD mortality registry + ventricular arrhythmias, death following emergency CABG + review of medical records	Un-specified SU, 67	Not SU (diet, insulin, or other oral diabetes medications), 118	NR (NR)	NR (NR)	(24)	(11)	Adjusted OR 2.53 (1.13-5.67); 0.024	OR ref

Appendix F: Evidence Table 21. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications for non-randomized trials and cohort studies: cardiovascular mortality

Author, year	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP1, initial dose in mg (fixed or esc) max dose	GP2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) p-value GP1	GP2 "X"R (95% CI) p-value GP2
Lomuscio, 1996 ¹¹	Cohort	Cardiovascular disease mortality/unclear mortality + heart failure	Glibenclamide, 106	Not glibenclamide, 126	at minimum 10 (NR)	NR (NR)	6 (50)	23 (85)	p<0.05 vs. GP2	
Lomuscio, 1996 ¹¹	Cohort	Cardiovascular disease mortality/death from arrhythmia	Glibenclamide, 106	Not glibenclamide, 126	at minimum 10 (NR)	NR (NR)	0 (0)	3 (11)	NSG vs. GP2	
Lomuscio, 1996 ¹¹	Cohort	Cardiovascular disease mortality/cardiac rupture	Glibenclamide, 106	Not glibenclamide, 126	at minimum 10 (NR)	NR (NR)	1 (8)	0 (0)	NSG vs. GP2	
Second Generation Sulfonylurea or Metformin vs. Metformin + Second Generation Sulfonylurea										
Fisman, 2001 ¹⁸⁶	Cohort	Cardiovascular disease mortality/CVD mortality + ICD-9 codes 410-414 + matched the patients ID number with their life status in the population registry + ischemic heart disease	Metformin, 79	Metformin + glyburide (no trade drug specified), 253	NR (NR)	NR (NR)	NR	NR	Age-adjusted IR 30 per 1000 person-years	Age-adjusted IR 31.2 per 1000 person-years
Fisman, 2001 ¹⁸⁶	Cohort	Cardiovascular disease mortality/CVD mortality + ICD-9 codes 410-414 + matched the patients ID number with their life status in the population registry + ischemic heart disease	Glyburide (no trade drug specified), 953	Metformin + glyburide (no trade drug specified), 253	NR (NR)	NR (NR)	NR	NR	Age-adjusted IR 24.5 per 1000 person-years	Age-adjusted IR 31.2 per 1000 person-years
Johnson, 2005 ¹³ Saskatchewan health database	Cohort	Cardiovascular disease mortality/CVD mortality registry + CVD mortality + ICD-9 codes 410, 411-414, 420-427, 429, 428, 430-432, 433-434, 436-438, 440	Un-specified SU, 2138	Metformin + un-specified SU, 1081	Various minimum doses	250 minimum dose Various minimum doses	14.4	10.9	HR 1 (ref)	Adjusted HR 0.59 (0.45-0.78)
Evans, 2006 ¹⁸⁰	Cohort	Cardiovascular mortality	Metformin, 2286	Metformin with later addition of SU, 985	NR (NR)	NR (NR)	NR	NR	RR 1 (ref)	Adjusted RR 2.29 (1.45-3.61)

Appendix F: Evidence Table 21. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications for non-randomized trials and cohort studies: cardiovascular mortality

Author, year	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP1, initial dose in mg (fixed or esc) max dose	GP2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) p-value GP1	GP2 "X"R (95% CI) p-value GP2
Evans, 2006 ¹⁸⁰	Cohort	Cardiovascular mortality	Metformin, 2286	SU with later addition of metformin, 1252	NR (NR)	NR (NR)	NR	NR	RR 1 (ref)	Adjusted RR 2.43 (1.61-3.66)
Olsson, 2000 ¹⁷⁸	Cohort	Cardiovascular disease mortality/ICD-8 codes for ischemic heart disease: 410-414	Un-specified SU, 741	Metformin + un-specified SU, 169	NR	NR (NR)	NR	NR	OR 1	Adjusted OR 1.73 (1.17-2.55)
Olsson, 2000 ¹⁷⁸	Cohort	Cardiovascular disease mortality/fatal stroke + ICD-8 codes for ischemic heart disease: 410-414 and ICD-8 codes for stroke: 430-438	Un-specified SU, 741	Metformin + un-specified SU, 169	NR	NR (NR)	NR	NR	OR 1	Adjusted OR 2.33 (1.17-4.63)
Johnson, 2002 ¹² Saskatchewan health database	Cohort	Cardiovascular disease mortality/fatal myocardial infarction + fatal stroke + CVD mortality + ICD-9 codes 390-398, 401-417, 420-438, 440-444, 446-448, 451-459	Un Specified SU, 3033	Metformin + un Specified SU, 4683	NR (NR)	NR (NR)	351 (11.6)	299 (6.4)	OR and RR 1.0 (ref)	Adjusted RR 0.63 (0.54-0.77) OR 0.64 (0.54-0.77)
Metformin or Second Generation Sulfonylurea vs. Placebo										
Simpson, 2006 ¹⁴	Cohort	Cardiovascular disease mortality/fatal myocardial infarction + CVD mortality + ICD-9 codes 410, 411-414	Glyburide high dose	Glyburide low dose	High dose/ below group median	Low dose/ below group median	17.6 per 1000 person-years	12 per 1000 person-years	Adjusted HR 1.37 (1.25-1.5)	HR1 (ref)
Simpson, 2006 ¹⁴	Cohort	Cardiovascular disease mortality/fatal myocardial infarction + CVD mortality + ICD-9 codes 410, 411-414	Metformin high dose	Metformin low dose	High dose/ above group median	Low dose/ below group median	11.5 per 1000 person-years	9.5 per 1000 person-years	Adjusted HR 1.1 (0.8-1.3)	HR 1 (ref)
Florkowski, 2001 ¹⁸⁷	Cohort	Cardiovascular disease mortality/CVD mortality registry	Metformin	Diet	NR (NR)	NR (NR)	NR	NR	(1) CAD absent at baseline: adjusted HR 1.07 (0.32-3.68); (2) CAD present at baseline: adjusted HR 0.78 (0.16-3.73)	HR 1 (ref)

Appendix F: Evidence Table 21. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications for non-randomized trials and cohort studies: cardiovascular mortality

Author, year Study group	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP1, initial dose in mg (fixed or esc) max dose	GP2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) p-value GP1	GP2 "X"R (95% CI) p-value GP2
Florkowski, 2001 ¹⁸⁷	Cohort	Cardiovascular disease mortality/CVD mortality registry	Un-specified SU	Diet	NR (NR)	NR (NR)	NR	NR	(1) CAD absent at baseline: adjusted HR 2.19 (0.84-5.65); (2) CAD present at baseline: adjusted HR 0.91 (0.23-3.69)	HR 1 (ref)
Metformin + Second Generation Sulfonylurea vs. Placebo										
Florkowski, 2001 ¹⁸⁷	Cohort	Cardiovascular disease mortality/CVD mortality registry	SU + metformin	Diet	NR (NR)	NR (NR)	NR	NR	1) CAD absent at baseline: Adjusted HR 1.66 (0.56-4.88) 2) CAD present at baseline: Adjusted HR 2.39 (0.57-10.06)	HR 1 (ref)

Comp = comparison; GP = group; mg = milligrams; esc = escalated; max = maximum; CI = confidence interval; IR = incidence rate; RR = relative risk; HR = hazard ratio; OR = odds ratio; SU = sulfonylurea; NR = not reported; ref = reference; NSG = not significant; ICD = International Classification of Diseases; CVD = cardiovascular disease; vs = versus; CABG = coronary artery bypass graft surgery; CAD = coronary artery disease

Appendix F: Evidence Table 22. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications for randomized controlled trials: cardiovascular morbidity

Author, year	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP1, initial dose in mg (fixed or esc) max dose	GP2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) p-value GP1	GP2 "X"R (95% CI) p-value GP2
Thiazolidinedione vs. Second Generation Sulfonylurea										
St John Sutto, 2002 ⁶⁷	RCT	Cardiovascular disease morbidity/heart disease	Rosiglitazone, 104	Glyburide (no trade drug specified), 99	4 bid (fixed)	NR (esc) 20	9	5	NR	NR
Lawrence, 2004 ⁵⁴	RCT	Cardiovascular disease morbidity/myocardial infarction (non-fatal)	Pioglitazone, 21	Gliclazide, 22	30 (esc) 45	80 od (esc) 160 bid	0	1	NR	NR
Thiazolidinedione vs. Metformin										
Virtanen, 2003 ¹⁴³ Hallsten, 2002 ⁵⁸	RCT	Cardiovascular disease morbidity/ischemic heart disease	Rosiglitazone + diet, 14	Metformin + diet, 13	2 bid (esc) 4 bid	500 bid (esc) 1000 bid	0	1	NR	NR
Lawrence, 2004 ⁵⁴	RCT	Cardiovascular disease morbidity/myocardial infarction (non-fatal)	Pioglitazone, 21	Metformin, 21	30 (esc) 45	500 bid (esc) 1000 tid	0	0	NR	NR
Hanefeld, 2004 ⁶⁰ QUARTET study group	RCT	Coronary heart diseases/cardiac disorders	Pioglitazone + un-specified SU + placebo, 319	Metformin + un-specified SU + placebo, 320	15 (esc) 45 NR	850 (esc) 850 tid NR	(3.1)	(4.1)	NR	NR
Metformin vs. Second Generation Sulfonylurea										
Lawrence, 2004 ⁵⁴	RCT	Cardiovascular disease morbidity/myocardial infarction (non-fatal)	Metformin, 21	Gliclazide, 22	500 bid (esc) 1000 tid	80 (esc) 160 bid	0 (0)	1 (4.5)	NR	NR
Hermann, 1994 ⁵⁷	RCT	Cardiovascular disease morbidity/unclear CHD	Metformin + diet, 38	Glyburide + diet, 34	1000 (esc) 3000	3.5 (esc) 10.5	2 (5)	3 (9)	NR	NR
Second Generation Sulfonylurea vs. Metformin + Second Generation Sulfonylurea										
Hermann, 1994 ⁵⁷	RCT	Cardiovascular disease morbidity/unclear CHD	Glyburide + diet, 34	Metformin + glyburide, 72	3.5 (esc) 10.5	500 (esc) 1500 1.75 (esc) 5.25	3 (9)	10 (14)	NR	NR

Appendix F: Evidence Table 22. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications for randomized controlled trials: cardiovascular morbidity

Author, year Study group	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP1, initial dose in mg (fixed or esc) max dose	GP2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) p-value GP1	GP2 "X"R (95% CI) p-value GP2
UKPDS, 1998 ¹⁵	RCT	Cardiovascular disease morbidity/myocardial infarction (non-fatal)	Un-specified SU + diet, 269	Metformin + un-specified SU + diet, 268	NR (NR)	NR (NR)	23	14	RR 1 (ref)	RR 0.62 (0.26-1.42)
UKPDS, 1998 ¹⁵	RCT	Cardiovascular disease morbidity/coronary heart disease	Un-specified SU + diet, 269	Metformin + un-specified SU + diet, 268	NR (NR)	NR (NR)	18	11	RR 1 (ref)	RR 0.64 (0.24-1.71)
UKPDS, 1998 ¹⁵	RCT	Cerebrovascular diseases/stroke	Un-specified SU + diet, 269	Metformin + un-specified SU + diet, 268	NR (NR)	NR (NR)	12	10	RR 1 (ref)	RR 0.68 (0.29-2.64)
Metformin vs. Other										
Rachmani, 2002 ¹⁵⁰	RCT	Cardiovascular disease morbidity/myocardial infarction (non-fatal)	Metformin continued + diet, 195	Metformin stopped + diet, 198	NR (NR)	NR (NR)	51 (26)	53 (27)	no significant differences between groups	
Rachmani, 2002 ¹⁵⁰	RCT	Cardiovascular disease morbidity/All CVD events	Metformin continued + diet, 195	Metformin stopped + diet, 198	NR (NR)	NR (NR)	102 (55)	108 (55)	no significant differences between groups	
Cryer, 2005 ¹⁷⁶ COSMIC Approach Study	RCT	Cardiovascular disease morbidity/CAD	Metformin + existing medications + diet, 7227	Diet + usual care, 1505	500 (esc) 2500	NR (NR)	(1)	(1.1)	NR	NR
Cryer, 2005 ¹⁷⁶ COSMIC Approach Study	RCT	Cardiovascular disease morbidity/myocardial infarction (non-fatal)	Metformin + existing medications + diet, 7227	Diet + usual care, 1505	500 (esc) 2500	NR (NR)	(0.7)	(0.7)	NR	NR
Cryer, 2005 ¹⁷⁶ COSMIC Approach Study	RCT	Cerebrovascular diseases/stroke	Metformin + existing medications + diet, 7227	Diet + usual care, 1505	500 (esc) 2500	NR (NR)	(0.4)	(0.7)	NR	NR
Metformin vs. Thiazolidinedione + Metformin										

Appendix F: Evidence Table 22. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications for randomized controlled trials: cardiovascular morbidity

Author, year	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP1, initial dose in mg (fixed or esc) max dose	GP2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) p-value GP1	GP2 "X"R (95% CI) p-value GP2
Weissman, 2005 ¹⁰⁰	RCT	Cardiovascular disease morbidity/myocardial infarction (non-fatal)	Metformin, 384	Rosiglitazone + metformin, 382	1000 (esc) 2000	4 (esc) 8 1000 (fixed)	0	2	NR	NR
Weissman, 2005 ¹⁰⁰	RCT	Cardiovascular disease morbidity/CAD or cardiac ischemia	Metformin, 384	Rosiglitazone + metformin, 382	1000 (esc) 2000	4 (esc) 8 1000 (fixed)	3 + 1 withdrew	5	NR	NR
Bailey, 2005 ¹⁰¹	RCT	Cardiovascular disease morbidity/myocardial infarction (non-fatal) + pulmonary edema with myocardial infarction	Metformin, 280	Rosiglitazone + metformin, 288	2500 (esc) 3000	4 (esc) 8 2000 (fixed)	0	1	NR	NR
Gomez-Perez, 2002 ¹⁰²	RCT	Cardiovascular disease morbidity/ischemic heart disease + bundle branch block + tachycardia	Metformin + placebo, 34	Rosiglitazone + metformin, 35	2500 (fixed)	2500 (fixed) 2 bid (fixed)	1	1	NR	NR
Gomez-Perez, 2002 ¹⁰²	RCT	Cardiovascular disease morbidity/ischemic heart disease + bundle branch block + tachycardia	Metformin + placebo, 34	Rosiglitazone + metformin, 36	2500 (fixed)	2500 (fixed) 4 bid (fixed)	1	2	NR	NR
Metformin vs. Metformin + Second Generation Sulfonylurea										
Hermann, 1994 ⁸⁷	RCT	Cardiovascular disease morbidity/unclear CHD	Metformin + diet, 38	Metformin + glyburide, 72	1000 (esc) 3000	500 (esc) 1500 1.75 (esc) 5.25	2 (5)	10 (14)	NR	NR
Metformin vs. Metformin XR										
Fujioka, 2003 ¹⁰⁵	RCT	Cardiovascular disease morbidity/angina + angina and heart failure	Metformin + placebo + diet	Metformin XR + placebo + diet, 146	1000 (esc) 1500	1000 (esc) 1500	0	1	NR	NR
Fujioka, 2003 ¹⁰⁵	RCT	Cerebrovascular diseases/stroke	Metformin + placebo + diet	Metformin XR + placebo + diet, 146	1000 (esc) 1500	1000 (esc) 1500	0	1	NR	NR
Second Generation Sulfonylurea vs. Second Generation Sulfonylurea										

Appendix F: Evidence Table 22. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications for randomized controlled trials: cardiovascular morbidity

Author, year	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP1, initial dose in mg (fixed or esc) max dose	GP2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) p-value GP1	GP2 "X"R (95% CI) p-value GP2
Sonnenberg, 1997 ¹⁹¹	RCT, cross-over	Cardiovascular disease morbidity/myocardial infarction (non-fatal) + 2 symptoms + WHO clinical criteria	Glimepiride, 48	Glimepiride, 46	3 (fixed)	6 (fixed)	0	1	NR	NR
Carlson, 1993 ¹⁰⁸	RCT	Cerebrovascular diseases/stroke + brainstem infarct resulting in death	Glyburide (Micro-nase), 104	Glyburide (Glynase Prestab), 102	3 (fixed)	5 (fixed)	1	0	NR	NR
Second Generation Sulfonylurea vs. Meglitinide										
Marbury, 1999 ¹¹⁶	RCT	Cardiovascular disease morbidity/unclear CHD	Glyburide (no trade drug specified) + placebo, 193	Repaglinide, 383	2.5 (esc) 15	0.5 (esc) 12	4	19	NR	NR
Wolffen-buttel, 1999 ¹¹⁷	RCT	Cardiac events NOS	Glyburide (no trade drug specified) + placebo, 139	Repaglinide, 286	1.75 (esc) 10.5	1.5 (esc) 12			Authors stated similar frequencies in each group, but no data given	
Metformin vs. Meglitinide										
Horton, 2000 ⁹⁶	RCT	Cardiovascular disease morbidity/electrocardiogram abnormalities	Metformin, 178	Nateglinide, 179	500 tid (fixed)	120 tid (fixed)	0	0	NR	NR
Thiazolidinedione vs. Placebo										
Virtanen, 2003 ¹⁴³	RCT	Cardiovascular disease morbidity/ischemic heart disease	Rosiglitazone + diet, 14	Placebo + diet, 14	2 bid (esc) 8 bid	NA	0	0	NR	NR
Aronoff, 2000 ¹⁶⁵	RCT	Cardiovascular disease morbidity/not stated	Pioglitazone, 329	Placebo, 79	7.5 (fixed)	NA	12 (3.6)	5 (6.3)	NR	NR

Appendix F: Evidence Table 22. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications for randomized controlled trials: cardiovascular morbidity

Author, year Study group	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP1, initial dose in mg (fixed or esc) max dose	GP2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) p-value GP1	GP2 "X"R (95% CI) p-value GP2
Dormandy, 2005 ¹⁸⁵ PROactive	RCT	Cerebrovascular diseases/stroke	Pioglitazone + existing diabetes medications, 2605	Placebo + existing diabetes medications, 2633	15 (esc) 45	NR (NR)	86	107	NR	NR
Dormandy, 2005 ¹⁸⁵ PROactive	RCT	Coronary heart diseases/myocardial infarction (non-fatal) + silent myocardial infarction	Pioglitazone + existing diabetes medications, 2605	Placebo + existing diabetes medications, 2633	15 (esc) 45	NR (NR)	119	144	HR 0.83 (0.65-1.06)	HR reference
Dormandy, 2005 ¹⁸⁵ PROactive	RCT	Coronary heart diseases/Acute coronary syndrome: patient received treatment in hospital for ischemic discomfort at rest that lasted at least 5 minutes and had electrocardiographic changes or raised cardiac serum markers not sufficiently high to indicate myocardial infarction or both	Pioglitazone + existing diabetes medications, 2605	Placebo + existing diabetes medications, 2633	15 (esc) 45	NR (NR)	56	72	HR 0.78 (0.55-1.11)	HR reference
Dormandy, 2005 ¹⁸⁵ PROactive	RCT	Coronary heart diseases/coronary artery bypass surgery + angioplasty + Coronary revascularization: percutaneous transluminal coronary intervention (e.g., angioplasty, stenting, atherectomy, laser ablation) or coronary artery bypass graft	Pioglitazone, 2605	Placebo, 2633	15 (esc) 45	NR (NR)	169	193	HR 0.88 (0.72-1.08)	HR reference

Appendix F: Evidence Table 22. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications for randomized controlled trials: cardiovascular morbidity

Author, year Study group	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP1, initial dose in mg (fixed or esc) max dose	GP2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) p-value GP1	GP2 "X"R (95% CI) p-value GP2
Barnett, 2003 ¹⁷²	RCT	Cardiovascular disease morbidity/myocardial infarction (non-fatal)	Rosiglitazone + existing unspecified SU, 84	Placebo + existing unspecified SU, 87	4 bid (fixed) NR (NR)	NR (NR)	1	0	NR	NR
Barnett, 2003 ¹⁷²	RCT	Cardiovascular disease morbidity/angina	Rosiglitazone + existing unspecified SU, 84	Placebo + existing unspecified SU, 87	4 bid (fixed) NR (NR)	NR (NR)	4 (5)	0 (0)	NR	NR
Kipnes, 2001 ¹⁶⁶	RCT	Cardiovascular disease morbidity/listed as "adverse cardiac events"	Pioglitazone + existing unspecified SU, 176	Placebo + existing unspecified SU, 181	15 (fixed) NR (fixed)	NR (fixed)	22 (6)	10 (5)	NR	NR
Vongthavaravat, 2002 ¹⁷⁰	RCT	Cerebrovascular diseases/unclear CBVD	Rosiglitazone + existing unspecified SU + diet, 164	Diet + existing unspecified SU + diet, 170	2 bid (fixed)	NR (NR)	2	2	NR	NR
Nishio, 2006 ¹⁵¹	RCT	Cardiovascular disease morbidity/major adverse cardiac events at 6 months - death, Q wave or non-Q wave myocardial infarction, coronary artery bypass grafting, and revascularization of the target lesion or vessel after the procedure	Pioglitazone, 26	Control group (no placebo), 28	30 (fixed)	NA	(7.7)	(60.7)	NR	NR
Takagi, 2003 ⁷⁶	RCT	Cardiovascular disease morbidity/angioplasty	Pioglitazone + existing medications, 23	Control group (conventional antidiabetic therapy), 21	30 (fixed)	NR (NR)	5 (19)	11 (46)	NR	NR

Appendix F: Evidence Table 22. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications for randomized controlled trials: cardiovascular morbidity

Author, year Study group	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP1, initial dose in mg (fixed or esc) max dose	GP2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) p-value GP1	GP2 "X"R (95% CI) p-value GP2
Choi, 2004 ¹⁴⁴	RCT	Cardiovascular disease morbidity/angioplasty	Rosiglitazone + existing medications, 38	Upitration of existing diabetes medications, 45	8 (other) 4	NR (esc)	9 (17.6)	21 (38.2)	NR	NR
Metformin vs. Placebo										
Teupe, 1991 ¹⁵⁵	RCT	Cardiovascular disease morbidity/myocardial infarction (non-fatal)	Metformin + diet, 50	Diet, 50	NR (esc) 1700	NA	1	0	NR	NR
Virtanen, 2003 ¹⁴³	RCT	Cardiovascular disease morbidity/ischemic heart disease	Metformin + diet, 13	Placebo + diet, 14	500 bid (esc) 1000 bid	NA	1	0	NR	NR
Horton, 2000 ⁹⁶	RCT	Cardiovascular disease morbidity/electrocardiogram abnormalities	Metformin, 178	Placebo, 172	500 tid (fixed)	NA	0	1	NR	NR
UKPDS, 1998 ¹⁵ UKPDS	RCT	Cardiovascular disease morbidity/myocardial infarction (non-fatal)	Metformin + diet, 342	Diet, 411	850 (esc) 2550	NA	24	40	RR 0.69 (0.35-1.34)	RR 1 (ref)
UKPDS, 1998 ¹⁵ UKPDS	RCT	Cerebrovascular diseases/nonfatal stroke	Metformin + diet, 342	Diet, 411	850 (esc) 2550	NA	6	16	RR 0.42 (0.12 – 1.45)	RR1 (ref)
Second Generation Sulfonylurea vs. Placebo										
Luis Bautista, 2003 ¹⁹³	RCT	Cerebrovascular diseases/used ICD-9 codes for CBVD + probable stroke/ TIA + unclear CBVD	Glimepi-ride + diet + exercise, 48	Placebo + diet + exercise, 22	1 (esc) 4	NA	0	1	NR	NR
UKPDS, 1998 ¹⁶ UKPDS	RCT	Cerebrovascular diseases/nonfatal stroke	Glibenclamide + diet, 615	Diet, 896	2.5 (esc) 20	NA	34	38	RR 1.30 (0.71-2.38)	RR 1 (ref)
UKPDS, 1998 ¹⁶ UKPDS	RCT	Cardiovascular disease morbidity/angina	Glibenclamide + diet, 615	Diet, 896	2.5 (esc) 20	NA	34	58	RR 0.84 (0.48-1.47)	RR1 (ref)

Appendix F: Evidence Table 22. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications for randomized controlled trials: cardiovascular morbidity

Author, year	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP1, initial dose in mg (fixed or esc) max dose	GP2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) p-value GP1	GP2 "X"R (95% CI) p-value GP2
UKPDS, 1998 ¹⁶ UKPDS	RCT	Cardiovascular disease morbidity/myocardial infarction (non-fatal) + 2 symptoms + WHO clinical criteria	Glibenclamide + diet, 615	Diet, 896	2.5 (esc) 20	NA	46	87	RR 0.74 (0.46-1.19)	RR 1 (ref)
Meglitinide vs. Placebo										
Jovanovic, 2000 ¹⁹⁴	RCT	Cardiovascular disease morbidity/myocardial infarction (non-fatal)	Repaglinide, 140	Placebo, 75	1 tid (fixed)	NA	1	0	NR	NR
Jovanovic, 2000 ¹⁹⁴	RCT	Cardiovascular disease morbidity/myocardial infarction (non-fatal)	Repaglinide, 146	Placebo, 75	4 tid (fixed)	NA	1	0	NR	NR
Horton, 2000 ⁹⁶	RCT	Cardiovascular disease morbidity/electrocardiogram abnormalities	Nateglinide, 179	Placebo, 172	120 (fixed)	NA	0	1	NR	NR
Alpha-Glucosidase Inhibitor vs. Placebo										
Hasche, 1999 ¹³⁸	RCT	Cardiovascular disease morbidity/angina + heart failure + cardiovascular disorder	Acarbose + diet, 36	Placebo + diet, 38	50 bid (esc) 100 tid	NA	1	2	NR	NR

Comp = comparison; GP = group; mg = milligrams; esc = escalated; max = maximum; CI = confidence interval; IR = incidence rate; RR = relative risk; HR = hazard ratio; OR = odds ratio; SU = sulfonylurea; NR = not reported; ref = reference; ICD = International Classification of Diseases; CHD = coronary heart disease; CAD = coronary artery disease; CBVD = cerebrovascular disease; TIA = transient ischemic attack; XR = extended release; WHO = World Health Organization; NOS = not otherwise specified; UKPDS = United Kingdom Prospective Diabetes Study; od = once daily; bid = twice daily; tid = three times daily; vs = versus

Appendix F: Evidence Table 23. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications for non-randomized trials and cohort studies: cardiovascular morbidity

Author, year	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP1, initial dose in mg (fixed or esc) max dose	GP2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) p-value GP1	GP2 "X"R (95% CI) p-value GP2
Metformin vs. Second Generation Sulfonylurea										
Johnson, 2005 ¹³ Saskatchewan health database	Cohort	Non-fatal cardiovascular hospitalization/used ICD-9 codes 410-414, 420-427, 429, 428, 440, 430-432, 433-434, 436-438	Metformin, 923	Un-specified SU, 2138	250 minimum dose	Various minimum doses	53.7	75.3	Adjusted HR 0.78 (0.63-0.97)	HR reference
Second Generation Sulfonylurea vs. Metformin + Second Generation Sulfonylurea										
Johnson, 2005 ¹³ Saskatchewan health database	Cohort	Non-fatal cardiovascular hospitalization/used ICD-9 codes 410-414, 420-427, 429, 428, 440, 430-432, 433-434, 436-438	Un-specified SU, 2138	Metformin + un-specified SU, 1081	Various minimum doses	250 minimum dose Various minimum doses	75.3	90.2	HR reference	Adjusted HR 1.09 (0.91-1.29)
Second Generation Sulfonylurea vs. Other Oral Diabetes Medications										
Garratt, 1999 ¹⁰	Cohort	Cardiovascular disease morbidity/subsequent myocardial infarction	Glibenclamide, 67	Diet, insulin, or other oral diabetes medication, 118	NR (NR)	NR (NR)	(19.9)	(23.1)		NSG vs. GP1
Garratt, 1999 ¹⁰	Cohort	Cardiovascular disease morbidity/coronary artery bypass surgery	Glibenclamide, 67	Diet, insulin, or other oral diabetes medication, 118	NR (NR)	NR (NR)	(23.3)	(31.7)		NSG vs. GP1
Garratt, 1999 ¹⁰	Cohort	Cardiovascular disease morbidity/Ventricular tachycardia or fibrillation while in hospital post myocardial infarction	Glibenclamide, 67	Diet, insulin, or other oral diabetes medication, 118	NR (NR)	NR (NR)	(27)	(22)		NSG vs. GP1
Garratt, 1999 ¹⁰	Cohort	Cardiovascular disease morbidity/angioplasty	Glibenclamide, 67	Diet, insulin, or other oral diabetes medication, 118	NR (NR)	NR (NR)	(17.8)	(46.7)		<0.05 vs. GP1

Appendix F: Evidence Table 23. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications for non-randomized trials and cohort studies: cardiovascular morbidity

Author, year Study group	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP1, initial dose in mg (fixed or esc) max dose	GP2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) p-value GP1	GP2 "X"R (95% CI) p-value GP2
Lomuscio, 1996 ¹¹	cohort	Coronary heart diseases/sustained ventricular tachycardia only	Glibenclamide, 106	Not glibenclamide, 126	at minimum 10 (NR)	NR (NR)	5 (4.7)	9 (7.2)		NSG vs. GP1
Lomuscio, 1996 ¹¹	cohort	Coronary heart diseases/unclear mortality + ventricular fibrillation only	Glibenclamide, 106	Not glibenclamide, 126	at minimum 10 (NR)	NR (NR)	2 (1.9)	6 (4.8)		<0.05 vs. GP1
Lomuscio, 1996 ¹¹	cohort	Coronary heart diseases/Ventricular fibrillation and/or sustained ventricular tachycardia	Glibenclamide, 106	Not glibenclamide, 126	at minimum 10 (NR)	NR (NR)	7 (6)	19 (15)		<0.05 vs. GP1
Thiazolidinedione and/or Metformin vs. Other Oral Diabetes Medications										
Inzucchi, 2005 ¹⁸⁴	Cohort	Cardiovascular disease morbidity/readmission for myocardial infarction (non-fatal) + Linkage with part A Medicare data	Un-specified TZD, 819	Non-insulin sensitizing antihyperglycemic, 6641	NR (NR)	NR (NR)	154 (18.8)	1247 (18.8)	Adjusted HR 0.92 (0.77-1.10)	HR 1 (ref)
Inzucchi, 2005 ¹⁸⁴	Cohort	Cardiovascular disease morbidity/readmission for myocardial infarction (non-fatal) + Linkage with part A Medicare data	Metformin, 1273	Non-insulin sensitizing antihyperglycemic, 6641	NR (NR)	NR (NR)	210 (16.5)	1247 (18.8)	Adjusted HR 1.02 (0.86-1.20)	HR 1 (ref)
Inzucchi, 2005 ¹⁸⁴	Cohort	Cardiovascular disease morbidity/readmission for myocardial infarction (non-fatal) + Linkage with part A Medicare data	Metformin + TZD, 139	Non-insulin sensitizing antihyperglycemic, 6641	NR (NR)	NR (NR)	1247 (18.8)	21 (15.1)	Adjusted HR 0.87 (0.68-1.12)	HR 1 (ref)
Thiazolidinedione vs. Thiazolidinedione										
Gegick, 2001 ¹⁹²	Cohort	Cerebrovascular diseases/unclear CVD mortality + cerebrovascular accident	Rosiglitazone, 67	Pioglitazone, 77	4 or 8 mg	15 - 45 (fixed)	0	1	NR	NR
Second Generation Sulfonylurea vs. Placebo										
Ikeda, 1994 ¹⁹⁵	Cohort	Cardiovascular disease morbidity/ prolonged QTc	Glibenclamide, 20	Diet, 20	1.25-5 (dose range)	NR (NR)	8 (0.4)	2 (0.1)	<0.05 vs. GP2	

Appendix F: Evidence Table 23. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications for non-randomized trials and cohort studies: cardiovascular morbidity

Comp = comparison; GP = group; mg = milligrams; esc = escalated; max = maximum; CI = confidence interval; IR = incidence rate; RR = relative risk; HR = hazard ratio; OR = odds ratio; SU = sulfonylurea; TZD = Thiazolidinedione; NR = not reported; ref = reference; CVD = cardiovascular disease; ICD = International Classification of Diseases; NSG = not significant; CHD = coronary heart disease; vs = versus

Appendix F: Evidence Table 24. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications in randomized controlled trials: peripheral vascular disease

Author, year	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP1, initial dose in mg (fixed or esc) max dose	GP2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) p-value GP1	GP2 "X"R (95% CI) p-value GP2
Second Generation Sulfonylurea vs. Metformin + Second Generation Sulfonylurea										
1998 ¹⁵ UKPDS	RCT	PVD/ limb amputation or death from PVD	SU, 269	Metformin + SU, 268	2.5 (esc) 20	500 (esc) 2550 2.5 (esc) 20	NR	NR	RR 1 (ref)	RR 2.12 (0.19-23.3)
Metformin or Second Generation Sulfonylurea vs. Diet										
1998 ¹⁵ UKPDS	RCT	PVD/ limb amputation or death from PVD	Metformin + diet, 342	Diet, 411	850 (esc) 2550	NA	6	9	RR 0.74 (0.26-2.09)	RR 1 (ref)
1998 ¹⁶ UKPDS	RCT	PVD/limb amputation or death from PVD	Glibenclamide + diet, 615	Diet, 896	2.5 (esc) 20	NA	0.8	1.6	RR 0.48 (0.17-1.31)	RR 1(ref)
Thiazolidinedione vs. Placebo										
Dormandy, 2005 ¹⁸⁵ PROactive	RCT	PVD/limb amputation	Pioglitazone, 2605	Placebo, 2633	15 (esc) 45	NA	26	26	HR 1.01 (0.58-1.73)	HR reference
Dormandy, 2005 ¹⁸⁵ PROactive	RCT	PVD/peripheral revascularization procedure	Pioglitazone, 2605	Placebo, 2633	15 (esc) 45	NA	80	65	HR 1.25 (0.9-1.73)	HR reference
Zhu, 2003 ¹⁸⁸	RCT	PVD/peripheral ischemia	Rosiglitazone + existing un-specified SU, 221	Placebo + existing un-specified SU, 112	2 bid (fixed) NR (fixed)	NR (fixed)	0	0	NR	NR
Zhu, 2003 ¹⁸⁸	RCT	PVD/peripheral ischemia	Rosiglitazone + existing un-specified SU, 221	Placebo + existing un-specified SU, 112	4 bid (fixed) NR (fixed)	NR (fixed)	1	0	NR	NR

Comp = comparison; GP = group; mg = milligrams; esc = escalated; max = maximum; CI = confidence interval; IR = incidence rate; RR = relative risk; HR = hazard ratio; OR = odds ratio; SU = sulfonylurea; NR = not reported; ref = reference; NA = not applicable; bid = twice a day; PVD = peripheral vascular disease; RCT = randomized controlled trial; UKPDS = United Kingdom Prospective Diabetes Study

Appendix F: Evidence Table 25. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications: retinopathy

Author, year	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP1, initial dose in mg (fixed or esc) max dose	GP2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI)	GP2 "X"R (95% CI)
Study group									p-value GP1	p-value GP2
Second Generation Sulfonylurea vs. Second Generation Sulfonylurea										
Baba, 1983 ¹³³	RCT	Diabetic retinopathy/ Fundoscopic examination + Scott's classification used	Glibenclamide, 95	Gliclazide, 97	2.5 (esc) 10	40 (esc) 160	NR	NR	Fundoscopy exam 11% aggravated cases (<0.05 vs. GP2) Scott's classification 6% improved 10% aggravated	Fundoscopy exam 3% aggravated cases Scott's classification 4% improved 1% aggravated
Akanuma, 1988 ¹⁹⁶ Diabetic Retinopathy Program	RCT	Diabetic retinopathy/proliferative retinopathy + mild non-proliferative + 4 grade scale of severity	Glipizide, 21	Un-specified SU, 19	40 (esc) 240	NR	NR	NR	IR 47.7 (baseline); 54.8 (followup)	IR 54.0 (baseline); 67.6 (followup)
Second Generation Sulfonylurea vs. Metformin + Second Generation Sulfonylurea										
UKPDS, 1998 ¹⁵	RCT	Diabetic retinopathy/ retinopathy requiring photocoagulation	Metformin + SU, 268	SU, 269	500 (esc) 2550 2.5 (esc) 20	2.5 (esc) 20	NR	NR	RR 1.08 (0.41-2.66)	ref
UKPDS, 1998 ¹⁵	RCT	Diabetic retinopathy/vitreous hemorrhage	Metformin + SU, 268	SU, 269	500 (esc) 2550 2.5 (esc) 20	2.5 (esc) 20	0	2	NR	NR
UKPDS, 1998 ¹⁵	RCT	Combined microvascular outcome (retinopathy and nephropathy)	Metformin + SU, 268	SU, 269	500 (esc) 2550 2.5 (esc) 20	2.5 (esc) 20	NR	NR	RR 0.84 (0.43-1.66)	ref
Metformin vs. Other Oral Diabetes Medications										
Rachmani, 2002 ¹⁵⁰	RCT	Diabetic retinopathy: total retinopathy/ proliferative retinopathy	Metformin continued + diet, 195	Metformin stopped + diet, 198	NR (NR)	NR (NR)	63/21 (initial); 70/22 (final)	66/22 (initial); 72/23 (final)	<0.01 vs. baseline; NSG vs. GP2	<0.01 vs. baseline; NSG vs. GP2
Metformin or Second Generation Sulfonylurea vs. Placebo										

Appendix F: Evidence Table 25. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications: retinopathy

Author, year Study group	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP1, initial dose in mg (fixed or esc) max dose	GP2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) p-value GP1	GP2 "X"R (95% CI) p-value GP2
Akanuma, 1988 ¹⁹⁶ Diabetic Retinopathy Program	RCT	Diabetic retinopathy/proliferative retinopathy + mild non-proliferative + 4 grade scale of severity	Glipizide, 21	Diet, 20	40 (esc) 240	NA	NR	NR	IR 47.7 (baseline); 54.8 (followup)	IR 51.3 (baseline); 73.0 (followup)
Akanuma, 1988 ¹⁹⁶ Diabetic Retinopathy Program	RCT	Diabetic retinopathy/proliferative retinopathy + mild non-proliferative + 4 grade scale of severity	Un-specified SU, 19	Diet, 20	NR (NR)	NA	NR	NR	IR 54.0 (baseline); 67.6 (followup)	IR 51.3 (baseline); 73.0 (followup)
UKPDS, 1998 ¹⁵	RCT	Diabetic retinopathy/retinopathy requiring photocoagulation	Metformin, 342	Diet, 411	NR (esc) 2550	NA	NR	NR	RR 0.69 (0.34-1.39)	ref
UKPDS, 1998 ¹⁵	RCT	Diabetic retinopathy/vitreous hemorrhage	Metformin, 342	Diet, 411	NR (esc) 2550	NA	NR	NR	RR 0.75 (0.07-7.62)	ref
UKPDS, 1998 ¹⁵	RCT	Combined microvascular outcome (retinopathy and nephropathy)	Metformin, 342	Diet, 411	NR (esc) 2550	NA	NR	NR	RR 0.71 (0.43-1.19)	ref
UKPDS, 1998 ¹⁶	RCT	Diabetic retinopathy/retinopathy requiring photocoagulation	Glibenclamide, 615	Diet, 896	2.5 (esc) 20	NA	NR	NR	RR 0.63 (0.40-1.00)	ref
UKPDS, 1998 ¹⁶	RCT	Diabetic retinopathy/vitreous hemorrhage	Glibenclamide, 615	Diet, 896	2.5 (esc) 20	NA	NR	NR	RR 0.73 (0.18-2.98)	ref
UKPDS, 1998 ¹⁶	RCT	Combined microvascular outcome (retinopathy and nephropathy)	Glibenclamide, 615	Diet, 896	2.5 (esc) 20	NA	NR	NR	RR 0.66 (0.47-0.93)	ref

Comp = comparison; GP = group; IR = incidence rate; CI = confidence interval; RR = relative risk; HR = hazard ratio; OR = odds ratio; SU = Sulfonylurea; RCT= randomized controlled trial; NR= not reported; NA = not applicable; vs=versus; mg=milligrams; max = maximum; esc=escalated; ref=reference; UKPDS = United Kingdom Prospective Diabetes Study; NSG = not significant

Appendix F: Evidence Table 26. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications: nephropathy

Author, year Study group	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) or GP1 baseline and followup p-value GP1	GP2 "X"R (95% CI) or GP2 baseline and followup p-value GP2
Thiazolidinedione vs. Second Generation Sulfonylurea										
Bakris, 2003 ⁶⁶	RCT	Diabetic nephropathy/number with normal albuminuria at baseline who progressed to microalbuminuria by study end	Rosiglitazone, 43	Glyburide (no trade drug specified), 47	4 bid (fixed)	NR (esc) 20	3 (7)	5 (10.6)	NR	NR
Bakris, 2003 ⁶⁶	RCT	Diabetic nephropathy/albumin/creatinine ratio	Rosiglitazone, 64	Glyburide (no trade drug specified), 57	4 bid (fixed)	NR (esc) 20	NR	NR	(-45 to -4); NSG vs. GP2	(-22 to 4)
Nakamura, 2000 ⁶⁴	RCT	Diabetic nephropathy/urinary albumin excretion	Pioglitazone, 15	Glibenclamide, 15	30 (fixed)	5 (fixed)	NR	NR	142.8 ug/min (baseline); 48.4 ug/min (followup) p < 0.05	Baseline and follow-up not reported; p > 0.05
Yanagawa, 2004 ⁶²	RCT	Diabetic nephropathy/urine albumin/creatinine	Pioglitazone, 19	Gliclazide, 21	NR	NR	NR	NR	F-statistic = 0.8; NSG vs. GP2	
Thiazolidinedione vs. Metformin										
Schern-thaner, 2004 ⁶⁶	RCT	Diabetic nephropathy/urinary albumin/creatinine ratio	Pioglitazone + placebo + diet, 588	Metformin + placebo + diet, 588	30 (esc) 45	850 up to 3 times/day (esc) 2550	NR (-19)	NR (-1)	p=0.002 vs. GP2	
Hanefeld, 2004 ⁶⁰ QUARTET study group	RCT	Diabetic nephropathy/albumin/creatinine ratio	Pioglitazone + un-specified SU + placebo, 319	Metformin + un-specified SU + placebo, 320	15 (esc) 45 NR	850 (esc) 850 tid NR	NR	NR	(0.73-0.97), p=0.017 vs. GP2	

Appendix F: Evidence Table 26. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications: nephropathy

Author, year	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) or GP1 baseline and followup p-value GP1	GP2 "X"R (95% CI) or GP2 baseline and followup p-value GP2
<p>Hanefeld, 2004⁶⁰</p> <p>QUARTET study group</p>	RCT	Diabetic nephropathy/microalbuminuria resolved	Pioglitazone + un-specified SU + placebo, 319	Metformin + un-specified SU + placebo, 320	15 (esc) 45 NR	850 (esc) 850 tid NR	(10.2)	(7.7)	NR	NR
Thiazolidinedione vs. Alpha-Glucosidase Inhibitor										
Nakamura, 2000 ⁶⁴	RCT	Diabetic nephropathy/proteinuria/albuminuria	Pioglitazone, 15	Voglibose, 15	30 (fixed)	0.6 (fixed)	NR	NR	142.8 ug/min (baseline); 48.4 ug/min (followup) p < 0.05 vs. baseline	Baseline and follow-up not reported; p > 0.05 vs. baseline
Metformin vs. Second Generation Sulfonylurea										
Amador-Licona, 2000 ⁸⁵	RCT	Diabetic nephropathy/change in glomerular filtration rate	Metformin, 28	Glibenclamide, 23	850 (esc) NR	5 (esc) NR	NR	NR	138 mL/min (baseline); 134 mL/min (followup); p=0.46 vs. baseline	136 mL/min (baseline); 151 mL/min (followup); p=0.04 vs. baseline
Amador-Licona, 2000 ⁸⁵	RCT	Diabetic nephropathy/change in microalbumin (mg/d)	Metformin, 28	Glibenclamide, 23	850 (esc) NR	5 (esc) NR	NR	NR	74 mg/d (baseline); 49 mg/d (followup); p=0.008 vs. baseline	83 mg/d (baseline); 102 mg/d (followup); p=0.09 vs. baseline
Metformin vs. Other Oral Diabetes Medications										
Rachmani, 2002 ¹⁵⁰	RCT	Diabetic nephropathy/urinary albumin/creatinine ratio in mg/g	Metformin continued + diet, 195	Metformin stopped + diet, 198	NR (NR)	NR (NR)	NR	NR	48 mg/g (baseline); 55 mg/g (followup); p<0.001 vs. baseline; NSG vs. GP2	46 mg/g (baseline); 57 mg/g (followup); p<0.001 vs. baseline

Appendix F: Evidence Table 26. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications: nephropathy

Author, year Study group	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) or GP1 baseline and followup p-value GP1	GP2 "X"R (95% CI) or GP2 baseline and followup p-value GP2
Rachmani, 2002 ¹⁵⁰	RCT	Diabetic nephropathy/ change serum creatinine	Metformin continued + diet, 195	Metformin stopped + diet, 198	NR (NR)	NR (NR)	NR	NR	163 umol/L (baseline); 179 umol/L (followup); p<0.01 vs. baseline	161 umol/L (baseline); 186 umol/L (followup); p<0.01 vs. baseline
Fujioka, 2003 ¹⁰⁵	RCT	Diabetic nephropathy/ urinary protein	Metformin + placebo + diet, 71	Metformin XR + placebo + diet, 75	1000 (esc) 1500	1000 (esc) 1500	2	0	NR	NR
Fujioka, 2003 ¹⁰⁵	RCT	Diabetic nephropathy/ urinary protein	Metformin + placebo + diet, 71	Metformin XR + placebo + diet, 71	1000 (esc) 1500	1000 (esc) 2000	2	0	NR	NR
Second Generation Sulfonylurea vs. Second Generation Sulfonylurea + Metformin										
UKPDS, 1998 ¹⁵	RCT	Diabetic nephropathy/death from renal disease	Metformin + SU, 268	SU, 269	500 (esc) 2550 2.5 (esc) 20	2.5 (esc) 20	1	1	RR 1.05 (0.08-39.9)	ref
UKPDS, 1998 ¹⁵	RCT	Diabetic nephropathy/renal failure	Metformin + SU, 268	SU, 269	500 (esc) 2550 2.5 (esc) 20	2.5 (esc) 20	0	4	NR	NR
Second Generation Sulfonylurea vs. Alpha-Glucosidase Inhibitor										
Nakamura, 2000 ⁶⁴	RCT	Diabetic nephropathy/ proteinuria/albuminuria	Glibenclamide, 15	Voglibose, 15	5 (fixed)	0.6 (fixed)	NR	NR	p > 0.05 vs. baseline	p > 0.05 vs. baseline
Metformin or Second Generation Sulfonylurea vs. Placebo										
UKPDS, 1998 ¹⁵	RCT	Diabetic nephropathy/ death from renal disease	Metformin, 342	Diet, 411	NR (esc) 2550	NA	2	1	RR 2.44 (0.10-57.46)	ref
UKPDS, 1998 ¹⁵	RCT	Diabetic nephropathy/ renal failure	Metformin, 342	Diet, 411	NR (esc) 2550	NA	2	2	RR 1.14 (0.09-14.94)	ref
UKPDS, 1998 ¹⁶	RCT	Diabetic nephropathy/death from renal disease	Glibenclamide, 615	Diet, 896	2.5 (esc) 20	NA	4	2	RR 2.84 (0.30-26.41)	ref

Appendix F: Evidence Table 26. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications: nephropathy

Author, year Study group	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) or GP1 baseline and followup p-value GP1	GP2 "X"R (95% CI) or GP2 baseline and followup p-value GP2
UKPDS, 1998 ¹⁶	RCT	Diabetic nephropathy/renal failure	Glibenclamide, 615	Diet, 896	2.5 (esc) 20	NA	4	8	RR 0.72 (0.15-3.50)	ref
Thiazolidinedione vs. Placebo										
Herz, 2003 ¹⁶³	RCT	Diabetic nephropathy/albumin/creatinine ratio	Pioglitazone, 99	Placebo, 99	45 (fixed)	NA	NR	NR	No treatment effect seen on urine albumin/creatinine ratios noted per author	No treatment effect seen on urine albumin/creatinine ratios noted per author
Herz, 2003 ¹⁶³	RCT	Diabetic nephropathy/albumin/creatinine ratio	Pioglitazone, 99	Placebo, 99	30 (fixed)	NA	NR	NR	No treatment effect seen on urine albumin/creatinine ratios noted per author	No treatment effect seen on urine albumin/creatinine ratios noted per author
Lebovitz, 2001 ¹⁶⁹	RCT	Diabetic nephropathy/albumin/creatinine ratio	Rosiglitazone, 142	Placebo, 132	2 bid (fixed)	NA	NR	NR	(-25.3 to -0.9)	(-9.1 to 18)
Lebovitz, 2001 ¹⁶⁹	RCT	Diabetic nephropathy/albumin/creatinine ratio	Rosiglitazone, 145	Placebo, 132	4 bid (fixed)	NA	NR	NR	(-30.6 to -11.3)	(-9.1 to 18)

Comp = comparison; GP = group; mg=milligrams; esc = escalated; max = maximum; CI = confidence interval; RR = relative risk; SU = sulfonylurea; NA=not applicable; vs=versus; d=day; mL= milliliter; L=liter; ug=micrograms; dL = deciliter; min = minute; g = gram; umol = micromole; XR = extended release; NR=not reported; NA = not applicable; min=minute; RCT=randomized controlled trial; ref=reference group; carbs=carbohydrates; NSG=not significant; bid = twice a day; tid = three times a day; UKPDS = United Kingdom Prospective Diabetes Study

Appendix F: Evidence Table 27. Comparative effectiveness of oral diabetes medications on distal diabetes-related complications: neuropathy

Author, year Study group	Study design	Main/specific outcome	Comp GP1, N	Comp GP2, N	GP1, initial dose in mg (fixed or esc) max dose	GP2, initial dose in mg (fixed or esc) max dose	GP1 events, n (%)	GP2 events, n (%)	GP1 "X"R (95% CI) p-value GP1	GP2 "X"R (95% CI) p-value GP2
Direct Comparisons										
Gomez-Perez, 2002 ¹⁰²	RCT	Neuropathy/ unclear neuropathy	Metformin + placebo, 34	Rosiglitazone + metformin, 35	2500 (fixed)	2500 (fixed) 2 bid (fixed)	1	0	NR	NR
Gomez-Perez, 2002 ¹⁰²	RCT	Neuropathy/ unclear neuropathy	Metformin + placebo, 34	Rosiglitazone + metformin, 36	2500 (fixed)	2500 (fixed) 4 bid (fixed)	1	0	NR	NR
Fujioka, 2003 ¹⁰⁵	RCT	Neuropathy/ unclear neuropathy	Metformin + placebo + diet, 71	Metformin XR + placebo + diet, 75	1000 (esc) 1500	1000 (esc) 1500	0	1	NR	NR
Fujioka, 2003 ¹⁰⁵	RCT	Neuropathy/ unclear neuropathy	Metformin + placebo + diet, 71	Metformin XR + placebo + diet, 71	1000 (esc) 1500	1000 (esc) 2000	0	0	NR	NR
Placebo-Controlled Trials										
Manzella, 2004 ¹⁴⁸	RCT	Neuropathy/ autonomic assessed by mean LF/HF ratio used as an index of cardiac sympathetic/ parasympathetic tone balance	Metformin + diet, 60	Placebo + diet, 60	850 bid (fixed)	NA	NR	NR	4.7 (baseline); 2.9 (followup); p<0.02 versus placebo	4.8 (baseline); 4.5 (followup)

Comp = comparison; GP = group; mg = milligrams; esc = escalated; max = maximum; CI = confidence interval; NR = not reported; NA = not applicable; RCT = randomized controlled trial; bid = twice a day; XR = extended release; LF/HF ratio = sympathovagal balance index

Appendix F: Evidence Table 28. Quality of randomized controlled trials evaluating comparative effectiveness of oral diabetes medications on distal diabetes-related complications

Author, year	Randomized	Randomization scheme described	Double blinded	Blinding described	Withdrawals described	Quality score
Nishio, 2006 ¹⁵¹	Yes	Not described	No	No	Yes	2
Weissman, 2005 ¹⁰⁰	Yes	Not described	Yes	Yes	Yes	4
Rosenstock, 2006 ¹²⁴	Yes	Not described	Yes	Not described	Yes	3
Bailey, 2005 ¹⁰¹	Yes	Yes	Yes	Not described	Yes	4
Dormandy, 2005 ¹⁸⁵	Yes	Yes	Yes	Yes	Yes	5
Cryer, 2005 ¹⁷⁶	Yes	Not described	No	No	Yes	2
Schernthaner, 2004 ⁵⁶	Yes	Yes	Yes	Yes	Yes	5
Choi, 2004 ⁷⁷	Yes	Not described	No	No	Yes	2
Baksi, 2004 ¹²⁶	Yes	Not described	Yes	Not described	Yes	3
Yanagawa, 2004 ⁶²	Yes	Not described	Nr	No	No	1
Manzella, 2004 ¹⁴⁸	Yes	Not described	No	No	Yes	2
Hanefeld, 2004 ⁶⁰	Yes	Not described	Yes	Yes	No	3
Lawrence, 2004 ⁵⁴	Yes	Not described	No	No	Yes	2
Garber, 2003 ⁸⁰	Yes	Yes	Yes	Yes	Yes	5
Takagi, 2003 ⁷⁸	Yes	Not described	No	No	No	1
Goldstein, 2003 ⁸²	Yes	Yes	No	No	Yes	3
Herz, 2003 ¹⁶³	Yes	Not described	Yes	Not described	Yes	3
Barnett, 2003 ¹⁷²	Yes	Not described	Yes	Yes	Yes	4
Fujioka, 2003 ¹⁰⁵	Yes	Not described	Yes	Yes	Yes	4
Luis Bautista, 2003 ¹⁹³	Yes	Not described	Yes	Yes	Yes	4
Vongthavaravat, 2002 ¹⁷⁰	Yes	Yes	No	No	No	2
Virtanen, 2003 ¹⁴³	Yes	Not described	Nr	Not described	Yes	2
Hallsten, 2002 ⁵⁸	Yes	Not described	No	No	Yes	2
St John Sutto, 2002 ⁶⁷	Yes	Not described	No	No	Yes	2
Rachmani, 2002 ¹⁵⁰	Yes	Yes	No	No	Yes	3
Gomez-Perez, 2002 ¹⁰²	Yes	Not described	Yes	Not described	Yes	3
Kipnes, 2001 ¹⁶⁶	Yes	Not described	Yes	Not described	Yes	3
Amador-Licona, 2000 ⁸⁵	Yes	Not described	No	No	Yes	2

Appendix F: Evidence Table 28. Quality of randomized controlled trials evaluating comparative effectiveness of oral diabetes medications on distal diabetes-related complications

Author, year	Randomized	Randomization scheme described	Double blinded	Blinding described	Withdrawals described	Quality score
Lebovitz, 2001 ¹⁶⁹	Yes	Not described	No	No	No	1
Fonseca, 2000 ¹⁰³	Yes	Yes	Yes	Yes	Yes	5
Nakamura, 2000 ⁶⁴	Yes	Not described	No	No	No	1
Horton, 2000 ⁹⁶	Yes	Not described	Yes	Yes	Yes	4
Aronoff, 2000 ¹⁶⁵	Yes	Not described	Yes	Not described	No	2
Hanefeld, 2000 ¹⁹⁰	Yes	Not described	Yes	Yes	No	3
Hasche, 1999 ¹³⁸	Yes	Not described	Yes	Not described	Yes	3
Jovanovic, 2000 ¹⁹⁴	Yes	Yes	Yes	Yes	Yes	5
Marbury, 1999 ¹¹⁶	Yes	Not described	Yes	Not described	Yes	3
Wolffenbuttel, 1999 ¹¹⁷	Yes	Not described	Yes	Yes	Yes	4
Goldberg, 1998 ¹³⁹	Yes	Not described	Yes	Not described	Yes	3
1998, ¹⁵	Yes	Not described	No	No	Yes	2
1998, ¹⁶	Yes	Yes	No	No	No	2
Rosenstock, 1996 ¹⁸⁹	Yes	Not described	Yes	Not described	Yes	3
DeFronzo, 1995 ⁸⁸	Yes	Not described	Yes	Yes	Yes	4
Hermann, 1994 ⁸⁷	Yes	Yes	Yes	Yes	No	4
Carlson, 1993 ¹⁰⁸	Yes	Not described	Yes	Not described	Yes	3
Teupe, 1991 ¹⁵⁵	Yes	Not described	No	No	Yes	2
Akanuma, 1988 ¹⁹⁶	Yes	Not described	No	No	Yes	2
Baba, 1983 ¹³³	Yes	Not described	Yes	Not described	Yes	3
Lester, 2005 ²⁴²	Yes	Not described	Yes	Not described	No	2
Zhu, 2003 ¹⁸⁸	Yes	Yes	Yes	Not described	Yes	4
Bakris, 2003 ⁸⁶	Yes	Not described	No	No	No	1
Sonnenberg, 1997 ¹⁹¹	Yes	Not described	Yes	Not described	Yes	3
Draeger, 1996 ¹¹²	Yes	Not described	Yes	Yes	Yes	4

Appendix F: Evidence Table 29. Study design characteristics table for studies reporting on quality of life (Key Question 3)

Author, year					
Study group	Study design	Country	Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Smith, 2005 ¹⁶¹	RCT	US	Yes	24 weeks (planned duration)	Age <35 or >75, any liver disease, any kidney disease, history of CVD, treatment experienced, no type 2 diabetes, other
Bailey, 2005 ¹⁰¹	RCT	UK, 14 European Countries	Yes	24 weeks (planned duration)	Age <18 or >70, history of CVD, no type 2 diabetes, other
Rosenstock, 2006 ¹²⁴	RCT	US, Canada	NR	NR	Age <60, history of CVD, no type 2 diabetes, other
Bech, 2003 ¹⁹⁷	RCT	Australia, Croatia, Czech Republic, France, Greece, Israel, Macedonia, Poland, Russia, Slovenia, Spain	Yes	NR	Age < 40 years, any liver disease, history of CVD, treatment experienced, no type 2 diabetes, other
Testa, 1998 ¹⁹⁸	RCT	US	Yes	15 weeks (planned duration)	Age <30, no type 2 diabetes, other

RCT = Randomized controlled trial; CVD = cardiovascular disease; US = United States; UK = United Kingdom; NR = not reported

Appendix F: Evidence Table 30. Study population table for studies reporting on quality of life (Key Question 3)

Author, year	Group, N	Mean age (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight (other measure)	Mean HbA1c %	Mean duration of diabetes
Rosenstock, 2006 ¹²⁴	Glipizide + rosiglitazone, N=116	68.7	(74.8)	NR	30.2	NR	7.72	6.8
	Placebo + glipizide, N=111	68.2	(71.8)	NR	30.5	NR	7.65	6.6
Bech, 2003 ¹⁹⁷	Repaglinide, N=164	56.9 (40-81)	(57.3)	AA: 1 (0.6); C: 161 (98.2); Asian: 0 (0); H: 0; O: 2 (1.2)	7.8	2.77	NR	NR
	Placebo, N=89	57.3 (40-76)	(58.4)	AA: 0 (0); C: 88 (98); Asian: 0 (0); H: 0; O: 1 (1.1)	7.6	2.81	NR	NR
Smith, 2005 ¹⁶¹	Placebo + diet, N=21	53.1	10	AA: 0; C: 16; Asian: 0; H: 0; O: 5	31.9	91.5	6.46	NR
	Diet + pioglitazone, N=21	56.2	9	AA: 0; C: 15; Asian: 0; H: 0; O: 6	32.1	93.5	6.88	NR
Bailey, 2005 ¹⁰¹	Metformin + rosiglitazone, N=288	58.1	168 (58)	AA: 2 (1); C: 280 (97); Asian: 3 (1); H: 0; O: 3 (1)	32.2	90.9	7.4	6
	Metformin, N=280	57.6	159 (57)	AA: 1 (<1); C: 273 (98); Asian: 3 (1); H: 0; O: 3 (1)	32.1	89.5	7.5	6.1
Testa, 1998 ¹⁹⁸	Placebo + diet, n=192	58.4 (30-82)	(58.9)	AA: (15.6); C: (72.9); Asian: 0; H: 0; O: (11.5)	30.3	NR	8.7	4.7
	Diet + glipizide GITS, N=377	58.7 (30-85)	(54.9)	AA: (16.7); C: (71.9); Asian: 0; H: 0; O: (11.4)	30.1	NR	8.5	5.6

BMI = body mass index; HbA1c = hemoglobin A1c; AA = African American; C = Caucasian; H = Hispanic; O = other; NR = not reported; GITS = gastrointestinal therapeutic system

Appendix F: Evidence Table 31. Comparative effectiveness of oral diabetes medications on quality of life

Author, year Study group	Quality of life assessment	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL2 - mean diff BL1	P-value for com- pari- sons with GP1	P-value for com- pari- sons with GP2
Smith, 2005 ¹⁶¹	Visual analog scale estimation of hunger and satiety	Pioglitazone + existing medication + diet, 21	Existing medication + placebo + diet, 21	30 (esc) 45	NR	NR NR NR	NR NR NR	NR	0.197 vs. GP2	
Bailey, 2005 ¹⁰¹	Diabetes treatment satisfaction questionnaire	Metformin, 258	Rosiglitazone + metformin, 270	2500 (esc) 3000	4 (esc) 8 2000 (fixed)	NR NR -1.1	NR NR -0.1	NR		<0.014 vs. GP1
Rosenstock, 2006 ¹²⁴	Diabetes treatment satisfaction questionnaire	Glipizide + placebo, 57	Rosiglitazone + glipizide, 90	10 (esc) 20	4 (fixed) 10 (esc) 20	NR NR -1.61	NR NR 1.15	-2.76		<0.001 vs. GP1
Rosenstock, 2006 ¹²⁴	Short Form-36 (mental health component)	Glipizide + placebo, 57	Rosiglitazone + glipizide, 90	10 (esc) 20	4 (fixed) 10 (esc) 20	NR NR -1.71	NR NR NR	NR	NSG vs. GP2	
Rosenstock, 2006 ¹²⁴	Short Form-36 (physical health component)	Glipizide + placebo, 57	Rosiglitazone + glipizide, 90	10 (esc) 20	4 (fixed) 10 (esc) 20	NR NR -2.43	NR NR NR	NR	NSG vs. GP2	
Bech, 2003 ¹⁹⁷	Diabetes treatment satisfaction questionnaire	Repaglinide, 164	Placebo, 89	0.5 (esc) 4 tid	NA	75.2 83.9 8.7	79.2 80.7 1.5	7.2	<0.05 vs. base- line	NSG vs. base- line
Bech, 2003 ¹⁹⁷	EuroQoL	Repaglinide, 164	Placebo, 89	0.5 (esc) 4 tid	NA	0.82 NR NR	0.83 NR NR	NR	NSG vs. base- line	NSG vs. base- line

Appendix F: Evidence Table 31. Comparative effectiveness of oral diabetes medications on quality of life

Author, year Study group	Quality of life assessment	Comp group 1, N	Comp group 2, N	Group 1, initial dose in mg (fixed or esc) max dose	Group 2, initial dose in mg (fixed or esc) max dose	GP1 BL mean (SD) GP1 final mean (SD) Mean diff from BL1	GP2 BL mean (SD) GP2 final mean (SD) Mean diff from BL2	Mean diff BL2 - mean diff BL1	P-value for com- pari- sons with GP1	P-value for com- pari- sons with GP2
Bech, 2003 ¹⁹⁷	WHO Wellbeing Questionnaire	Repaglinide, 136	Placebo, 63	0.5 (esc) 4 tid	NA	74.5 74.3 -0.2	77 76.5 -0.5	0.3	NSG vs. base- line	NSG vs. base- line
Testa, 1998 ¹⁹⁸	Visual analog scale – perceived health	Glypizide GITS + diet, 377	Placebo + diet, 192	5 (esc) 20	NA	NR NR NR	NR NR NR	0.36	0.004 vs. GP2	
Testa, 1998 ¹⁹⁸	Visual analog scale – symptom distress	Glypizide GITS + diet, 377	Placebo + diet, 192	5 (esc) 20	NA	NR NR NR	NR NR NR	0.59	<.001 vs. GP2	
Testa, 1998 ¹⁹⁸	Visual analog scale – mental and emotional health	Glypizide GITS + diet, 377	Placebo + diet, 192	5 (esc) 20	NA	NR NR NR	NR NR NR	0.16	0.22 vs. GP2	
Testa, 1998 ¹⁹⁸	Visual analog scale – overall VAS	Glypizide GITS + diet, 377	Placebo + diet, 192	5 (esc) 20	NA	NR NR NR	NR NR NR	0.24	0.04 vs. GP2	
Testa, 1998 ¹⁹⁸	Visual analog scale – cognitive functioning	Glypizide GITS + diet, 377	Placebo + diet, 192	5 (esc) 20	NA	NR NR NR	NR NR NR	0.34	0.005 vs. GP2	

Comp = comparison; BL = baseline; GP = group; mg = milligrams; esc = escalated; max = maximum; SD = standard deviation; diff = difference; mmol = millimole; NR = not reported; NA = not applicable; QoL = quality of life; WHO = World Health Organization; VAS = visual analog scale; GITS = gastrointestinal therapeutic system

Appendix F: Evidence Table 32. Quality of randomized controlled trials evaluating comparative effectiveness of oral diabetes medications on quality of life

Author, year	Randomized	Randomization scheme described	Double blinded	Blinding described	Withdrawals described	Quality score
Rosenstock, 2006 ¹²⁴	Yes	Not Described	Yes	Not described	Yes	3
Bailey, 2005 ¹⁰¹	Yes	Yes	Yes	Not described	Yes	4

Appendix F: Evidence Table 32. Quality of randomized controlled trials evaluating comparative effectiveness of oral diabetes medications on quality of life

Smith, 2005 ¹⁶¹	Yes	Not Described	Yes	Yes	No	3
Bech, 2003 ¹⁹⁷	Yes	Not Described	Yes	Not described	No	2
Testa, 1998 ¹⁹⁸	Yes	Not Described	Yes	Not described	Yes	3

Author, year

Study group

Study design

Country

Pharmaceutical
support

Study duration
(planned/mean)

Exclusion criteria

Appendix F: Evidence Table 33. Study Design Characteristics Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year			Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Study group	Study design	Country			
Kane, 2004 ²¹⁹	Cohort	US	No	24 weeks (Mean follow-up)	No type 2 diabetes, Other
Ballary, 2003 ²²⁷	trial without control arm	India	Yes	NR	Age <36 or >65, Any liver disease, Any kidney disease, History of CVD, Neuropathy, Retinopathy, HbA1c <8%, No type 2 diabetes, Other
Swislocki, 1999 ²¹⁰	Cohort	US	No	NR	No type 2 diabetes, Other
Rosenbaum, 2002 ¹⁵³	RCT	Brazil	No	24 weeks (Planned duration)	Age <40 or >65, Any liver disease, Any kidney disease, Treatment experienced, No type 2 diabetes, Other
Stang, 1999 ²³⁵	Cohort	US, Canada	No	NR	No type 2 diabetes, Other
Simpson, 2006 ¹⁴	Cohort	Canada	No	249.6 for 234 subjects taking lower daily doses, 234 subjects taking higher doses (Mean follow-up)	Age <30, Other
Nishio, 2006 ¹⁵¹	RCT	Japan	No	6 months (Planned duration)	Any liver disease, Any kidney disease, No type 2 diabetes, Other
Weissman, 2005 ¹⁰⁰	RCT	US	Yes	24 weeks (Planned duration)	Age <18 and >75, Any liver disease, Any kidney disease, History of CVD, HbA1c <6.5 or >8.5 for patients having received prior combination treatment; <7 or >10 prior monotherapy or drug naive patients, No type 2 diabetes, Other
Rosenstock, 2006 ¹²⁴	RCT	US, Canada	No	NR	Age <60, History of CVD, No type 2 diabetes, Other
Bailey, 2005 ¹⁰¹	RCT	UK, 14 European Countries	Yes	24 weeks (Planned duration)	Age <18 or >70, History of CVD, No type 2 diabetes, Other

Appendix F: Evidence Table 33. Study Design Characteristics Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year			Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Study group Kardas, 2005 ¹¹⁴ , DIACOM	Study design RCT	Country Poland	No	NR	Age <40 and >75, HbA1c >9.0%, No type 2 diabetes, Other
Forst, 2005 ¹⁴⁵	RCT	Germany	Yes	24 weeks (Planned duration)	Age < 40 or >75, Any liver disease, Any kidney disease, History of CVD, HbA1c <6.6 or >9.9, No type 2 diabetes, Other
Hartung, 2005 ²³¹	Case-control	US	No	NR	Age <18, No type 2 diabetes, Other
Bhansali, 2005 ²¹⁴	pre-post	UK, India	Yes	NR	Age <40, Any liver disease, Any kidney disease, History of CVD, HbA1c >8.5 or FPG>120mg/dl, No type 2 diabetes, Other
Yamanouchi, 2005 ⁵⁷	RCT	Japan	No	12 months (Planned duration)	Any liver disease, Any kidney disease, History of CVD, Treatment experienced, Neuropathy, Retinopathy, HbA1c <7.0%, No type 2 diabetes, Other
Kahara, 2005 ²³⁴	Non-randomized trial	Japan	No	3 months (Planned duration)	No type 2 diabetes, Other
Goldberg, 2005 ⁵²	RCT	US, Puerto Rico, Mexico, and Colombia	Yes	24 weeks (Planned duration)	Age <35, Any liver disease, Any kidney disease, History of CVD, Treatment experienced, HbA1c <7 or >11.5 if naive to anihyperglycemic therapy; <7 or >9.5 if previously treated with oral anihyperglycemic therapy, No type 2 diabetes, Other
Pfutzner, 2005 ⁶⁸	RCT	Germany	Yes	26 weeks (Planned duration)	Age <40 or >75, Any liver disease, Any kidney disease, History of CVD, HbA1c <6.6% or >9.9%, Other

Appendix F: Evidence Table 33. Study Design Characteristics Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year			Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Study group	Study design	Country			
Derosa, 2005 ⁵³	RCT	Italy	No	NR	Any liver disease, Any kidney disease, History of CVD, Neuropathy, Retinopathy, HbA1c <7.5%, No type 2 diabetes, Other
Derosa, 2005 ⁷²	RCT	Italy	No	12 months (Planned duration)	Age <18, Any liver disease, Any kidney disease, History of CVD, Neuropathy, Retinopathy, HbA1c <7.5, No type 2 diabetes, Other
Chalasani, 2005 ²²²	Cohort	US	No	duration of therapy=357 days for group 1 and 423 days in group 2 (Mean follow-up)	No type 2 diabetes, Other
Langenfeld, 2005 ¹⁴⁶	RCT	Germany	Yes	24 weeks (Planned duration)	Age <40 or age>75, Any liver disease, Any kidney disease, History of CVD, HbA1c <6.6% or >9.9%, No type 2 diabetes, Other
Rajagopalan, 2005 ²²³	Cohort	US	Yes	294.2, 296.1, 300.1, 321.9, 295.9, 319.9 Groups 1 and 2: Pioglitazone vs. rosiglitazone; Groups 3 and 4: Pioglitazone vs. sulfonylurea; Groups 5 and 6: Pioglitazone vs. metformin (Mean follow-up)	Age <18, Any liver disease, No type 2 diabetes, Other
Feinglos, 2005 ¹⁰⁴	RCT	US	Yes	16 weeks (Planned duration)	Age <30 or age >81, Any liver disease, Any kidney disease, History of CVD, HbA1c <7.0% or >8.5%, No type 2 diabetes, Other
Evans, 2005 ³²⁵	Case-control	Scotland	No	NR	No type 2 diabetes
Goke, 2002 ⁷⁵ , German Pio Study Group	RCT	Germany	Yes	26 weeks (Planned duration)	Any liver disease, Any kidney disease, History of CVD, HbA1c <7.5% or >11.5%, No type 2 diabetes, Other

Appendix F: Evidence Table 33. Study Design Characteristics Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year					
Study group	Study design	Country	Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Charbonnel, 2005 ⁶³	RCT	14 European countries, Australia, Canada, South Africa and Israel	Yes	52 weeks (Planned duration)	Age <35 and >75, Treatment experienced, HbA1c <7.5% and >11%, No type 2 diabetes, Other
Tan, 2005 ⁶¹ , this is a one yr extension study for Quartet study group (ref 11) but only half the original centers included (98/208 centers)	RCT	Canada, UK, Australia, Finland, Poland, the Slovak republic and South Africa	Yes	104 weeks (Planned duration)	Age <35 >75, Treatment experienced, HbA1c <7.5% or >11% with diet alone, No type 2 diabetes, Other
Cryer, 2005 ¹⁷⁶ , COSMIC Approach Study	RCT	US	Yes	12 months (Planned duration)	Age <18, Any liver disease, Any kidney disease, No type 2 diabetes, Other
McCluskey, 2004 ⁷⁶	RCT	US	Yes	30 weeks (Planned duration)	Age <18 >80, Treatment experienced, HbA1c <7.5% & >9.5%, No type 2 diabetes, Other
Maru, 2005 ²³² , UK General Practice Research Database	Cohort	UK	Yes	130 (Mean follow-up)	Age <35, Treatment experienced, No type 2 diabetes, Other
Schemthaler, 2004 ⁵⁶	RCT	Europe	No	12 months (Planned duration)	Age <35 or >75, Treatment experienced, HbA1c <7.5% or >11%, No type 2 diabetes,
Smith, 2005 ¹⁶¹	RCT	US	Yes	24 weeks (Planned duration)	Age <35 or >75, Any liver disease, Any kidney disease, History of CVD, Treatment experienced, No type 2 diabetes, Other
Rajagopalan, 2004 ³²⁷ , PharMetrics Patient-Centered Database	Cohort	US	No	45.9 weeks (Mean follow-up)	Age <18, No type 2 diabetes, Other

Appendix F: Evidence Table 33. Study Design Characteristics Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year					
Study group	Study design	Country	Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Choi, 2004 ⁷⁷	RCT	Korea	No	6 months (Planned duration)	Any liver disease, Any kidney disease, Other
Matthews, 2005 ⁷⁰	RCT	Europe and Australia	Yes	52 months (Planned duration)	Age <35 or >75, History of CVD, HbA1c <7.5% or >11%, No type 2 diabetes, Other
Nichols, 2005 ²³⁰ , Kaiser Permanente database	Cohort	US	Yes	144.4 total sulfonylurea monotherapy group- mean MONTHS of followup is 26.4; metformin monotherapy- mean MONTHS of followup is 23.1; sulfonylurea + metformin- mean months of followup is 28.3 (Mean follow-up)	Other
Derosa, 2004 ⁹⁰	RCT	Italy	No	12 months (Planned duration)	Age <46 or >67, Any liver disease, Any kidney disease, History of CVD, Treatment experienced, No type 2 diabetes, Other
Schemthaner, 2004 ¹⁰⁶	RCT	154 clinical centres in Austria, Belgium, the Czech Republic, France, Germany, Hungary, Italy, the Netherlands, Poland, Slovakia, Spain, and the United Kingdom	No	27 weeks (Planned duration)	Age <35, Any liver disease, Any kidney disease, HbA1c < 6.9 or > 11.5, No type 2 diabetes, Other
Tan, 2004 ⁶⁵	RCT	22 centres in Denmark, Finland, Norway, and Sweden.	Yes	52 weeks (Planned duration)	Treatment experienced, HbA1c <7.5 or > 11 for pts not receiving OAM, <7.5, > 9.5 for patients receiving OAM, No type 2 diabetes, Other
Bell, 1997 ²⁰⁸	interview of patients over 3 months asking if they have ever experienced hypoglycemia	US	No	NR	No type 2 diabetes

Appendix F: Evidence Table 33. Study Design Characteristics Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year					
Study group	Study design	Country	Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Baksi, 2004 ¹²⁶	RCT	7 European countries	Yes	26 weeks (Planned duration)	Age <35 or >80, Any liver disease, History of CVD, Treatment experienced, Neuropathy, No type 2 diabetes, Other
Tan, 2004 ⁶⁹	RCT	Mexico	Yes	NR	Any liver disease, Any kidney disease, History of CVD, HbA1c < 7.5% to > 11% in patients who were not receiving OAMs, and <7.5% to >9.5% in patients who were receiving OAM monotherapy, No type 2 diabetes, Other
Saad, 2004 ¹⁶⁴	RCT	US	Yes	12 weeks (Planned duration)	Age <18 or >73, Any liver disease, Any kidney disease, History of CVD, Treatment experienced, Other
Rosenstock, 2004 ¹³¹	RCT	US	Yes	16 weeks (Planned duration)	Age <18, Females, Treatment experienced, No type 2 diabetes, Other
Raskin, 2004 ⁷⁴	RCT	US	Yes	12 titration and 12 maintenance weeks (Planned duration)	Age <18, HbA1c <7 or >12% during previous monotherapy with sulfonylurea or metformin at 50% or more of maximal recommended dose for at least 3 months, No type 2 diabetes, Other
Manzella, 2004 ¹⁴⁸	RCT	Italy	No	4 months (Planned duration)	History of CVD, Treatment experienced, Neuropathy, No type 2 diabetes, Other
Feinbock, 2003 ¹³⁰	RCT	Austria	Yes	26 weeks (Planned duration)	Age <36 or >80, Any liver disease, Any kidney disease, Treatment experienced, HbA1c <7.8%, No type 2 diabetes, Other

Appendix F: Evidence Table 33. Study Design Characteristics Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year					
Study group	Study design	Country	Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Kerenyi, 2004 ¹²⁵	RCT	15 countries	Yes	26 weeks (Planned duration)	Age <35 or >80, Any liver disease, Any kidney disease, History of CVD, No type 2 diabetes, Other
Jovanovic, 2004 ⁷³	RCT	US	Yes	12 week titration then 12 week maintenance (Planned duration)	Age <18, HbA1c <7 or >12, No type 2 diabetes, Other
Hanefeld, 2004 ⁶⁰ , QUARTET study group	RCT	Canada, UK, Hungary, Finland, U.K., Slovak Republic, Belgium, Estonia, Lithuania, Denmark, Italy, Greece, Sweden, and the Netherlands	Yes	NR	Age <35 or >75, History of CVD, HbA1c <7.5 or >11, No type 2 diabetes, Other
Lawrence, 2004 ⁵⁴	RCT	UK	Yes	12 titration, 12 maintenance weeks (Planned duration)	Age <45 or >80, Any liver disease, Any kidney disease, History of CVD, HbA1c for diet treated diabetes: <7% or >10% for low-dose oral hypoglycemic therapy: >7.5%, No type 2 diabetes, Other
Delea, 2003 ²²⁸ , Phametrics Integrated Outcomes Database	Cohort	US	Yes	6 years (Mean follow-up)	Age 48, Other
Garber, 2003 ⁸⁰	RCT	US	Yes	16 weeks (Planned duration)	NR
Takagi, 2003 ⁷⁸	RCT	Japan	No	NR	Any liver disease, Any kidney disease, No type 2 diabetes, Other
Tosi, 2003 ⁹⁵	RCT, cross-over	Italy	Yes	6 months (Planned duration)	Any liver disease, Any kidney disease, History of CVD, Treatment experienced, HbA1c <6.3, No type 2 diabetes, Other
Goldstein, 2003 ⁸²	RCT	US	Yes	18 weeks (Planned duration)	Any liver disease, Any kidney disease, History of CVD, HbA1c <7.5 and >12.0, Other

Appendix F: Evidence Table 33. Study Design Characteristics Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year					
Study group	Study design	Country	Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Herz, 2003 ¹⁶³	RCT	Canada, Spain	Yes	16 weeks (Planned duration)	Any liver disease, Any kidney disease, Treatment experienced, HbA1c HbA1c < 6.5% or HbA1c>9.8%, No type 2 diabetes, Other
Ko, 2003 ³²⁸	Non-randomized trial	Korea	No	12 weeks (Planned duration)	Onset of diabetes <40 old, Any liver disease, Any kidney disease, History of CVD, No type 2 diabetes, Other
Derosa, 2003 ⁹⁷	RCT	Italy	No	12 months (Planned duration)	Any kidney disease, History of CVD, Treatment experienced, HbA1c < 7 %, No type 2 diabetes, Other
Barnett, 2003 ¹⁷²	RCT	UK	No	26 weeks (Planned duration)	Age <30 or Age > 80, Any liver disease, HbA1c < 7.5%, No type 2 diabetes, Other
Fujioka, 2003 ¹⁰⁵	RCT	US	Yes	24 weeks (Planned duration)	Any liver disease, Any kidney disease, History of CVD, HbA1c >8.5% and FPG>200 mg/dL while on MIR for >=8 weeks, No type 2 diabetes, Other
Zhu, 2003 ¹⁸⁸	RCT	China	Yes	24 weeks (Planned duration)	Age <40 or age>70, Any liver disease, Any kidney disease, History of CVD, Neuropathy, Retinopathy, HbA1c <7.5%, No type 2 diabetes, Other
Del Prato, 2003 ¹⁴⁹	RCT	France, Italy, Netherlands	No	29 weeks (Planned duration)	Age <35 or age>70, HbA1c <7.5% or >10% after run-in period, No type 2 diabetes, Other
Pavo, 2003 ⁵⁹	RCT	Russia and Hungary	Yes	32 weeks (Planned duration)	Age <40, Any liver disease, Any kidney disease, History of CVD, Treatment experienced, HbA1c <7.5% or >11.0%, No type 2 diabetes, Other

Appendix F: Evidence Table 33. Study Design Characteristics Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year					
Study group	Study design	Country	Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Chandrasekharan, 2002 ²¹²	Cohort	India	Yes	NR	Age < 30 or > 65, Any liver disease, Any kidney disease, History of CVD, HbA1c <= 8%, No type 2 diabetes, Other
Leese, 2003 ²⁰¹ , DARTS/MEMO	Cohort	Scotland	Yes	NR	No type 2 diabetes
Luis Bautista, 2003 ¹⁹³	RCT	US	Yes	NR	Age <35 or >80, HbA1c <8.0% or >10.5%, No type 2 diabetes, Other
Jun, 2003 ²³³	Cohort	US	No	NR	Age <=18, HbA1c <8% and have not had an HbA1c measurement within one month before the start of the study medication and have not had >=2 HbA1c measurements at 3 month intervals during the 6 month study period, No type 2 diabetes, Other
Vongthavaravat, 2002 ¹⁷⁰	RCT	India, Thailand, The Philippines, Tunisia, Argentina and Brazil	Yes	26 weeks (Planned duration)	Age <40 or >80, Any liver disease, Any kidney disease, History of CVD, Treatment experienced, Neuropathy, Retinopathy, No type 2 diabetes, Other
Virtanen, 2003 ¹⁴³	RCT	Finland	Yes	26 weeks (Planned duration)	Age <45 or >75, Any liver disease, Any kidney disease, History of CVD, Treatment experienced, Neuropathy, Retinopathy, No type 2 diabetes, Other
Vakkilainen, 2002 ¹²²	RCT	Finland	Yes	12 weeks (Planned duration)	Age <18 or >75, Any liver disease, Any kidney disease, HbA1c <6.5 or >10, No type 2 diabetes, Other
Cefalu, 2002 ³²³	RCT	US	No	18 weeks (Planned duration)	Age <35 or age>70, HbA1c <7%, No type 2 diabetes, Other

Appendix F: Evidence Table 33. Study Design Characteristics Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year					
Study group	Study design	Country	Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Hallsten, 2002 ⁵⁸	RCT	Finland	Yes	26 weeks (Planned duration)	Any liver disease, Any kidney disease, History of CVD, No type 2 diabetes, Other
Scherbaum, 2002 ¹⁴¹	RCT	Germany	Yes	26 weeks (Planned duration)	Age <35 or age>70, Any liver disease, History of CVD, HbA1c <7.5% or >12%, No type 2 diabetes, Other
Blonde, 2002 ⁸¹	RCT	US	Yes	16 weeks (Planned duration)	Age <30 or >75, Any liver disease, Any kidney disease, History of CVD, HbA1c <7.4%, No type 2 diabetes, Other
St John Sutto, 2002 ⁶⁷	RCT	US	Yes	52 weeks (Planned duration)	Age <40 or age>80, Any liver disease, Any kidney disease, History of CVD, No type 2 diabetes, Other
Rachmani, 2002 ¹⁵⁰	RCT	Israel	No	4 years (Planned duration)	Age < 40 or > 75, No type 2 diabetes, Other
Saloranta, 2002 ²⁴¹	RCT	12 countries Argentina, Australia, Belgium, Canada, Finland, France, Germany, Italy, Netherlands, New Zealand, Sweden, USA	Yes	24 weeks (Planned duration)	Age <30, Any liver disease, Any kidney disease, History of CVD, No type 2 diabetes, Other
Kubo, 2002 ²²⁵	Non-randomized trial	Japan	No	12 weeks (Planned duration)	Any liver disease, Any kidney disease, History of CVD, Neuropathy, Retinopathy, No type 2 diabetes, Other
Rosenstock, 2002 ³³⁰	NR	NR	No	NR	NR
Marre, 2002 ⁸⁴	RCT	Netherlands, Denmark, Portugal, France, Belgium	Yes	4 months (Planned duration)	Age <18, Any liver disease, Any kidney disease, History of CVD, Other
Garber, 2002 ⁷⁹	RCT	US	Yes	20 weeks (Planned duration)	Any liver disease, Any kidney disease, Treatment experienced, HbA1c <7% or >11%, No type 2 diabetes, Other

Appendix F: Evidence Table 33. Study Design Characteristics Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year			Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Study group	Study design	Country			
Gomez-Perez, 2002 ¹⁰²	RCT	Mexico	Yes	26 weeks (Planned duration)	Age <40 or >80, Any liver disease, Any kidney disease, History of CVD, Treatment experienced, No type 2 diabetes, Other
Deerochanawong, 2001 ³³¹	Trial without control arm	Thailand	Yes	NR	Age <35 or >75, Any liver disease, Any kidney disease, Treatment experienced, No type 2 diabetes, Other
Holstein, 2001 ²⁰²	Cohort	Germany	No	NR	Other
Charpentier, 2001 ²⁰⁶			No	NR	Age <35 or age>70, No type 2 diabetes, Other
Charpentier, 2001 ⁸⁹	RCT	France	Yes	20 weeks (Planned duration)	Age ≤ 34 or ≥ 71, Any kidney disease, History of CVD, No type 2 diabetes, Other
Rosenblatt, 2001 ¹⁶²	RCT	US	Yes	16 weeks (Planned duration)	Any liver disease, Any kidney disease, History of CVD, Treatment experienced, Neuropathy, Retinopathy, HbA1c < 8.0%, No type 2 diabetes, Other
Emslie-Smith, 2001 ³³²	Cohort	Scotland	No	NR	No type 2 diabetes, Other
Madsbad, 2001 ¹¹⁹	RCT	Denmark, Scandinavia	Yes	12 months (Planned duration)	Age ≤ 39 or ≥ 76, Any liver disease, Any kidney disease, HbA1c < 6.5 or > 10%, No type 2 diabetes, Other
Kipnes, 2001 ¹⁶⁶	RCT	US	Yes	NR	Age <30 or >75, Any liver disease, Any kidney disease, History of CVD, Neuropathy, Retinopathy, HbA1c < 8, No type 2 diabetes, Other

Appendix F: Evidence Table 33. Study Design Characteristics Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year						
Study group	Study design	Country	Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria	
Gegick, 2001 ¹⁹²	Cohort	US	Yes	12.8 (Mean follow-up)	HbA1c Had not had at least two baseline determinations while receiving maintenance troglitazone therapy, No type 2 diabetes, Other	
Mertes, 2001 ²¹³	Cohort	Germany	No	NR	No type 2 diabetes	
Amador-Licona, 2000 ⁸⁵	RCT	Mexico	No	12 weeks (Planned duration)	Age >65, Any liver disease, History of CVD, Other	
Lebovitz, 2001 ¹⁶⁹	RCT	US	No	26 weeks (Planned duration)	Age < 36 or >81, Any liver disease, Any kidney disease, History of CVD, No type 2 diabetes, Other	
Patel, 1999 ¹⁶⁷	RCT	US	No	12 weeks (Planned duration)	Age < 30 or > 80, Any liver disease, Any kidney disease, History of CVD, No type 2 diabetes, Other	
Phillips, 2001 ¹⁶⁸	RCT	US	Yes	26 weeks (Planned duration)	Age < 40 or >80, Any liver disease, Any kidney disease, Neuropathy, No type 2 diabetes, Other	
Moses, 2001 ²¹⁸	RCT	13 countries	Yes	16 weeks (Planned duration)	Age <40, Any liver disease, History of CVD, Treatment experienced, No type 2 diabetes, Other	
Einhom, 2000 ¹⁶⁰	RCT	US	Yes	16 weeks (Planned duration)	Any liver disease, Any kidney disease, History of CVD, Neuropathy, Retinopathy, HbA1c <8.0, No type 2 diabetes, Other	
Fonseca, 2000 ¹⁰³	RCT	US	No	26 weeks (Planned duration)	Age <40 or >80, Any liver disease, Any kidney disease, History of CVD, Treatment experienced, Neuropathy, No type 2 diabetes, Other	
Abbasi, 2000 ²⁶⁵	Cohort	US	No	NR	Any kidney disease, No type 2 diabetes, Other	

Appendix F: Evidence Table 33. Study Design Characteristics Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year			Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Study group	Study design	Country			
Bytzer, 2001 ²¹⁶	Cross-sectional	Australia	No	NR	No type 2 diabetes, Other
Horton, 2000 ⁹⁶	RCT	US	Yes	24 weeks (Planned duration)	Age <30, Any kidney disease, HbA1c <6.8% or >11%, No type 2 diabetes, Other
Aronoff, 2000 ¹⁶⁵	RCT	US	Yes	26 weeks (Planned duration)	Any liver disease, Any kidney disease, History of CVD, Neuropathy, Retinopathy, HbA1c <7%, No type 2 diabetes, Other
Hanefeld, 2000 ¹⁹⁰	RCT	Europe, multicenter	Yes	12 weeks (Planned duration)	Age <30 or >75, Any kidney disease, History of CVD, Neuropathy, Retinopathy, HbA1c mean level of two tests <6.8 or >10.5, No type 2 diabetes, Other
King, 2000 ¹⁴²	Non-randomized trial	US	No	4 months (Planned duration)	Other
Hasche, 1999 ¹³⁸	RCT	Germany	No	104 weeks (Planned duration)	Age < 40 or >80, Any liver disease, Any kidney disease, History of CVD, Treatment experienced, Retinopathy, HbA1c <7.5 or >9.5%, No type 2 diabetes, Other
Wolffenbuttel, 2000 ¹⁷¹	RCT	Italy, UK, France, Spain, Holland and Switzerland	Yes	26 weeks (Planned duration)	Age < 30 or >80, Any liver disease, Any kidney disease, Neuropathy, HbA1c < 7.5%, No type 2 diabetes, Other
Gregorio, 1999 ¹²⁹	RCT	Italy	No	18 weeks (Planned duration)	Age < 70, Any liver disease, Any kidney disease, History of CVD, HbA1c < 9%, No type 2 diabetes, Other
Klamann, 2000 ¹⁸³	Cohort	Germany	No	NR	No type 2 diabetes, Other

Appendix F: Evidence Table 33. Study Design Characteristics Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year						
Study group	Study design	Country	Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria	
Jovanovic, 2000 ¹⁹⁴	RCT	US	Yes	24 weeks (Planned duration)	Age <40 or > 75, Any liver disease, Any kidney disease, History of CVD, HbA1c with OHA (naive): <6.5%; with OHA-treatment: > 12%, No type 2 diabetes, Other	
Willms, 1999 ⁹⁹	RCT	Germany	Yes	12 weeks (Planned duration)	Age <18, Any liver disease, Any kidney disease, History of CVD, HbA1c <7% or >13%, No type 2 diabetes, Other	
Lysy, 1999 ²²⁰	Cross-sectional	Israel	No	NR	NR	
Erle, 1999 ¹²⁷	RCT	US, Italy	Yes	6 months (Planned duration)	No type 2 diabetes, Other	
Landgraf, 1999 ¹²¹	RCT	Germany, Austria, and Netherlands	Yes	14 weeks (Planned duration)	Any liver disease, Any kidney disease, History of CVD, Treatment experienced, No type 2 diabetes, Other	
Marbury, 1999 ¹¹⁶	RCT	US, Canada	Yes	12 months (Planned duration)	Age >37 or <75, Any liver disease, Any kidney disease, History of CVD, Treatment experienced, Retinopathy, HbA1c <6.5% or 14.6%, No type 2 diabetes, Other	
Selby, 1999 ²³⁷	Cohort	US	Yes	5.6 months for HbA1c outcome only (Mean follow-up)	HbA1c <6.7, No type 2 diabetes, Other	
Wolffenbuttel, 1999 ¹¹⁷	RCT	Germany, Austria, Netherlands	No	12 months (Planned duration)	Age <40 or >75, Any liver disease, Any kidney disease, History of CVD, Treatment experienced, HbA1c <6.5 if treated w/diet only; >12% if treated with diet plus oral, Other	
Testa, 1998 ¹⁹⁸	RCT	US	Yes	15 weeks (Planned duration)	Age <30, No type 2 diabetes, Other	
Goldberg, 1998 ¹³⁹	RCT	US	Yes	18 weeks (Planned duration)	Age <40 and >75, No type 2 diabetes, Other	

Appendix F: Evidence Table 33. Study Design Characteristics Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year					
Study group	Study design	Country	Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
1998, ¹⁵ , UKPDS	RCT	UK	Yes	NR	Age <25 or >65, Treatment experienced, No type 2 diabetes, Other
1998, ¹⁶ , UKPDS	RCT	UK	Yes	NR	Age <25 or >65, Any kidney disease, History of CVD, Treatment experienced, Retinopathy, No type 2 diabetes, Other
Schade, 1998 ¹³⁵	RCT	US	Yes	12 weeks (Planned duration)	Age <30 or >75, Any liver disease, Any kidney disease, History of CVD, Treatment experienced, No type 2 diabetes, Other
1998, ¹²⁸ , UKPDS	RCT	UK	Yes	3 years (Planned duration)	Age <25 or >65, Any kidney disease, History of CVD, Other
Cathelineau, 1997 ²⁰⁹	trial without control arm	France	No	NR	Any liver disease, Any kidney disease, History of CVD, No type 2 diabetes, Other
Garber, 1997 ²¹⁷	RCT	US	Yes	14 weeks (Planned duration)	Age <30, Treatment experienced, No type 2 diabetes, Other
Sonnenberg, 1997 ¹⁹¹	RCT, cross-over	US	Yes	4 weeks (Planned duration)	Age <40 or >80, Any liver disease, Any kidney disease, Treatment experienced, No type 2 diabetes, Other
Simonson, 1997 ¹³⁶	RCT	US	Yes	16 weeks (Planned duration)	Age < 30, Any liver disease, Any kidney disease, History of CVD, Treatment experienced, Retinopathy, HbA1c <6 % at the end of week 2 of placebo administration, No type 2 diabetes, Other
Rosenstock, 1996 ¹⁸⁹	NR	NR	No	NR	No type 2 diabetes, Other

Appendix F: Evidence Table 33. Study Design Characteristics Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year						
Study group	Study design	Country	Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria	
Dills, 1996 ¹⁰⁷	RCT	US	Yes	12 months (Planned duration)	Age <30 or >80, Any liver disease, Any kidney disease, No type 2 diabetes, Other	
Draeger, 1996 ¹¹²	RCT	UK, Europe, Asia, South Africa and South America	No	12 months (Planned duration)	Age < 40 or > 80, Any liver disease, Any kidney disease, Treatment experienced, No type 2 diabetes, Other	
Goldberg, 1996 ¹³⁴	RCT	US	Yes	NR	Age <30 or >75, Any liver disease, Any kidney disease, No type 2 diabetes, Other	
Gregorio, 1996 ²²¹	pre-post	Italy	No	NR	Age <70, Any liver disease, Any kidney disease, HbA1c <9%, No type 2 diabetes, Other	
Grant, 1996 ¹⁵⁴	RCT	UK	Yes	24 weeks (Planned duration)	No type 2 diabetes, Other	
Vray, 1995 ¹³⁷	RCT, factorial	France, China	Yes	3 months (Planned duration)	Age <40 or >70, Any liver disease, Any kidney disease, Treatment experienced, No type 2 diabetes, Other	
DeFronzo, 1995 ⁸⁸	RCT	US	No	29 weeks (Planned duration)	Age <40 or >70, Any liver disease, Any kidney disease, History of CVD, Treatment experienced, No type 2 diabetes, Other	
Tsumura, 1995 ³³³		NR	No	NR	NR	
1995, ⁹² , UKPDS	RCT	UK	Yes	3 years (Planned duration)	Age <25 or >65, Any liver disease, Any kidney disease, History of CVD, Treatment experienced, Retinopathy, No type 2 diabetes, Other	

Appendix F: Evidence Table 33. Study Design Characteristics Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year					
Study group	Study design	Country	Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Hermann, 1994 ⁸⁷	RCT	Sweden	Yes	6 months (Planned duration)	No type 2 diabetes, Other
Birkeland, 1994 ¹¹⁰	RCT	Norway	Yes	15 months (Planned duration)	Any liver disease, Any kidney disease, History of CVD, Treatment experienced, HbA1c <7% or >11%, No type 2 diabetes, Other
Rosenstock, 1993 ¹⁰⁹	RCT	US	Yes	4 months (Planned duration)	Age < 65, Any liver disease, Any kidney disease, Treatment experienced, No type 2 diabetes, Other
Carlson, 1993 ¹⁰⁸	RCT	US	Yes	12 weeks (Planned duration)	Age <30 or >75, Any liver disease, Any kidney disease, No type 2 diabetes, Other
Wolffenbuttel, 1993 ¹²⁰	RCT	Netherlands	Yes	12 (4 week titration, 8 week treatment) (Planned duration)	Any liver disease, Any kidney disease, HbA1c <7.0 or >12.0%, No type 2 diabetes, Other
Aguilar, 1992 ²³⁶	Cohort	Mexico	No	4.92 years (Mean follow-up)	No type 2 diabetes, Other
Haupt, 1991 ²¹¹	trial without the control arm	Germany	No	NR	Age < 40 -biologic age taken in to account for patients > 65, Any kidney disease, No type 2 diabetes, Other
Teupe, 1991 ¹⁵⁵	RCT	Germany	No	2 years (Planned duration)	Age >70, Any liver disease, Any kidney disease, History of CVD, No type 2 diabetes, Other
Noury, 1991 ⁸⁶	RCT	France	No	3 months (Planned duration)	Any liver disease, Any kidney disease, No type 2 diabetes, Other

Appendix F: Evidence Table 33. Study Design Characteristics Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year					
Study group	Study design	Country	Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Hermann, 1991 ⁹⁴	RCT	Sweden	Yes	6 months (Planned duration)	Any liver disease, Any kidney disease, History of CVD, No type 2 diabetes, Other
Hermann, 1991 ¹⁵⁹	RCT	Sweden	No	6 months (Planned duration)	No type 2 diabetes, Other
Jennings, 1989 ²⁰³	Cohort	UK	Yes	NR	Age <40 or >65, No type 2 diabetes, Other
Menzies, 1989 ³³⁴	Non-randomized trial	Scotland	Yes	3 months (Planned duration)	Any kidney disease, No type 2 diabetes, Other
Kilo, 1988 ¹⁴⁷	RCT	US	No	3 months (Planned duration)	Treatment experienced, No type 2 diabetes, Other
Rosenstock, 1987 ²⁰⁷	Cohort	US	No	NR	Age <20, >80, Any liver disease, Any kidney disease, History of CVD, No type 2 diabetes, Other
Baba, 1983 ¹³³	RCT	Japan	No	24 weeks (Planned duration)	No type 2 diabetes, Other
Dandona, 1983 ²¹⁵	Case-control	UK	No	NR	Other
Tseng, 2005 ¹⁴⁰	RCT	Taiwan	No	12 weeks (Planned duration)	No type 2 diabetes, Other
Inzucchi, 2005 ¹⁸⁴	Cohort	US	No	NR	Age <65, No type 2 diabetes, Other
Schofl, 2003 ²²⁶	Cohort	Germany	Yes	16.74 weeks (Mean follow-up)	Age <18, Any liver disease, No type 2 diabetes, Other
Frenchman, 2003 ²⁰⁰	Cohort	US	Yes		No type 2 diabetes, Other
Turner, 1998 ⁹³ , UKPDS	RCT	UK	Yes	6 years (Planned duration)	Age <25 or >=65, Any kidney disease, History of CVD, Treatment experienced, Retinopathy, No type 2 diabetes, Other

Appendix F: Evidence Table 33. Study Design Characteristics Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year					
Study group	Study design	Country	Pharmaceutical support	Study duration (planned/mean)	Exclusion criteria
Garber, 2006 ⁷¹	RCT	US	Yes	24 weeks (Planned duration)	Age <20 or age>78, Any liver disease, Any kidney disease, History of CVD, HbA1c <=7.0% or >=12.0%, No type 2 diabetes, Other
Manley, 2003 ²³⁹	Cohort	US	No	NR	No type 2 diabetes, Other
Chan, 2003 ²²⁴	Cohort	US	Yes	NR	No type 2 diabetes, Age >18 years, Other
Masoudi, 2005 ²²⁹	Cohort	US	No	NR	Age< 65 years, No Type 2 Diabetes, Other
Staa, 1997 ²⁰⁴	Cohort	UK	No	NR	Age<20 years, No Type 2 Diabetes, Other
Shorr, 1996 ²⁰⁵	Cohort	US	No	4 years (Planned duration)	Age<65 years, No Type 2 Diabetes, Other

RCT = Randomized controlled trial; CVD = cardiovascular disease; HbA1c = Hemoglobin A1c; FPG = fasting plasma glucose; OAM= oral antihypoglycemic medication; OHA =oral hyperglycemic agent; ODM = oral diabetes medication

Appendix F: Evidence Table 34. Study Population Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year		Mean age in years (age range)			Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes
Study group	Group, n		Male, n (%)	Race, n (%)				
Kane, 2004 ²¹⁹	Pioglitazone, 316	62.9 (49.4 - 76.4)	(48.9%)	NR	34.1	97.4	7.3	12.5
Ballary, 2003 ²²⁷	Metformin + rosiglitazone, 189	NR	NR	NR	NR	NR	NR	NR
Swislocki, 1999 ²¹⁰	Metformin + unspecified sulfonylurea, 152	62.4	147	AA: 33 (20%); C:100 (61%); Asian: 4 (2%); H: 3 (2%); O: 24 (14%)	31.5	99.5	9.41	8.5
Rosenbaum, 2002 ¹⁵³	Placebo, 20	62	8	NR	31.7	80.2	6.3	NR
	Acarbose, 20	59.8	6	NR	30.3	75.1	6.4	NR
Stang, 1999 ²³⁵	Metformin, 11797	NR	NR	NR	NR	NR	NR	NR
Simpson, 2006 ¹⁴	Metformin, 769	63.2	419 (54%)	NR	NR	NR	NR	NR
	Metformin, 768	64.6	409 (53%)	NR	NR	NR	NR	NR
	Glyburide, 2071	66.4	1148 (55%)	NR	NR	NR	NR	NR
	Glyburide, 2067	67.8	1239 (60%)	NR	NR	NR	NR	NR
Nishio, 2006 ¹⁵¹	Control group (no placebo), 28	67.5	20 (71.4%)	AA: 0; C: 0; Asian: 0; H: 0; O: (100%)	24.6	NR	6.9	NR
	Pioglitazone, 26	66.2	19 (73.1%)	AA:0; C:0; Asian:0; H:0; O: (100%)	24.6	NR	7.7	NR
Weissman, 2005 ¹⁰⁰	Metformin + rosiglitazone, 358	55.5	NR	NR	34.4	98.2	8.05	NR
	Metformin, 351	55.7	NR	NR	33.8	96.7	7.97	NR
Rosenstock, 2006 ¹²⁴	Glipizide + rosiglitazone, 116	68.7	(74.8%)	NR	30.2	NR	7.72	6.8
	Placebo glipizide, 111	68.2	(71.8%)	NR	30.5	NR	7.65	6.6
Bailey, 2005 ¹⁰¹	Metformin + rosiglitazone, 288	58.1	168 (58%)	AA: 2 (1%); C: 280 (97%); Asian: 3 (1%); H: 0; O: 3 (1%)	32.2	90.9	7.4	6
	Metformin, 280	57.6	159 (57%)	AA: 1 (<1%); C: 273 (98%); Asian: 3 (1%); H: 0; O: 3 (1%)	32.1	89.5	7.5	6.1
Kardas, 2005 ¹¹⁴	Glyclazide, 55	60.9	(53%)	NR	27.1	79	7.1	2.2

Appendix F: Evidence Table 34. Study Population Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes
	Glibenclamide, 50	62.4	(38%)	NR	26.3	75	7.2	3.5
Forst, 2005 ¹⁴⁵	Glimepiride, 84	63 (+/- 7.4)	52	NR	31.8	NR	7.44	6.9
	Pioglitazone, 89	62.2 (+/- 8.4)	55	NR	31.7	NR	7.52	7.4
Hartung, 2005 ²³¹	Cases (hospitalized for heart failure), 288	67 (NR)	97 (33.7%)	AA: 0; C: 261 (90.6%); Asian: 0; H: 0; O: 27 (9.4%)	NR	NR	NR	NR
	Controls (not hospitalized for heart failure), 1652	66.4 (NR)	544 (32.9%)	AA: 0; C: 1437 (87%); Asian: 0; H: 0; O: 215 (13%)	NR	NR	NR	NR
Bhansali, 2005 ²¹⁴	Diet + metformin XR, 40	57.3 (40-74)	NR	NR	25.6	NR	6.9	10.3
Yamanouchi, 2005 ⁵⁷	Diet + exercise + pioglitazone, 38	55.2 (46 - 64.4)	18	AA: 0; C: 0; Asian: 0; H: 0; O: (100%)	25.8	NR	10.2	3.2 months
	Diet + exercise + metformin, 39	54.7 (44.9 - 64.5)	20	AA: 0; C: 0; Asian: 0; H: 0; O: (100%)	26.2	NR	9.9	3 months
	Diet + exercise + glimepiride, 37	55.6 (46.3 - 64.9)	19	AA: 0; C: 0; Asian: 0; H: 0; O: (100%)	25.6	NR	9.8	3.3 months
Kahara, 2005 ²³⁴	Pioglitazone, 49	64	34 (69.3%)	NR	24	61.4	7.3	NR
	Diet + pioglitazone, 369	55.9	199 (53.9%)	AA: 9 (2.4%); C: 239 (64.8%); Asian: 10 (2.7%); H: 105 (28.5%); O: 6 (1.6%)	33.7	93.7	7.6	3.9
	Diet + rosiglitazone, 366	56.3	201 (54.9%)	AA: 10 (2.7%); C: 219 (59.8%); Asian: 12 (3.3%); H: 118 (32.2%); O: 7 (1.9%)	32.6	92.5	7.5	4
Pfutzner, 2005 ⁶⁸	Pioglitazone, 89	62.2	58 (61.8%)	AA: 0; C: 88 (98.8%); Asian: 0; H: 0; O: 1 (1.1%)	31.7	NR	7.52	7.4
	Glimepiride, 84	63	52 (61.9%)	AA: 0; C: 81 (96.4%); Asian: 0; H: 0; O: 3 (3.7%)	31.8	NR	7.44	6.9
Derosa, 2005 ⁵³	Diet + exercise + glimepiride + pioglitazone, 45	53 (47 - 59)	21	AA: 0; C: 0; Asian: 0; H: 0; O: (100%)	24.4	68.9	8.2	5
	Diet + exercise glimepiride + rosiglitazone, 42	54 (49 - 59)	22	AA: 0; C: 0; Asian: 0; H: 0; O: (100%)	24.3	67.8	8	6
Derosa, 2005 ⁷²	Diet + exercise +	52 (47 -57)	23	NR	26.8	NR	7.9	4

Appendix F: Evidence Table 34. Study Population Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes
	behavioral therapy + metformin + glimepiride, 47							
	Diet + exercise + behavioral therapy + metformin + rosiglitazone, 48	54 (50 -58)	25	NR	26.6	NR	8	5
Chalasani, 2005 ²²²	Rosiglitazone, 210	53 (42 - 64)	(43%)	AA: (36%); C: (56%); Asian: 0; H: 0; O: 0	NR	232lb	9.3	NR
	Rosiglitazone, 628	55 (44 - 66)	(32%)	AA: (47%); C: (47%); Asian: 0; H: 0; O: 0	NR	229lb	9.4	NR
Langenfeld, 2005 ¹⁴⁶	Pioglitazone, 89	62	55 (61.8%)	AA: 0; C: 88 (98.9%); Asian: 0; H: 0; O: (1.1%)	31.7	NR	7.52	7.4
	Glimepiride, 84	63	52 (61.9%)	AA: 0; C: 81 (96.4%); Asian: 0; H: 0; O: (3.6%)	31.8	NR	7.44	6.9
Rajagopalan, 2005 ²²³	Pioglitazone, 1847	54.3 (18-91)	(52.4%)	NR	NR	NR	NR	NR
	Rosiglitazone, 1847	54.3 (18-92)	(51.8%)	NR	NR	NR	NR	NR
	Pioglitazone, 1474	54.6 (18-91)	(54.3%)	NR	NR	NR	NR	NR
	Unspecified sulfonylurea, 1474	54.5 (19-94)	(52.9%)	NR	NR	NR	NR	NR
	Pioglitazone, 1137	52.7 (18-90)	(50%)	NR	NR	NR	NR	NR
	Metformin, 1137	52.5 (19-88)	(49.6%)	NR	NR	NR	NR	NR
Feinglos, 2005 ¹⁰⁴	Metformin + glipizide, 61	57.7 (30-80)	28	AA: 5 (8.2%); C: 48 (78.7%); Asian: 2 (3.3%); H: 5 (8.2%); O: 1 (1.6%)	31.7	90	7.45	6.5
	Placebo + metformin, 61	58.8 (40-81)	25	AA: 10 (16.4%); C: 42 (68.9%); Asian: 2 (3.3%); H: 5 (8.2%); O: 2 (3.3%)	32.1	90.8	7.64	4.6
Evans, 2005 ³²⁵	Cases (admitted with malignant cancer), 923	73	488 (53%)	NR	NR	NR	NR	8.5
	Controls (no cancer diagnosis), 1846	NR-age- matched	NR-gender- matched	NR	NR	NR-but matched on year of	NR	NR

Appendix F: Evidence Table 34. Study Population Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes
						diagnosis of diabetes		
Goke, 2002 ⁷⁵	Pioglitazone, 129	58.9	69 (53.5%)	NR	30.9	NR	8.98	57.0 months
	Acarbose, 136	58.8	74 (54.5%)	NR	30.8	NR	9.03	59.1 months
Charbonnel, 2005 ⁶³	Pioglitazone, about 635 (NR)	NR	NR	NR	NR	NR	8.7	NR
	Glyclazide, about 635 (NR)	NR	NR	NR	NR	NR	8.7	NR
Tan, 2005 ⁶¹	Pioglitazone, 270	57	171 (63.3%)	AA: 0; C: 253 (93.7%); Asian: 0; H: 0; O: 17 (6.3%)	32	91.7	NR	2.7
	Glyclazide, 297	56	182 (61.3%)	AA: 0; C: 275 (92.6%); Asian: 0; H: 0; O: 22 (7.4%)	32	89.2	NR	2.9
Cryer, 2005 ¹⁷⁶	Diet + metformin, 7227	58.3	(49.3%)	AA: (16.2%); C: (78%); Asian: (2.9%); H: 0; O: (2.8%)	NR	92.5	NR	4.9
	Diet+ usual care on existing medications, 1505	58.8	(49.5%)	AA: (17.5%); C: (76.2%); Asian: (2.7%); H: 0; O: (3.6%)	NR	92.2	NR	4.7
McCluskey, 2004 ⁷⁶	Glimepiride + rosiglitazone, 25	60.2 (46 - 76)	11 (44%)	AA: 0; C: 24 (96%); Asian: 0; H: 0; O: NR	NR	100.5	7.9	7.2
	Placebo + rosiglitazone, 15	50.8 (35 - 69)	6 (40%)	AA: 0; C: 12 (80%); Asian: 0; H: 0; O: NR	NR	99.4	8.4	4.6
Maru, 2005 ²³²	No diabetes medications, 21245	63	11516 (54.2%)	NR	(BMI)≥30, n=5702)	NR	NR	NR
	Unspecified sulfonylurea, 11350	64	5953 (52.5%)	NR	(BMI)≥30, n=2422)	NR	NR	NR
	Metformin, 4579	59	2206 (48.2%)	NR	(BMI)≥30, n=2197)	NR	NR	NR
Scherthaner, 2004 ⁵⁶	Placebo + diet + pioglitazone, 597	57	314 (52.6%)	31.2	NR	88.2	8.7	3.4
	Placebo + diet + metformin, 597	56	345 (57.8%)	31.4	NR	89.7	8.7	3.1
Smith, 2005 ¹⁶¹	Placebo + Diet + existing oral diabetes medications, 21	53.1	10	AA: 0; C: 16; Asian: 0; H: 0; O: 5	31.9	91.5	6.46	NR

Appendix F: Evidence Table 34. Study Population Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year	Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes
		Diet + pioglitazone + existing medications, 21	56.2	9	AA: 0; C: 15; Asian: 0; H: 0; O: 6	32.1	93.5	6.88	NR
Rajagopalan, 2004 ³²⁷		Pioglitazone, 1668	51.1 (50.8 - 51.4)	851 (51%)	NR	NR	NR	NR	NR
Choi, 2004 ⁷⁷		Rosiglitazone + existing oral diabetes medications, 38	60.9	24	NR	24.9	67.6	7.79	7.5
		Control group (existing oral diabetes medications), 45	59.9	34	NR	24.8	68.1	7.72	7.2
Matthews, 2005 ⁷⁰		Diet+ metformin + pioglitazone, 317	56	161 (50.8%%)	AA: 0; C: 315 (99.4%%); Asian: 2 (0.6%); H: 0; O: 0	32.6	NR	8.71	5.8
		Diet + metformin + glidazide, 313	57	154 (49.2%%)	AA: 0; C: 313 (100%%); Asian: 0 (0%); H: 0; O: 0	32.6	NR	8.53	5.5
Nichols, 2005 ²³⁰		Unspecified sulfonylurea, 1085	62	(55.9%)	NR	NR	NR	8	4
		Metformin, 272	60	(51.1%)	NR	NR	NR	7.8	4.3
		Metformin + unspecified sulfonylurea, 1834	61.1	(52.4%)	NR	NR	NR	8.3	5.8
Derosa, 2004 ⁹⁰		Placebo + diet + exercise + glimepiride, 81	56	38	NR	27.6	NR	8.5	NR
		Placebo + diet + exercise + metformin, 83	58	42	NR	28.1	NR	8.4	NR
Scherthaner, 2004 ¹⁰⁶		Glyclazide MR + existing oral diabetes medications, 405	60.5	(51%)	NR	30.5	83.1	8.4	5.6
		Glimepiride + existing oral diabetes medications, 440	60.6	(52%)	NR	30.6	83.8	8.2	5.8
Tan, 2004 ⁶⁵		Glibenclamide, 109	57.9	80 (73%)	AA: 0; C: 109 (100%); Asian: 0;	29.6	89	8.5	62.6 months

Appendix F: Evidence Table 34. Study Population Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes
				H: 0; O: 0				
	Pioglitazone, 91	60	56 (62%)	AA: 0; C: 90 (99%); Asian: 0; H: 0; O: 1 (1%)	30.2	88.4	8.4	57.1 months
Bell, 1997 ²⁰⁸	Unspecified sulfonylurea, 90	64.7	46	NR	NR	NR	NR	8.9
Baksi, 2004 ¹²⁶	Glyclazide, 241	61.9	151 (62.7%)	AA: 1 (0.4%); C: 235 (97.5%); Asian: 1 (0.4%); H: 0; O: 4 (1.7%)	29.7	NR	8.6	6.9
	Glyclazide + rosiglitazone, 225	61.1	129 (57.3%)	AA: 1 (0.4%); C: 219 (97.3%); Asian: 3 (1.3%); H: 0; O: 2 (0.9%)	30.2	NR	8.5	6.5
Tan, 2004 ⁶⁹	Pioglitazone, 121	55.1	54 (45%)	AA: 0; C: 0 (0%); Asian: 0; H: 121 (100%); O: 0	29.3	74.2	8.54	77.8 months
	Glimepiride, 123	55.7	65 (53%)	AA: 0; C: 1 (1%); Asian: 0; H: 122 (99%); O: 0	28.8	74.5	8.45	81.2 months
Saad, 2004 ¹⁶⁴	Placebo, 30	54	18	NR	31	NR	8.1	NR
	Pioglitazone, 28	55	11	NR	31	NR	8.5	NR
Rosenstock, 2004 ¹³¹	Repaglinide, 76	50.9	41	AA: 6; C: 60; Asian: 0; H: 9; O: 1	33	NR	8.9	3.5
	Nateglinide, 74	54	42	AA: 3; C: 59; Asian: 1; H: 9; O: 2	32.9	NR	8.9	4.3
Raskin, 2004 ⁷⁴	Repaglinide, 63	58.5	39	AA: 10; C: 40; Asian: 0; H: 1; O: 12	NR	NR	7.2	NR
	Rosiglitazone, 62	56.6	33	AA: 8; C: 42; Asian: 0; H: 0; O: 12	NR	NR	7.4	NR
Manzella, 2004 ¹⁴⁸	Placebo + diet, 60	57 (all patients)	33	NR	29.2	NR	8.1	NR
	Diet + metformin, 60	57 (all patients)	31	NR	29.5	NR	8	NR
Feinbock, 2003 ¹³⁰	Glimepiride, 111	57.7	66	AA: 0; C: 110; Asian: 1; H: 0; O: 0	29.2	85	9.1	36.3 months
	Acarbose, 108	57.1	58	AA: 0; C: 107; Asian: 1; H: 0; O: 0	29.1	83	9.4	43.1 months
Kerenyi, 2004 ¹²⁵	Diet + glibenclamide,	59.9	105	AA: 2; C: 163; Asian: 4; H: 0;	29.2	NR	8.1	6.7

Appendix F: Evidence Table 34. Study Population Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes
	170			O: 1				
	Diet + glibenclamide + rosiglitazone, 165	60	91	AA: 1; C: 160; Asian: 3; H: 0; O: 1	30.7	NR	7.9	5.6
Jovanovic, 2004 ⁴³	Repaglinide, 61	57.8	36	AA: 7; C: 46; Asian: 0; H: 3; O: 5	31.2	NR	9	6.9
	Pioglitazone, 62	56.2	31	AA: 7; C: 51; Asian: 0; H: 2; O: 2	32.1	NR	9.1	6.1
Hanefeld, 2004 ⁶⁰	Placebo + unspecified sulfonylurea + pioglitazone, 31	60	171 (53.6%)	AA: 2 (0.6%); C: 317 (99.4%); Asian: 0; H: 0; O: 0 (0%)	30.2	85.3	8.82	7
	Placebo + metformin + unspecified sulfonylurea, 320	60	175 (54.7%)	AA: 3 (0.9%); C: 315 (98.4%); Asian: 0; H: 0; O: 2 (0.6%)	30	84.9	8.8	7.1
Lawrence, 2004 ⁵⁴	Metformin, 20	59.5	12	NR	median 29.2	NR	8.04	NR
	Glyclazide, 20	63.5	13	NR	median 28.7	NR	7.85	NR
	Pioglitazone, 20	60.4	14	NR	median 30.6	NR	7.43	NR
Delea, 2003 ²²⁸	Thiazolidinedione, 5441	57.2	(56.6%)	NR	NR	NR	NR	NR
	No thiazolidinedione, 28103	58.8	(57.2%) (57.2%)	NR	NR	NR	NR	NR
Garber, 2003 ⁸⁰	Metformin + glyburide, 171	55.6	76 (44%)	AA: 18 (10.5%); C: 132 (77.2%); Asian: 0; H: 15 (8.8%); O: 6 (3.5%)	31.4	91.9	8.8	3
	Metformin, 164	54.7	71 (43.3%)	AA: 11 (6.7%); C: 132 (80.5%); Asian: 0; H: 15 (9.1%); O: 6 (3.7%)	31.4	92.8	8.5	2.6
	Glyburide, 151	55.3	66 (43.7%)	AA: 11 (7.3%); C: 123 (81.5%); Asian: 0; H: 12 (7.9%); O: 5 (3.3%)	31.1	91	8.7	3
Takagi, 2003 ⁷⁸	pioglitazone + existing oral diabetes	64	20	NR	25.6	NR	6.8	NR

Appendix F: Evidence Table 34. Study Population Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes
	medications, 23							
	Other (existing oral diabetes medications), 21	65	14	NR	24.5	NR	6.7	NR
Tosi, 2003 ⁹⁵	Glibenclamide, 20	NR	NR	NR	NR	NR	NR	NR
	Metformin + glibenclamide, 41	NR	NR	NR	NR	NR	NR	NR
	Metformin, 19	NR	NR	NR	NR	NR	NR	NR
Goldstein, 2003 ⁸²	Metformin + glipizide, 87	54.6	(58.6%)	AA: (11.5%); C: (72.4%); Asian: (0%); H: (16.1%); O: 0	31.7	94	8.7	5.9
	Glipizide, 84	57.4	(64.3%)	AA: (11.9%); C: (71.4%); Asian: (2.4%); H: (14.3%); O: 0	30.6	89.9	8.9	6.5
	Metformin, 76	56.6	(61.8%)	AA: (15.8%); C: (65.8%); Asian: (1.3%); H: (17.1%); O: 0	31.6	93.8	8.7	7.3
Herz, 2003 ¹⁶³	Placebo, 99	58 (33-85)	49 (49.5%)	AA: 0 (0%); C: 96 (97%); Asian: 3 (3%); H: 0 (0%); O: 0	31.7	86.3	7.5	NR
	Pioglitazone, 99	59 (24-79)	59 (59.6%)	AA: 0 (0%); C: 97 (98%); Asian: 1 (1%); H: 1 (1%); O: 0	31.7	86.6	7.5	NR
	Pioglitazone, 99	58.1 (24-84)	52 (52.5%)	AA: 0 (0%); C: 93 (93.9%); Asian: 1 (3%); H: 3 (3%); O: 0	30.8	84.1	7.6	NR
Ko, 2003 ³²⁸	Control (existing oral diabetes medications), 69	60	25	AA: 0 (0%); C: 0 (0%); Asian: 0 (0%); H: 0 (0%); O: 69 (100%)	26.1	NR	9.6	6.3
	Rosiglitazone + existing oral diabetes medications, 49	61.6	15	AA: 0 (0%); C: 0 (0%); Asian: 0 (0%); H: 0 (0%); O: 49 (100%)	25.3	NR	9.4	9.3
Derosa, 2003 ⁹⁷	Diet + exercise + repaglinide, 56	55	29	NR	25.2	70.2	7.6	4
	Diet + exercise + metformin, 56	52	27	NR	24.7	72.3	7.4	5
Barnett, 2003 ¹⁷²	Placebo + unspecified sulfonylurea, 87	54.1 (32-78)	(75%)	AA: 0 (0%); C: 0 (0%); Asian: 0 (0%); H: 0 (0%); O: (100%)	26.4	NR	9.06	6.5
	Unspecified sulfonylurea +	54.3 (28-76)	(80%)	AA: 0 (0%); C: 0 (0%); Asian: 0 (0%); H: 0 (0%); O: (100%)	26.8	NR	9.21	6.5

Appendix F: Evidence Table 34. Study Population Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes
	rosiglitazone, 84							
Fujioka, 2003 ¹⁰⁵	Placebo + diet + metformin XR, 75	54	34	NR	32	92	7	3
	Placebo + diet + metformin XR, 71	55	28	NR	31	88	7	3
	Placebo + diet + metformin, 71	54	31	NR	33	96	7.1	3
Derosa, 2003 ¹¹⁸	Placebo + repaglinide, 62	56	31	NR	26.1	76.4	8	NR
	Placebo + glimepiride, 62	54	30	NR	26.4	77.1	7.8	NR
Zhu, 2003 ¹⁸⁸	Placebo + unspecified sulfonylurea, 105	58.8	(46%)	AA: 0; C: 0; Asian: (100%); H: 0; O: 0	25.1	NR	9.8	7.6
	Unspecified sulfonylurea + rosiglitazone, 215	59	(41%)	AA: 0; C: 0; Asian: (100%); H: 0; O: 0	24.8	NR	9.8	7.2
	Unspecified sulfonylurea + rosiglitazone, 210	58.9	(48%)	AA: 0; C: 0; Asian: (100%); H: 0; O: 0	24.9	NR	9.9	7.9
Del Prato, 2003 ¹⁴⁹	Placebo, 144	56	91	NR	29.9	NR	NR	NR
	Placebo + metformin, 284	56	68	NR	29.7	NR	NR	NR
Pavo, 2003 ⁵⁹	Placebo + pioglitazone, 105	54.2	(43.8%)	NR	31.3	86.6	8.6	0.47
	Placebo + metformin, 100	55.8	(56%)	NR	31.1	88.9	8.6	0.53
Chandrasekharan, 2002 ²¹²	Nateglinide, 105	48.44	70	NR	NR	NR	8.51	4.74
Leese, 2003 ²⁰¹	Unspecified sulfonylurea, 2823	65.4	(52.2%)	NR	29.6	NR	7.16	6.3
Luis Bautista, 2003 ¹⁹³	Diet + exercise + glimepiride, 48	48.4	27 (56.3%)	AA: 0; C: 0; Asian: 0; H: (100%); O: 0	NR	83.3	10	4.2
	Placebo + diet + exercise, 22	50.7	11 (50%)	AA: 0; C: 0; Asian: 0; H: (100%); O: 0	NR	76.3	10.5	5.7

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Author, year		Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes
Study group	Group, n							
Jun, 2003 ²³³	Pioglitazone, 54	54.6 (27-68)	9 (16.7%)	AA: 0; C: 0; Asian: 0; H: 54 (100%); O: 0	32	NR	10.4	10.3
Vongthavaravat, 2002 ¹⁷⁰	Diet + unspecified sulfonylurea + rosiglitazone, 164	54.6 (30-76)	75 (45.7%)	AA: 6 (3.7%); C: 66 (40.2%); Asian: 91 (55.5%); H: 0; O: 1 (0.6%)	27.1	69	9.1	5
	Diet + unspecified sulfonylurea, 170	57.3 (37-77)	72 (42.4%)	AA: 4 (2.4%); C: 62 (36.5%); Asian: 101 (59.4%); H: 0; O: 3 (1.8%)	27.1	68.8	8.9	6
Virtanen, 2003 ¹⁴³	Placebo + diet, 14	58	10	NR	30.3	88.3	6.3	NR
	Diet + rosiglitazone, 14	58	10	NR	29.1	83.7	6.8	NR
	Diet + metformin, 13	58	8	NR	29.9	88.8	6.9	NR
Vakkilainen, 2002 ¹²²	Placebo + nateglinide, 23	63	NR	AA: 0; C: (100%); Asian: 0; H: 0; O: 0	27.8	NR	7.6	NR
	Placebo + glibenclamide, 20	63	NR	AA: 0; C: (100%); Asian: 0; H: 0; O: 0	28.8	NR	7.6	NR
Cefalu, 2002 ³²³	Metformin + glypizide XL, 46	53.5	30	NR	32.5	94	10.4	7.7
	Metformin + glypizide XL, 45	55.8	25	NR	32.1	95	10	6.3
Hallsten, 2002 ⁵⁸	Placebo + diet, 14	57.7	10	NR	30.3	NR	6.3	NR
	Diet + metformin, 13	57.8	8	NR	29.9	NR	6.9	NR
	Diet + rosiglitazone, 14	58.6	10	NR	29.3	NR	6.8	NR
Scherbaum, 2002 ¹⁴¹	Placebo + diet, 84	59.1	47	NR	29.2	84.8	8.75	5.6
	Diet + pioglitazone, 89	58	56	NR	29.9	87.2	9.33	5.4
	Diet + pioglitazone, 78	59.6	32	NR	29.3	82	9.06	4.6
Blonde, 2002 ⁸¹	Glyburide, 164	55.8	94 (57.3%)	AA: 20 (12.2%); C: 109 (66.5%); Asian: 0; H: 28 (17.1%); O: 7 (4.3%)	30.3	88	9.64	7.01
	Metformin, 153	57.6	95 (62.1%)	AA: 16 (10.5%); C: 105 (69.3%); Asian: 0; H: 26 (17%); O: 5 (3.3%)	30.6	89.5	9.51	8.18

Appendix F: Evidence Table 34. Study Population Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes
	Metformin + glyburide, 160	55.4	89 (55.6%)	AA: 20 (12.5%); C: 112 (70%); Asian: 0; H: 25 (15.6%); O: 3 (1.9%)	30.7	89.4	9.41	7.36
	Metformin + glyburide, 162	55.6	103 (63.6%)	AA: 15 (9.3%); C: 110 (67.9%); Asian: 0; H: 31 (19.1%); O: 6 (3.7%)	30.6	89.6	9.42	6.97
St John Sutton, 2002 ⁶⁷	Glyburide, 99	56.1 (40-76)	(71%)	AA: (3%); C: (76%); Asian: 0; H: 0; O: (21%)	65.7% ≥27	9.5	6.2	NR
	Rosiglitazone, 104	55.1 (40-77)	(75%)	AA: (5%); C: (73%); Asian: 0; H: 0; O: (22%)	67.3% ≥27	9.1	5.3	NR
Rachmani, 2002 ¹⁵⁰	Diet + metformin stopped, 198	64	102	NR	28.4	NR	8.6	14
	Diet + metformin continued, 195	65	103	NR	28.7	NR	8.6	15
Saloranta, 2002 ²⁴¹	nateglinide, 166	61	105 (63.3%)	AA: 2 (1.2%); C: 162 (97.6%); Asian: 1 (0.6%); H: 0; O: 1 (0.6%)	28.95	NR	6.55	3.8
	nateglinide, 175	61.1	107 (61.1%)	AA: 1 (0.6%); C: 163 (93.1%); Asian: 3 (4.6%); H: 0; O: 8 (4.6%)	28.92	NR	6.53	3.6
	nateglinide, 171	59.6	112 (65.5%)	AA: 2 (1.2%); C: 163 (95.3%); Asian: 4 (1.2%); H: 0; O: 2 (1.2%)	29.12	NR	6.57	3.7
	Placebo, 163	59.1	98 (60.1%)	AA: 2 (1.2%); C: 157 (96.3%); Asian: 1 (1.8%); H: 0; O: 3 (1.8%)	28.78	NR	6.45	3.2
Kubo, 2002 ²²⁵	Pioglitazone, 18	63.4	4	AA: 0; C: 0; Asian: (100%); H: 0; O: 0	27.8	NR	8.6	NR
	Glyclazide, 18	61.2	5	NR	26.7	NR	8.2	NR
	Glyclazide + pioglitazone, 19	64.1	5	NR	26.7	NR	8.6	NR
Marre, 2002 ⁸⁴	Metformin, 104	57.5	62	NR	29.9	84.9	8.09	5.4
	Glibenclamide, 103	58.7	57	NR	29.3	82.5	7.88	6.6
	Metformin +	58	50	NR	30.1	84.7	7.89	5.9

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Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes
Garber, 2002 ⁹	glibenclamide, 101							
	Metformin + glibenclamide, 103	60.7	56	NR	29.7	83.1	7.62	6.7
	Placebo, 161	55.4	76	AA: 16; C: 122; Asian: 0; H: 17; O: 6	30.2	86.2	8.21	2.76
	Glyburide, 161	56.5	82	AA: 15; C: 126; Asian: 0; H: 14; O: 6	30.3	87.2	8.21	2.81
	Metformin, 161	56	93	AA: 7; C: 130; Asian: 0; H: 20; O: 4	30.4	88.6	8.26	2.98
	Metformin + glyburide, 158	56.9	91	AA: 20; C: 117; Asian: 0; H: 18; O: 3	30.1	88.8	8.25	3.52
Gomez-Perez, 2002 ¹⁰²	Metformin + glyburide, 165	58.1	96	AA: 10; C: 131; Asian: 0; H: 16; O: 8	29.6	86.7	8.18	3.3
	Placebo + metformin, 34	53.4 (40-68)	10	AA: 0; C: 1; Asian: 0; H: 26; O: 7	28.5	NR	NR	9.1
	Metformin + rosiglitazone, 35	51.7 (40-73)	10	AA: 0; C: 0; Asian: 0; H: 28; O: 7	28	NR	NR	11.1
Deerochanawong, 2001 ³³¹	Metformin + rosiglitazone, 36	54.2 (42-76)	7	AA: 0; C: 4; Asian: 0; H: 26; O: 6	27.6	NR	NR	10.7
	Glimepiride, 89	52.2	29	NR	25.5	NR	10	NR
Holstein, 2001 ²⁰²	Glimepiride + glibenclamide, 1	84	(100%)	NR	24.8	NR	5.6	4
	Glibenclamide, 38	83.5	(36.8%)	NR	22.9	NR	5.25	6
	Glimepiride, 6	83.5	(33.3%)	NR	28.2	NR	4.7	16
Charpentier, 2001 ²⁰⁶	Glimepiride, 980	57.9	576 (59%)	NR	30	NR	8.9	3.7
Charpentier, 2001 ⁸⁹	Placebo + metformin, 75	56.7 (36-69)	45 (60%)	NR	29.2	82.2	6.8	7
	Placebo + glimepiride, 150	55.4 (35-70)	87 (58%)	NR	29.3	81	6.5	5.3
	Metformin + glimepiride, 147	56.8 (36-70)	87 (59%)	NR	29.5	81.2	6.4	5.6

Appendix F: Evidence Table 34. Study Population Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes
Rosenblatt, 2001 ¹⁶²	Placebo, 96	55.2	(46.2%)	AA: (11.5%); C: (61.5%); Asian: 0; H: (24%); O: (3.1%)	30.7	87.2	10.42	NR
	Pioglitazone, 101	53.8	(50.5%)	AA: (8.9%); C: (69.3%); Asian: 0; H: (19.8%); O: (2%)	31.5	89.8	10.65	NR
Emslie-Smith, 2001 ³³²	Metformin, 1847	63.4	(47.6%)	NR	NR	NR	NR	NR
Madsbad, 2001 ¹¹⁹	Repaglinide, 175	60.2	107	NR	28	82.9	7.3	8.1
	Placebo + glipizide, 81	62	52	NR	28	83.6	7.2	7
Kipnes, 2001 ¹⁶⁶	Placebo + unspecified sulfonylurea, 187	56.9	109	AA: 25; C: 141; Asian: 3; H: 18; O: 0	32	NR	9.9	19
	Unspecified sulfonylurea + pioglitazone, 184	56.5	109	AA: 20; C: 146; Asian: 3; H: 15; O: 0	31.4	NR	10	29
	Unspecified sulfonylurea + pioglitazone, 189	56.6	113	AA: 17; C: 156; Asian: 3; H: 13; O: 0	32.4	NR	9.9	26
Gegick, 2001 ¹⁹²	Pioglitazone, 67	66 (57 - 75)	NR	NR	98.3	7.1	14	NR
	Rosiglitazone, 77	59 (48.6 - 69.4)	NR	NR	103	6.97	12	NR
Mertes, 2001 ²¹³	Acarbose, 1954	63	(46%)	NR	27.4	78.3	8.4	5.2
Amador-Licona, 2000 ⁸⁵	Glibenclamide, 23	48.2	7	NR	30.4	73.2	8.4	4
	Metformin, 28	49.3	11	NR	26.8	70.7	8.5	4.5
Lebovitz, 2001 ¹⁶⁹	Placebo, 158	59	104	NR	29.9	NR	9.0	4.6
	Rosiglitazone, 166	60	107	NR	30.2	NR	9.0	4.8
	Rosiglitazone, 169	61	113	NR	29.1	NR	8.8	5.4
Patel, 1999 ¹⁶⁷	Placebo, 75	56.8 (34-83)	52 (69.3%)	AA: 2; C: 55; Asian: 0; H: 0; O: 18	28.9	NR	9.1	4.2

Appendix F: Evidence Table 34. Study Population Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes
	Rosiglitazone, 74	56.7 (30-76)	49 (66.2%)	AA: 4; C: 55; Asian: 0; H: 0; O: 15	29.4	NR	9.1	4.9
	Rosiglitazone, 72	55.8 (31-74)	51 (70.8%)	AA: 6; C: 53; Asian: 0; H: 0; O: 13	28.6	NR	8.9	6.7
	Rosiglitazone, 79	59.8 (37-79)	51 (64.6%)	AA: 4; C: 63; Asian: 0; H: 0; O: 12	29.5	NR	9	4.4
	Rosiglitazone, 80	59.7 (41-81)	55 (68.8%)	AA: 5; C: 58; Asian: 0; H: 0; O: 17	28.4	NR	9	5.8
Phillips, 2001 ¹⁶⁸	Placebo, 173	57.7	119 (68.8%)	AA: 16 (9.2%); C: 137 (79.2%); Asian: 0; H: 0; O: 20 (11.6%)	29.1	NR	8.9	6.6
	Rosiglitazone, 181	57.5	106 (58.6%)	AA: 23 (12.7%); C: 138 (76.2%); Asian: 0; H: 0; O: 20 (11%)	29.9	NR	8.9	5.4
	Rosiglitazone, 186	56.8	110 (59.1%)	AA: 15 (8.1%); C: 145 (78%); Asian: 0; H: 0; O: 26 (14%)	30	NR	8.9	5.5
	Rosiglitazone, 181	58.9	119 (65.7%)	AA: 13 (7.2%); C: 145 (80.1%); Asian: 0; H: 0; O: 23 (12.7%)	30	NR	8.9	6.1
	Rosiglitazone, 187	56.5	122 (65.2%)	AA: 20 (10.7%); C: 133 (71.1%); Asian: 0; H: 0; O: 34 (18.2%)	29.9	NR	9	5.9
Moses, 2001 ²¹⁸	Repaglinide, 260	57.5	(53.5%)	AA: (0.4%); C: (98.8%); Asian: (0%); H: 0; O: (0.8%)	30	84	7.8	2.99
	Placebo, 134	57.4	(57.5%)	AA: (0%); C: (98.5%); Asian: (0%); H: 0; O: (1.5%)	30.9	86.6	7.6	3.07
Einhorn, 2000 ¹⁶⁰	Diet + metformin + pioglitazone, 168	55.5	92 (54.8%)	AA: 14 (8.3%); C: 136 (81%); Asian: 0; H: 17 (10.1%); O: 1 (0.6%)	32.11	NR	9.86	NR
	Placebo + diet + metformin, 160	55.7	96 (60%)	AA: 10 (6.3%); C: 139 (86.9%); Asian: 0; H: 6 (3.8%); O: 5 (3.1%)	32.12	NR	9.75	NR
Fonseca, 2000 ¹⁰³	Placebo + metformin, 113	58.8	74.3	AA: (3.5%); C: (81.4%); Asian: 0; H: 0; O: (15%)	30.3	NR	8.6	7.3
	Metformin + rosiglitazone, 116	57.5	62.1	AA: (6.9%); C: (80.2%); Asian: 0; H: 0; O: (12.9%)	30.2	NR	8.9	7.5

Appendix F: Evidence Table 34. Study Population Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes
	Metformin + rosiglitazone, 110	58.3	68.2	AA: (10%); C: (77.3%); Asian: 0; H: 0; O: (12.7%)	29.8	NR	8.9	8.3
Abbasi, 2000 ²⁶⁵	Metformin, 110	60.69 (27-85)	57	NR	NR	NR	NR	NR
Bytzer, 2001 ²¹⁶	Metformin, 211	61.9 (51.1 - 62.7)	(54.3%)	NR	NR	NR	NR	NR
	Unspecified sulfonylurea, 206	63 (50.7 - 75.3)	(52.9%)	NR	NR	NR	NR	NR
Horton, 2000 ⁹⁶	Nateglinide, 179	58.6	110	AA: (9.5%); C: (82.1%); Asian: (2.8%); H: 0; O: (5.6%)	29.6	NR	8.3	4.7
	Metformin, 178	56.8	121	AA: (9.6%); C: (79.2%); Asian: (2.2%); H: 0; O: (9%)	29.6	NR	8.4	7.5
	Placebo, 172	59.6	104	AA: (16.9%); C: (78.5%); Asian: (0.6%); H: 0; O: (4.1%)	29.2	NR	8.3	4.6
Aronoff, 2000 ¹⁶⁵	Placebo, 79	53.7 mean (29-75) – for all groups combined	(58%) -for all groups combined	AA: (8%); C: (78%); Asian: (2%); H: (12%); O: (1%) – for all groups combined	NR	90.4	10.4	NR
	Pioglitazone, 81	53.7 mean (29-75) – for all groups combined	(58%) -for all groups combined	AA: (8%); C: (78%); Asian: (2%); H: (12%); O: (1%) – for all groups combined	NR	93.5	10	NR
	Pioglitazone, 81	53.7 mean (29-75) – for all groups combined	(58%) -for all groups combined	AA: (8%); C: (78%); Asian: (2%); H: (12%); O: (1%) – for all groups combined	NR	91.2	10.2	NR
	Pioglitazone, 87	53.7 mean (29-75) – for all groups combined	(58%) -for all groups combined	AA: (8%); C: (78%); Asian: (2%); H: (12%); O: (1%) – for all groups combined	NR	90.3	10.2	NR
	Pioglitazone, 80	53.7 mean (29-75) – for all groups combined	(58%) -for all groups combined	AA: (8%); C: (78%); Asian: (2%); H: (12%); O: (1%) – for all groups combined	NR	90.8	10.3	NR

Appendix F: Evidence Table 34. Study Population Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year		Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes
Study group	Group, n							
Hanefeld, 2000 ¹⁹⁰	Placebo, 60	57.4	36	NR	28.3	NR	8.5	5.4
	Nateglinide, 51	58	36	NR	29	NR	8.4	4.5
	Nateglinide, 58	56.1	41	NR	28.1	NR	8.3	6.2
	Nateglinide, 63	54.4	44	NR	28.6	NR	8.3	4.4
	Nateglinide, 57	56.5	36	NR	28.8	NR	8.5	3.7
King, 2000 ¹⁴²	Rosiglitazone, 36	59.2	(50%)	NR	NR	92.1	8.73	NR
	Pioglitazone, 30	60.2	(38%)	NR	NR	87.2	8.72	NR
Hasche, 1999 ¹³⁸	Diet + acarbose, 36	63.8	17	NR	26.1	74.3	8.5	1
	Placebo + diet, 38	63.1	19	NR	26.7	75.5	8.3	1
Wolffenbuttel, 2000 ¹⁷¹	Placebo + unspecified sulfonylurea, 192	61.9	110	AA: 2; C: 186; Asian: 0; H: 0; O: 4	28.1	NR	9.21	8
	Unspecified sulfonylurea + rosiglitazone, 199	61	125	AA: 2; C: 190; Asian: 0; H: 0; O: 7	28.0	NR	9.2	7
	Unspecified sulfonylurea + rosiglitazone, 183	60.6	101	AA: 2; C: 180; Asian: 0; H: 0; O: 1	28.3	NR	9.23	7
Gregorio, 1999 ¹²⁹	Glibenclamide or glyclazide, 85	75.73	40	NR	NR	76.61	10.32	14.67
	Metformin + (glibenclamide or glyclazide), 89	75.42	42	NR	NR	76.44	10.33	15.11
Klamann, 2000 ¹⁸³	Glibenclamide, 76	72	37	NR	26.8	73	8.4	10
	Non-glibenclamide, 89	73	54	NR	26.8	71	7.7	8
Jovanovic, 2000 ¹⁹⁴	Placebo, 75	58.5	49 (65%)	AA: 11 (15%); C: 51 (68%); Asian: 1 (1%); H: 0; O: 12 (16%)	29.8	NR	8.6	6.8
	Repaglinide, 140	57.9	96 (69%)	AA: 14 (10%); C: 107 (76%); Asian: 0 (0%); H: 0; O: 19 (14%)	29.4	NR	8.9	6.6
	Repaglinide, 146	57.6	87 (60%)	AA: 18 (12%); C: 110 (75%); Asian: 2 (1%); H: 0; O: 16	29.5	NR	8.7	6.3

Appendix F: Evidence Table 34. Study Population Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes
				(11%)				
Willms, 1999 ⁹⁹	Acarbose, 31	60.3	15	NR	NR	86.1	10.6	134.8 months
	Placebo, 29	59.2	17	NR	NR	90.2	10.6	119.6 months
	Metformin, 27	53.4	13	NR	NR	88.6	10.6	111.9 months
Lysy, 1999 ²²⁰	Metformin, 706	62.6 (male)/ 63.4 (female)	365	NR	NR	NR	NR	9.4 (male)/9.2 (female)
Erle, 1999 ¹²⁷	Glyburide, 20	60 for both groups combined	21 (for both groups combined)	NR	30.5 (for both groups combined)	85.2	7.37	NR
	Metformin + glyburide, 20	60 for both groups combined	21 (for both groups combined)	NR	30.5 (for both groups combined)	85.5	7.67	NR
Landgraf, 1999 ¹²¹	Repaglinide, 94	61	56	AA: 0; C: 90; Asian: 0; H: 0; O: 4	27.6	80	7.8	10
	Placebo + glibenclamide, 100	63	57	AA: 6; C: 93; Asian: 0; H: 0; O: 1	27.5	79	8	10
Marbury, 1999 ¹¹⁶	Repaglinide, 362	58.3	242 (67%)	AA: 33 (9%); C: 279 (77%); Asian: 0; H: 0; O: 50 (14%)	29.4	NR	8.7	7.2
	Placebo + glyburide, 182	58.7	120 (66%)	AA: 16 (9%); C: 144 (79%); Asian: 0; H: 0; O: 22 (12%)	29.1	NR	8.9	8.3
Selby, 1999 ²³⁷	Started on metformin, 9875	NR	(47.5%)	NR	(71% >= BMI of 27)	NR	NR	NR
	Not started on metformin, 54382	NR	(53.6%)	NR	(60% >= BMI of 27)	NR	NR	NR
Wolffenbuttel, 1999 ¹¹⁷	Repaglinide, 286	61	(62%)	NR	28.4	81.5	7.1	median 6
	Placebo + glyburide, 139	61	(68%)	NR	28	81.3	7	median 6
Testa, 1998 ¹⁹⁸	Placebo + diet, 192	58.4 (30-82)	(58.9%)	AA: (15.6%); C: (72.9%); Asian: 0; H: 0; O: (11.5%)	30.3	NR	8.7	4.7
	Diet + glipizide XL, 377	58.7 (30-85)	(54.9%)	AA: (16.7%); C: (71.9%); Asian: 0; H: 0; O: (11.4%)	30.1	NR	8.5	5.6

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Author, year		Mean age in years (age range)			Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes
Study group	Group, n		Male, n (%)	Race, n (%)				
Goldberg, 1998 ¹³⁹	Placebo, 33	56.4	25 (76%)	AA: 0; C: 29 (88%); Asian: 0; H: 0; O: 4 (12%)	30	NR	8.1	5.1
	Repaglinide, 67	58.7	49 (74%)	AA: 0; C: 58 (88%); Asian: 0; H: 0; O: 8 (12%)	30.6	NR	8.3	5.6
UKPDS, 1998 ¹⁵	Diet, 411	53	193 (47%)	AA: 0; C: (86%); Asian: (6%); H: 0; O: (8%)	31.8	87	7.1	NR
	Diet + metformin, 342	53	157 (46%)	AA: 0; C: (85%); Asian: (4%); H: 0; O: (11%)	31.6	87	7.3	NR
	Diet + glibenclamide, 277	53	127 (46%)	AA: 0; C: (87%); Asian: (4%); H: 0; O: (9%)	31.5	86	7.2	NR
	Diet + unspecified sulfonylurea, 269	58	164 (61%)	AA: 0; C: (77%); Asian: (13%); H: 0; O: (10%)	29.4	82	7.6	NR
	Diet + metformin + unspecified sulfonylurea, 268	59	158 (59%)	AA: 0; C: (77%); Asian: (11%); H: 0; O: (12%)	29.7	83	7.5	NR
UKPDS, 1998 ¹⁶	Diet, 896	54	555	AA: 0; C: (83%); Asian: 0; H: 0; O: (16%)	27.5	77	6.2	NR
	Diet+ unspecified sulfonylurea, 619	54	359	AA: 0; C: (79%); Asian: 0; H: 0; O: (21%)	27	75	6.3	NR
	Diet + glibenclamide, 615	54	381	AA: 0; C: (84%); Asian: 0; H: 0; O: (15%)	27.4	77	6.3	NR
Schade, 1998 ¹³⁵	Glimepiride, 123	52	NR	NR	NR	86.8	9.1	3.1
	Placebo, 126	54	NR	NR	NR	87.3	8.9	3.1
UKPDS, 1998 ¹²⁸	Diet + metformin + glibenclamide, 291	59	(59%)	AA: (14%); C: (78%); Asian: (8%); H: 0; O: 0	29.2	81	Median 7.4	NR
	Diet + glibenclamide, 300	58	(60%)	AA: (11%); C: (78%); Asian: (11%); H: 0; O: 0	29.1	81	Median 7.3	NR
Lee, 1998 ²⁵⁹	Placebo + diet + metformin, 24	59 (56 - 62)	0	NR	40	112.8	8.3	4
	Placebo + diet, 24	61 (59 - 63)	0	NR	39.6	108.6	8.1	3
Cathelineau, 1997 ²⁰⁹	Diet + glyclazide, 5572	58.5	3225	NR	28.5	NR	8.7	1.2
Garber, 1997 ²¹⁷	Placebo, 79	55	(56%)	AA: (22%); C: (66%); Asian: 0; H: (11%); O: (1%)	NR	90.9	9.9	NR

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Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes
	Metformin, 73	57	(62%)	AA: (11%); C: (62%); Asian: 0; H: (14%); O: (1%)	NR	90	10.1	NR
	Metformin, 73	55	(55%)	AA: (12%); C: (55%); Asian: 0; H: (10%); O: (1%)	NR	90	10	NR
	Metformin, 76	59	(63%)	AA: (12%); C: (63%); Asian: 0; H: (15%); O: (2%)	NR	89.6	9.7	NR
	Metformin, 73	60	(53%)	AA: (14%); C: (53%); Asian: 0; H: (12%); O: (4%)	NR	89.1	10.1	NR
	Metformin, 77	59	(65%)	AA: (10%); C: (65%); Asian: 0; H: (10%); O: (0%)	NR	94.5	10	NR
Sonnenberg, 1997 ¹⁹¹	Glimepiride, 50	61	(70%)	NR	NR	86	NR	7.2
	Glimepiride, 48	61	(70%)	NR	NR	86	NR	7.2
	Placebo, 53	61	(70%)	NR	NR	86	NR	7.2
Simonson, 1997 ¹³⁶	Glipizide, 68	57.4 (33-81)	40	AA: 10; C: 50; Asian: 0; H: 0; O: 8	29	185lb	8.5	6.9
	Glipizide, 42	58.7 (34-78)	25	AA: 4; C: 32; Asian: 0; H: 0; O: 6	28.4	181lb	8.8	8.8
	Glipizide, 42	55.5 (130-271)	26	AA: 4; C: 30; Asian: 0; H: 0; O: 8	29.5	187.3lb	8.6	6.5
	Glipizide, 69	59.3 (128-312)	47	AA: 7; C: 54; Asian: 0; H: 0; O: 8	28.8	186.7lb	8.7	7.8
	Glipizide, 28	61.7 (144-267)	17	AA: 1; C: 25; Asian: 0; H: 0; O: 2	29.6	196.2lb	8.4	6.6
	Glipizide, 29	56.9 (142-270)	23	AA: 1; C: 24; Asian: 0; H: 0; O: 4	30.5	201.1lb	8.6	5.3
	Placebo, 69	60.2 (125-280)	53	AA: 8; C: 50; Asian: 0; H: 0; O: 11	29.78	191.7lb	8.3	7.5
Rosenstock, 1996 ¹⁸⁹	Placebo, 79	61.1	(67%)	NR	NR	85.9	8	median 6
	Glimepiride, 88	61.8	(74%)	NR	NR	82.9	8.1	median 7
	Glimepiride, 81	58.8	(70%)	NR	NR	86.3	8.1	median 6
	Glimepiride, 83	59.6	(66%)	NR	NR	84.2	8	median 5
	Glimepiride, 85	61.7	(72%)	NR	NR	86.8	8.3	median 7
Dills, 1996 ¹⁰⁷	Glimepiride, 289	59	(61%)	AA: 0; C: (86%); Asian: 0; H: 0;	NR	192lb	8.5	5

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Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes
				O: (14%)				
	Glyburide, 288	60	(58%)	AA: 0; C: (87%); Asian: 0; H: 0; O: (13%)	NR	192lb	8.5	5
Draeger, 1996 ¹¹²	Glibenclamide, 520	60.7 (26-81)	340	AA: 0; C: 0; Asian: (74%); H: 0; O: (26%) – both groups combined	26.5	NR	8.1	5
	Glimepiride, 524	59.7 (27-81)	325	AA: 0; C: 0; Asian: (74%); H: 0; O: (26%) – both groups combined	26.5	NR	8.1	5
Goldberg, 1996 ¹³⁴	Placebo, 74	60.4	48	AA: 0; C: 60; Asian: 0; H: 0; O: 14	NR	85	7.8	6
	Glimepiride, 78	58.9	56	AA: 0; C: 65; Asian: 0; H: 0; O: 13	NR	83.9	7.8	7
	Glimepiride, 76	57.8	41	AA: 0; C: 60; Asian: 0; H: 0; O: 16	NR	86.1	7.7	5
	Glimepiride, 76	59.6	43	AA: 0; C: 64; Asian: 0; H: 0; O: 12	NR	85.3	7.8	6
Gregorio, 1996 ²²¹	Metformin + unspecified sulfonylurea, 76	76.44 (70- 88)	31	NR	BMI<25: 24; BMI>25: 52	NR	10.38	15.08
Grant, 1996 ¹⁵⁴	Placebo, 23	NR	NR	NR	NR	NR	NR	NR
	Metformin, 25	NR	NR	NR	NR	NR	NR	NR
	Metformin, 27	NR	NR	NR	NR	NR	NR	NR
Vray, 1995 ¹³⁷	Placebo, 56	56.8	(36%)	NR	F 23.7; M 23.8	NR	10	3.9
	Glibenclamide, 56	55.8	(36%)	NR	F 24.5; M 23.7	NR	9.6	2.4
	Placebo, 50	56	(50%)	NR	F 23.8; M 25.0	NR	9.6	2.5
	Glibenclamide, 54	53.3	(65%)	NR	F 23.7; M 24.1	NR	9.3	2.2
DeFronzo, 1995 ⁸⁸	Metformin, 143	53	62	NR	29.9	94.4	8.4	6
	Placebo, 53	53	62	NR	29.2	92.2	8.2	6

Appendix F: Evidence Table 34. Study Population Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes
	Placebo + metformin, 210	55	96	NR	29.4	92.6	8.9	8.4
	Placebo + glyburide, 209	56	103	NR	29.1	92.6	8.5	8.7
	metformin + glyburide, 213	55	98	NR	29	92.1	8.8	7.8
UKPDS, 1995 ⁹²	Diet, 664	NR	NR	NR	NR	NR	NR	NR
	Diet + glibenclamide, 472	NR	NR	NR	NR	NR	NR	NR
	Diet + metformin, 262	NR	NR	NR	NR	NR	NR	NR
Hermann, 1994 ⁸⁷	Diet + metformin, 25	NR	NR	NR	NR	78.6	6.9	NR
	Diet + glibenclamide, 21	NR	NR	NR	NR	82.6	6.7	NR
	Diet + metformin + glibenclamide, 54	NR	NR	NR	NR	80.2	6.8	NR
	Diet + metformin + glibenclamide, 13	NR	NR	NR	NR	84.6	7.8	NR
	Diet + metformin + glibenclamide, 13	NR	NR	NR	NR	76	7.8	NR
	Diet + metformin + glibenclamide, 18	NR	NR	NR	NR	83.2	8.4	NR
Birkeland, 1994 ¹¹⁰	Diet + glipizide, 15	59 (for all groups combined)	22 (for all groups combined)	NR	26.4 (for all groups combined)	NR	8	3.5 (for all groups combined)
	Diet + glyburide, 15	59 (for all groups combined)	22 (for all groups combined)	NR	26.4 (for all groups combined)	NR	8	3.5 (for all groups combined)
	Placebo + diet, 16	59 (for all groups combined)	22 (for all groups combined)	NR	26.4 (for all groups combined)	NR	8.1	3.5 (for all groups combined)
Rosenstock, 1993 ¹⁰⁹	Glyburide, 70	71.4	39	AA: 0; C: 65; Asian: 0; H: 2; O: 3	NR	79.6	5.7	11
	Glyclazide, 69	70.2	48	AA: 0; C: 64; Asian: 0; H: 2; O: 3	NR	80.5	5.8	11

Appendix F: Evidence Table 34. Study Population Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes
Carlson, 1993 ¹⁰⁸	Glyburide, 104	59.2 (33-80)	61	AA: 11; C: 81; Asian: 0; H: 7; O: 5	NR	NR	7.6	N=15/32/57 for <1/1-5/>5 yrs
	Glyburide, 102	60.3 (38-78)	62	AA: 13; C: 81; Asian: 0; H: 4; O: 4	NR	NR	7.6	N=6/42/54 for <1/1-5/>5 yrs
Wolffenbuttel, 1993 ¹²⁰	Repaglinide, 29	62 (45-75)	25	NR	26.1	74	range7.0-12.0	9
	Glibenclamide, 15	62 (45-75)	25	NR	26.1	70.9	range7.0-12.0	9
Aguilar, 1992 ²³⁶	Metformin + unspecified sulfonylurea, 157	48	NR	NR	NR	NR	NR	9.5
Haupt, 1991 ²¹¹	Diet + metformin + unspecified sulfonylurea, 1823	59.8 (men) / 62.6 (women)	705	NR	NR	78.9	11	7.7
Teupe, 1991 ¹⁵⁵	Diet, 50	56	20	NR	NR	86.1	9.6	6.4
	Diet + metformin, 50	51.5	20	NR	NR	89.1	10	8.1
Noury, 1991 ⁸⁶	Metformin, 30	55	16	NR	29.1	80.4	9.75	3
	Glyclazide, 27	54.9	12	NR	28	79	9.72	3
Hermann, 1991 ⁹⁴	Diet + metformin, 16	60 (38-73) (for all groups combined)	(64%) – for all groups combined	NR	27	76.5	6.7	NR
	Diet + glibenclamide, 17	60 (38-73) (for all groups combined)	(64%) – for all groups combined	NR	29.2	84.1	6.6	NR
	Diet + metformin + glibenclamide, 12	60 (38-73) (for all groups combined)	(64%) – for all groups combined	NR	30	87.3	7.7	NR
	Diet + metformin + glibenclamide, 11	60 (38-73) (for all	(64%) – for all groups	NR	26.1	74.4	7.8	NR

Appendix F: Evidence Table 34. Study Population Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes
		groups combined)	combined					
Schneider, 1991 ¹⁷³	Placebo, 16	61.5	9	NR	27.1	NR	6.48	NR
	Metformin, 18	60.4	8	NR	26.1	NR	6.76	NR
Hermann, 1991 ¹⁵⁹	Diet + metformin + glibenclamide, 72	60 (34-74) – all groups combined	79	NR	28.4 – all groups combined	82.3 – all groups combined	NR	NR
	Diet + metformin, 38	60 (34-74) – all groups combined	NR	NR	28.4 – all groups combined	82.3 – all groups combined	NR	NR
	Diet + glibenclamide, 34	60 (34-74) – all groups combined	NR	NR	28.4 – all groups combined	82.3 – all groups combined	NR	NR
	Diet, 14	60 (34-74) – all groups combined	NR	NR	28.4 – all groups combined	82.3 – all groups combined	NR	NR
Doran, 1991 ²⁶⁰	Metformin, 30	55	(53%)	NR	30	NR	11.7	NR
	Placebo, 30	55	(30%)	NR	30	NR	11.8	NR
Jennings, 1989 ²⁰³	Glyburide, 74	NR	NR	NR	NR	NR	NR	NR
	Glyclazide, 80	NR	NR	NR	NR	NR	NR	NR
Menzies, 1989 ³³⁴	Metformin, 39	63.7 (both groups combined)	26 (both groups combined)	NR	78.3 (both groups combined)	NR	10.28	8.4 (both groups combined)
	Metformin, 25	63.7 (both groups combined)	26 (both groups combined)	NR	78.3 (both groups combined)	NR	10.83	8.4 (both groups combined)
Kilo, 1988 ¹⁴⁷	Glyburide, 47	66 (both groups combined)	NR	NR	NR	NR	NR	NR
	Glipizide, 52	66(both groups combined)	NR	NR	NR	NR	NR	NR
Rosenstock, 1987 ²⁰⁷	Glipizide, 79	61.4	45 (57%)	AA: 27 (34%); C: 40 (51%); Asian: 0; H: 10 (13%); O: 2	NR	181.9lb	10	NR

Appendix F: Evidence Table 34. Study Population Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes
				(3%)				
Baba, 1983 ¹³³	Glyclazide, 146	(<39 - >70)	78 (53.42%)	NR	Obesity Index: <119%: 71.9%; >120%: 28.1%	NR	NR	N=35/25/39/47 for <1/1-4/5- 9/>=10 yrs
	Glibenclamide, 131	(<39 - >70)	55 (41.98%)	NR	Obesity Index: <119%: 71%; >120%: 29%	NR	NR	N=30/35/31/35 for <1/1-4/5- 9/>=10 yrs
Dandona, 1983 ²¹⁵	Metformin, 54	NR	NR	NR	NR	NR	NR	NR
	Metformin + unspecified sulfonylurea, 45	NR	NR	NR	NR	NR	NR	NR
	Unspecified sulfonylurea, 53	NR	NR	NR	NR	NR	NR	NR
	Diet, 35	NR	NR	NR	NR	NR	NR	NR
Tseng, 2005 ¹⁴⁰	Unspecified sulfonylurea + pioglitazone, 23	58	8	AA: 0; C: 0; Asian: 0; H: 0; O: (100%)	NR	61.3	NR	
	Placebo + unspecified sulfonylurea, 25	54	9	AA: 0; C: 0; Asian: 0; H: 0; O: (100%)	NR	62.6	NR	NR
Inzucchi, 2005 ¹⁸⁴	Non-insulin sensitizer, 6641	76.8	3108 (46.8%)	AA: 0; C: 5811 (87.5%); Asian: 0; H: 0; O: 0	NR	NR	NR	NR
	Metformin, 1273	75.2	659 (51.8%)	AA: 0; C: 1164 (91.4%); Asian: 0; H: 0; O: 0	NR	NR	NR	NR
	Unspecified TZD, 819	75.8	385 (47%)	AA: 0; C: 731 (89.3%); Asian: 0; H: 0; O: 0	NR	NR	NR	NR
	Metformin + unspecified thiazolidinedione, 139	73.6	74 (53.2%)	AA: 0; C: 123 (88.5%); Asian: 0; H: 0; O: 0	NR	NR	NR	NR

Appendix F: Evidence Table 34. Study Population Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes
Schoffl, 2003 ²²⁶	Pioglitazone, 8760	61 (18 - 99)	4600 (52.8%)	29.4	NR	85.4	8.43	NR
Frenchman, 2003 ²⁰⁰	Unspecified sulfonylurea, 121	women 80.2, men 73.7 (all groups combined)	61	NR	NR	Overall N=121 with greater than ideal body weight	NR	NR
	Metformin, 48	women 80.2, men 73.7 (all groups combined)	61	NR	NR	Overall N=121 with greater than ideal body weight	NR	NR
	Rosiglitazone, 13	women 80.2, men 73.7 (all groups combined)	61	NR	NR	Overall N=121 with greater than ideal body weight	NR	NR
	Pioglitazone, 11	women 80.2, men 73.7 (all groups combined)	61	NR	NR	Overall N=121 with greater than ideal body weight	NR	NR
Turner, 1998 ⁹³	Non-obese patients in the primary diet failure group, 287	50	(69%)	AA: (9%); C: (83%); Asian: (8%); H: 0; O: 0	22.5	NR	10.9	NR
	Obese patients in the primary diet failure group, 171	50	(26%)	AA: (8%); C: (89%); Asian: (3%); H: 0; O: 0	31.8	NR	10.4	NR
	Non-obese patients in the main randomization group, 789	53	(71%)	AA: (10%); C: (76%); Asian: (14%); H: 0; O: 0	23.8	NR	7	NR
	Obese patients in the main randomization group, 831	52	(42%)	AA: (9%); C: (86%); Asian: (5%); H: 0; O: 0	31.2	NR	7.1	NR

Appendix F: Evidence Table 34. Study Population Table for Studies Reporting on Adverse Events (Key Question 4)

Author, year Study group	Group, n	Mean age in years (age range)	Male, n (%)	Race, n (%)	Mean BMI in kg/m ² (other measure)	Mean weight in kg (other measure)	Mean HbA1c %	Mean duration of diabetes
Chalmers, 1992 ³³⁶	Metformin + unspecified sulfonylurea, 70	63 (25-84)	26	NR	30	NR	10.36	8.2
Profozic, 1987 ³³⁷	Glyclazide, 467	56 (28-81)	208 (44.54%)	NR	NR	81.7	NR	4.7
Garber, 2006 ⁷¹	Diet + metformin + glibenclamide, 160	56 (31-78)	90	AA: 8 (5%); C: 128 (80%); Asian: 4 (3%); H: 17 (11%); O: 3 (2%)	32	93	8.5	5
	Diet + metformin + rosiglitazone, 158	56 (24-78)	102	AA: 9 (6%); C: 125 (79%); Asian: 4 (3%); H: 16 (10%); O: 4 (3%)	32	94	8.4	6
Manley, 2003 ²³⁹	Rosiglitazone, 15	63.79	26	NR	NR	NR	8.59	NR
	Pioglitazone, 25	64.63	NR	NR	NR	NR	NR	NR
Chan, 2003 ²²⁴	Entire cohort, 171,143 (not broken down by med type)	57.9	(53.5%)	NR	NR	NR	NR	NR
Masoudi, 2005 ²²⁹	Metformin, 1861	75.8	(43%)	C: (87%); O: (13%)	NR	NR	NR	NR
	Thiazolidinedione, 2226	75.9	(39%)	C: (88%); O: (12%)	NR	NR	NR	NR
	No Insulin sensitizer, 12069	77	(42%)	C: (84%); O: (16%)	NR	NR	NR	NR
Staa, 1997 ²⁰⁴	Glibenclamide, 18740	67.4	(49.8%)	NR	NR	NR	NR	NR
	Glyclazide, 7418	68	(49.4%)	NR	NR	NR	NR	NR
	Glipizide, 2012	68.2	(49.5%)	NR	NR	NR	NR	NR
Shorr, 1996 ²⁰⁵	Glyburide or glipizide, 8576 person-years	78	(16%)	C: (47%); O: (53%)	NR	NR	NR	NR

AA = African American; C = Caucasian; H = Hispanic; O = Other; BMI = Body-Mass Index; Wt = weight; n or N = number; NR=not reported; kg=kilograms; m²=meters squared; %=percent; HbA1c=hemoglobin A1c; BMI= body mass index.

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Thiazolidinedione vs Thiazolidinedione										
Derosa, 2005 ⁵³	RCT	Rosiglitazone + glimepiride + diet + exercise, 42	Pioglitazone + glimepiride + diet + exercise, 45	4 mg (fixed) 4 (2 bid) mg (fixed)	15 mg (fixed) 4 (2 bid) mg (fixed)			Transient flatulence 2 (4.8) total for GP1 1 (2.2) total for GP2		ALT>1.5 times ULN + AST>1.5 times ULN 2 (4.8) total for GP1 1 (2.2) total for GP2
Frenchman, 2003 ²⁰⁰	Cohort	Rosiglitazone (none received second medication), 13	Pioglitazone + Second medication was added in 66.7% of patients: 2 SU, 2 metformin, 2 insulin, 11	NR (NR)	NR (NR)	Low FPG (unspecified) 2 (15.4) total for GP1 1 (9.1) total for GP2	Edema 0 (0) total for GP1 1 (9.1) total for GP2	Nausea + vomiting + diarrhea 0 (0) withdrawn for GP1 0 (0) total for GP1 0 (0) withdrawn for GP2 4 (36.4) total for GP2		Total adverse events 2 (15.4) total for GP1 8 (72.7) total for GP2 Decreased dose due to unspecified adverse event 0 (0) total for GP1 1 (9.1) total for GP2
Manley, 2003 ²³⁹	Cohort	Rosiglitazone, 15	Pioglitazone, 25	NR (NR)	NR (NR)					Anemia 34.89% baseline Hct level for GP1 34.00% final Hct level for GP2 (p=0.024)

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
King, 2000 ¹⁴²	Non-randomized trial	Rosiglitazone, 36	Pioglitazone, 30	8 mg (fixed)	45 mg (fixed)		Edema not reported 3 (7.9) total for GP1 2 (6.7) total for GP2		Other side effects + abdominal pain, rash, dizziness, felt bad, noncardiac chest pain. 4 (11.1) total for GP1 1(3.3) total for GP2	Elevated aminotransferase levels/2 times the upper limit of normal 1 (2.6) total for GP1 0 (0) total for GP2
Gegick, 2001 ¹⁹²	Cohort	Rosiglitazone, 86	Pioglitazone, 77	4 or 8 mg (fixed)	15 - 45 mg (fixed)		Edema not reported 3 (3.5) withdrawn for GP1 3 (3.5) total for GP1 4 (5.2) withdrawn for GP2 4 (5.2) total for GP2		Perceived medication intolerance with non-specific symptoms 3 (3.5) withdrawn for GP1 3 (3.5) total for GP1 3 (3.9) withdrawn for GP2 3 (3.9) total for GP2	

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Rajagopalan, 2005 ²²³	Cohort	Pioglitazone, 1847	Rosiglitazone, 1847	NR (NR)	NR (NR)					<p>Liver failure/2-year IR of liver failure or hepatitis (principal or secondary diagnosis) 0.5 for GP1 0.4 for GP2</p> <p>Liver failure/2-year IR of liver failure or hepatitis (principal diagnosis) 0.3 for GP1 0.4 for GP2</p> <p>Liver failure/2-year IR of liver failure only (principal or secondary diagnosis) 0.0 for GP1 0.1 for GP2</p>
Thiazolidinedione vs Metformin										
Hallsten, 2002 ⁵⁸	RCT	Rosiglitazone + diet, 14	Metformin + diet, 13	4 mg (2 mg for 2 weeks twice daily, thereafter 4 mg twice daily) 8 mg	1000 mg (500 mg for 2 weeks twice daily, thereafter 1000 mg twice daily) 2000 mg				Withdrawn due to unspecified adverse event 0 (0) withdrawn for GP1 2 (15.4) withdrawn for GP2	

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Yamanouchi, 2005 ⁵⁷	RCT	Pioglitazone + diet + exercise, 38	Metformin + diet + exercise, 39	30 for women and 45 for men mg (fixed)	750 mg (fixed)	Not reported 0 (0) serious for GP1 0 (0) total for GP1 0 (0) serious for GP2 0 (0) total for GP2	Edema 2 (5.3) withdrawn for GP1 4 (10.5) total for GP1 0 (0) total for GP2			ALT>1.5 times ULN + AST>1.5 times ULN 0 (0) total for GP1 0 (0) total for GP2
Lawrence, 2004 ⁵⁴	RCT	Pioglitazone, 21	Metformin, 21	30 mg (esc) 45 mg od	500 mg (esc) 1 g tid		Ankle edema 1 (4.8) withdrawn for GP1 0 (0) withdrawn for GP2			
Pavo, 2003 ⁵⁹	RCT	Pioglitazone + placebo, 105	Metformin + placebo, 100	30 mg (esc) 45 mg	850 mg (esc) 2550 mg		Lower limb edema 13 (12.4) total for GP1 4 (4.0) total for GP2	Diarrhea 4 (3) total for GP1 16 (16) total for GP2	Withdrawn due to unspecified adverse events 2 (1.9) withdrawn for GP1 0 (0) withdrawn for GP2	AST -2.2 mean change for GP1 0.7 mean change for GP2 ALT -6.8 mean change for GP1 1.2 mean change for GP2

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Schemthaner, 2004 ⁵⁶	RCT	Pioglitazone + placebo + diet, 597	Metformin + placebo + diet, 597	30 mg (esc) 45	850 mg (esc) 2550		Peripheral edema 5 (0.8) withdrawn for GP1 27 (4.5) total for GP1 2 (0.3) withdrawn for GP2 10 (1.7) total for GP2 Edema nos 13 (2.2) total for GP1 1 (0.2) total for GP2	Diarrhea 3 (0.5) withdrawn for GP1 19 (3.2) total for GP1 9 (1.5) withdrawn for GP2 66 (11.1) total for GP2 Nausea 14 (2.3) total for GP1 25 (4.2) total for GP2		ALT > 3 times ULN + AST > 3 times ULN 0 (0) withdrawn for GP1 2 (0.3) serious for GP1 2 (0.3) withdrawn for GP2 1 (0.2) serious for GP2 Hypertension nos 15 (2.5) total for GP1 17 (2.8) total for GP2
Hanefeld, 2004 ⁶⁰ QUARTET study group	RCT	Pioglitazone + unspecified sulfonylurea + placebo, 319	Metformin + unspecified sulfonylurea + placebo, 320	15 mg (12 week titration, 40 week maintenance) 45 mg NR (fixed)	850 mg (12 week titration, 40 week maintenance) 2550 mg NR (fixed)	Not reported 0 (0) serious for GP1 0 (0) serious for GP2	Edema not reported 22 (6.9) total for GP1 5 (1.6) total for GP2	Included diarrhea 9 (2.8) withdrawn for GP1 39 (12.2) total for GP1 7 (2.2) withdrawn for GP2 75 (23.4) total for GP2	Unspecified adverse events 20 (6.3) withdrawn for GP1 19 (5.9) withdrawn for GP2	Elevated aminotransferase levels Nsg Anemia Nsg

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Frenchman, 2003 ²⁰⁰	Cohort	Rosiglitazone (none received second med), 13	Metformin + second med was added in 47.6% of patients: 9 sulfonylureas, and 1 insulin), 48	NR (NR)	NR (NR)	Low fpg (unspecified) 2 (15.4) total for GP1 2 (4.2) total for GP2	Edema 0 (0) total for GP1 2 (4.2) total for GP2	Nausea + vomiting + diarrhea 0 (0) withdrawn for GP1 0 (0) total for GP1 1 (2.1) withdrawn for GP2 5 (10.4) total for GP2	Total adverse events 2 (15.4) total for GP1 21 (43.8) total for GP2 Decreased dose due to unspecified adverse event 0 (0) total for GP1 6 (12.5) total for GP2	
Frenchman, 2003 ²⁰⁰	Cohort	Pioglitazone + second med was added in 66.7% of patients: 2 SU, 2 metformin, 2 insulin), 11	Metformin + second med was added in 47.6% of patients: 9 sulfonylureas, and 1 insulin), 48	NR (NR)	NR (NR)	Low FPG (unspecified) 1 (9.1) total for GP1 2 (4.2) total for GP2	Edema 1 (9.1) total for GP1 2 (4.2) total for GP2	Nausea + vomiting + diarrhea 0 (0) withdrawn for GP1 4 (36.4) total for GP1 1 (2.1) withdrawn for GP2 5 (10.4) total for GP2	Total adverse events 8 (72.7) total for GP1 21 (43.8) total for GP2 Decreased dose due to unspecified adverse event 1 (9.1) total for GP1 6 (12.5) total for GP2	

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Rajagopalan, 2005 ²²³	Cohort	Pioglitazone, 1137	Metformin, 1137	NR (NR)	NR (NR)					<p>Liver failure/2-year IR of liver failure or hepatitis (principal or secondary diagnosis) 0.4 for GP1 0.8 for GP2</p> <p>Liver failure/2-year IR of liver failure or hepatitis (principal diagnosis) 0.2 for GP1 0.5 for GP2</p> <p>Liver failure/2-year IR of liver failure only (principal or secondary diagnosis) 0.0 for GP1 0.1 for GP2</p>
Inzucchi, 2005 ¹⁸⁴	Cohort	Unspecified TZD, 819	Metformin, 1273	NR (NR)	NR (NR)		Medical record for CHF 402 (49.1) total for GP1 435 (34.2) total for GP2			

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Inzucchi, 2005 ¹⁸⁴	Cohort	Unspecified TZD, 819	Metformin + TZD, 139	NR (NR)	NR (NR)		Medical record for CHF 402 (49.1) total for GP1 54 (38.8) total for GP2			
Thiazolidinedione vs. Sulfonylurea										
Yamanouchi, 2005 ⁵⁷	RCT	Pioglitazone + diet + exercise, 38	Glimepiride + diet + exercise, 37	30 for women and 45 for men mg (fixed)	1.0 mg (esc) 2.0 after 1 month in 8 cases. Rest on 1 mg	Not reported 0 (0) serious for GP1 0 (0) total for GP1 0 (0) serious for GP2 1 (2.7) total for GP2	Edema 2 (5.3) withdrawn for GP1 4 (10.5) total for GP1 0 (0) total for GP2			ALT>1.5 times ULN + AST>1.5 times ULN 0 (0) total for GP1 0 (0) total for GP2
St John Sutton, 2002 ⁶⁷	RCT	Rosiglitazone, 104	Glyburide (no trade drug specified), 99	4 mg (fixed)	NR (titrated 1st 8 weeks then fixed) 20 mg/day	Signs and symptoms 0 (0) withdrawn for GP1 0 (0) serious for GP1 0 (0) withdrawn for GP2 3 (3.0) serious for GP2 7 (7.1) total for GP2	Chf not reported 1 (1.0) total for GP1 0 (0) total for GP2 Edema not reported 6 (6) total for GP1 1 (1) total for GP2		Withdrawn due to unspecified adverse event 8 (7.7) withdrawn for GP1 4 (4.0) withdrawn for GP2	Anemia 7 (7) total for GP1 2 (2) total for GP2 Elevated aminotransferase levels 0 (0) total for GP1 0 (0) total for GP2

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Charbonnel, 2005 ⁶³	RCT	Pioglitazone, 635	Gliclazide, 635	(forced titration to maximum tolerated dose during first 16 weeks) 45mg	(forced titration to maximum tolerated dose during first 16 weeks) 320mg	Not reported 0 (0) serious for GP1 22 (3.5) total for GP1 1 (0.2) serious for GP2 63 (10.1) total for GP2	Edema not reported 54 (8.7) total for GP1 28 (4.5) total for GP2	Diarrhea 18 (2.9) total for GP1 21 (3.4) total for GP2 nausea 27 (4.3) total for GP1 32 (5.1) total for GP2		Elevated aminotransferase levels 3 (0.5) total for GP1 10 (1.6) total for GP2
Lawrence, 2004 ⁵⁴	RCT	Pioglitazone, 21	Gliclazide, 22	30 mg (esc) 45 mg od	80 mg (esc) 160 mg bid		Ankle edema 1 (4.8) withdrawn for GP1 0 (0) withdrawn for GP2			
Tan, 2005 ⁶¹ one year extension study for Quartet study group	RCT	Pioglitazone, 270	Gliclazide, 297	15 mg (esc) 45	80 mg (esc) 320				Withdrew due to unspecified event 33 (12.2) withdrawn for GP1 33 (12.2) total for GP1 25 (8.4) withdrawn for GP2 25 (8.4) total for GP2	
Tan, 2004 ⁶⁵	RCT	Pioglitazone, 91	Glibenclamide, 109	30 mg (esc) 45mg	1.75 mg (esc) 10.5mg	Symptoms or self monitored bg < 50mg/dl 4 (4) total for GP1 32 (29) total for GP2	Pedal 24 (26) total for GP1 9 (8) total for GP2		Unknown 6 (6.6) withdrawn for GP1 10 (9.2) withdrawn for GP2	

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Forst, 2005 ¹⁴⁶	RCT	Pioglitazone + other medication, except metformin & glimepiride), 89	Glimepiride + other medication, except g-cell stimulatory drugs & ppar-p agonists, 84	45 mg (fixed)	1-6 mg (to attain blood glucose level less than 6.7mmol/l) 6mg	Unknown 21 (23.6) total for GP1 26 (31.0) total for GP2	Worsening of preexisting heart failure 2 (2.2) total for GP1 0 (0) total for GP2 Edema 21 (23.6) total for GP1 2 (2.4) total for GP2		Withdrawn due to drug related side effects 1 (1.1) withdrawn for GP1 0 (0) withdrawn for GP2	
Frenchman, 2003 ²⁰⁰	Cohort	Rosiglitazone (none received second med), 13	Unspecified sulfonylurea + second med added in 17.7% of patients: 9 metformin, 2 insulin, 2 rosiglitazone, and 1 pioglitazone), 121	NR (NR)	NR (NR)	Low fpg (unspecified) 2 (15.4) total for GP1 18 (14.9) total for GP2	Edema 0 (0) total for GP1 3 (2.5) total for GP2	Nausea + vomiting + diarrhea 0 (0) withdrawn for GP1 0 (0) total for GP1 0 (0) withdrawn for GP2 3 (2.5) total for GP2	Total adverse events 2 (15.4) total for GP1 29 (24) total for GP2 Decreased dose due to unspecified adverse event 0 (0) total for GP1 6 (5) total for GP2	

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Frenchman, 2003 ²⁰⁰	Cohort	Pioglitazone + second med was added in 66.7% of patients: 2 SU, 2 metformin, 2 insulin), 11	Unspecified sulfonylurea + second med added in 17.7% of patients: 9 metformin, 2 insulin, 2 rosiglitazone, and 1 pioglitazone), 121	NR (NR)	NR (NR)	Low FPG (unspecified) 1 (9.1) total for GP1 18 (14.9) total for GP2	Edema 1 (9.1) total for GP1 3 (2.5) total for GP2	Nausea + vomiting + diarrhea 0 (0) withdrawn for GP1 4 (36.4) total for GP1 0 (0) withdrawn for GP2 3 (2.5) total for GP2	Total adverse events 8 (72.7) total for GP1 29 (24) total for GP2 Decreased dose due to unspecified adverse event 1 (9.1) total for GP1 6 (5) total for GP2	

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Rajagopalan, 2005 ²²³	Cohort	Pioglitazone, 1474	Unspecified sulfonylurea, 1474	NR (NR)	NR (NR)					<p>Liver failure/2-year IR of liver failure or hepatitis (principal or secondary diagnosis) 0.6 for GP1 1.0 for GP2</p> <p>Liver failure/2-year IR of liver failure or hepatitis (principal diagnosis) 0.3 for GP1 0.7 for GP2</p> <p>Liver failure/2-year IR of liver failure only (principal or secondary diagnosis) 0.0 for GP1 0.1 for GP2</p>
Kubo, 2002 ²²⁵	Non-randomized trial	Pioglitazone, 18	Gliclazide, 18	30 mg (fixed)	40 mg (fixed)		Edema not reported 3 (16.7) total for GP1			Elevated aminotransferase levels 0 (0) serious for GP1 0 (0) total for GP1
Thiazolidinedione + Metformin vs. Sulfonylurea + Metformin										

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Garber, 2006 ⁷¹	RCT	Rosiglitazone + metformin + diet, 155	Glibenclamide + metformin + diet, 159	4 mg (esc) 8 1500 or 2000 depending on dose of metformin prior to study mg (esc) 2000	5 mg (esc) 10 1000 mg (esc) 2000	Symptoms and fbs <50 mg/dl 0 (0) withdrawn for GP1 2 (1) total for GP1 7 (4.4) withdrawn for GP2 60 (38) total for GP2		Diarrhea 5 (3) total for GP1 10 (6) total for GP2 Abdominal pain 2 (1.3) withdrawn for GP1 6 (4) total for GP1 9 (5.7) withdrawn for GP2 10 (6) total for GP2 Diarrhea + abdominal pain + other gi symptoms 16 (10) total for GP1 18 (11) total for GP2	Withdrawn due to unspecified event 2 (1.3) withdrawn for GP1 9 (5.6) withdrawn for GP2	
Derosa, 2005 ⁷²	RCT	Rosiglitazone + metformin + diet + exercise + behavioral therapy, 48	Glimepiride + metformin + diet + exercise + behavioral therapy, 47	4 mg (fixed) 1500 mg (fixed)	2 mg (fixed) 1500 mg (fixed)			Transient flatulence 2 (4.2) total for GP1 1 (2.1) total for GP2		ALT>1.5 ULN + AST>1.5 ULN 3 (6.3) total for GP1 0 (0) total for GP2
Thiazolidinedione vs Meglitinide										

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Raskin, 2004 ⁴⁴	RCT	Rosiglitazone, 62	Repaglinide, 63	2 mg bid (12 week dose titration then 12 week maintenance) 4 mg bid	0.5 mg per meal if hba1c≤8 or 1 mg if >8 (12 week dose titration, 12 week maintenance) 4 mg per meal	Fsg<2.8 mmol/l 0 (0) serious for GP1 1 (2) total for GP1 0 (0) serious for GP2 4 (6) total for GP2	Peripheral 2 (3) total for GP1 0 (0) total for GP1		Withdrew due to unspecified adverse event 6 (9.7) withdrawn for GP1 4 (6.3) withdrawn for GP2	ALT> 3 times normal + AST> 3 times normal 0 (0) serious for GP1 1 (1.6) serious for GP2
Jovanovic, 2004 ⁷³	RCT	Pioglitazone, 62	Repaglinide, 61	30 mg (fixed)	0.5 mg if hba1c<8 or 1 mg if hba1c>8 (titrated up for 12 weeks, then fixed for 12 weeks) 4 mg per meal	Symptoms only or symptoms with bg level not < 50mg/dl 4 (7) total for GP1 8 (13) total for GP2 Fsg<50 mg/dl 0 (0) serious for GP1 2 (3) total for GP1 0 (0) serious for GP2 5 (8) total for GP2	Peripheral 1 (2) total for GP1 0 (0) total for GP2	Diarrhea 2 (3) total for GP1 3 (5) total for GP2	Withdrew due to unspecified adverse event 1 (1.6) withdrawn for GP1 3 (4.9) withdrawn for GP2	Anemia/mean changes in levels of hemoglobin ALT> 3 times nl + AST> 3 times normal 0 (0) total for GP1 0 (0) total for GP2
Thiazolidinedione vs Alpha-Glucosidase Inhibitors										

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Goke, 2002 ⁷⁶ German Pio Study Group	RCT	Pioglitazone, 129	Acarbose, 136	45 mg (fixed)	50 mg once daily (esc) 300 mg divided up into tid dosing		Chf not reported 0 (0) withdrawn for GP1 2 (1.5) withdrawn for GP2 Edema not reported 1 (0.8) withdrawn for GP1 6 (4.7) total for GP1 0 (0) withdrawn for GP2 NR for GP2	Abdominal distension/flatulence 0 (0) withdrawn for GP1 NR for GP1 1 (0.7) withdrawn for GP2 46 (33.8) total for GP2		Elevated aminotransferase levels 0 (0) withdrawn for GP1 2 (1.5) withdrawn for GP2
Other Thiazolidinedione Comparisons										
Takagi, 2003 ⁷⁸	RCT	Pioglitazone + (conventional anti-diabetics therapy: insulin (22%), SU (52%), acarbose (9%)), 23	(conventional anti-diabetics therapy: insulin (14%), SU (33%), acarbose (71%)), 21	30 mg (fixed) NR (NR)	NR (NR)		Chf not reported 0 (0) total for GP1 0 (0) total for GP2 Edema not reported 2 (8.7) total for GP1 0 (0) total for GP2			

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Nishio, 2006 ¹⁵¹	RCT	Pioglitazone, 26	Control (no placebo), 28	30 mg (fixed)	NR (NR)		Severe CHF 0 (0) serious for GP1 0 (0) serious for GP2 Edema not reported 0 (0) total for GP1			ALT>2 times ULN + AST> 2 x ULN 0 (0) total for GP1
Choi, 2004 ⁷⁷	RCT	Rosiglitazone (could be on metformin + unspecified sulfonylurea + unspecified alpha-glucosidase inhibitor + insulin), 38	Up-titration of control group (could be on metformin + unspecified sulfonylurea + unspecified alpha-glucosidase inhibitor + insulin), 45	8 mg (changed to 4mg/ day after catheterization)	NR (NR)					Elevated aminotransferase levels 0 (0) withdrawn for GP1 0 (0) total for GP1 0 (0) withdrawn for GP2 0 (0) total for GP2
Ko, 2003 ³²⁸	Non-randomized trial	Rosiglitazone (some on insulin or unspecified SU), 60	Existing medications (metformin + unspecified sulfonylurea (some on insulin), 72	4 mg (fixed)	NR (NR)		Edema or weight gain 6 (10) withdrawn for GP1 0 (0) withdrawn for GP2			

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Delea, 2003 ²²⁸ Pharmetrics Integrated Outcomes Database	Cohort	Unspecified TZD, 4441	Non-TZD, 28103	NR (NR)	NR (NR)		Icd-9 code for CHF 1.76 (1.43-2.17) HR (95% CI)			
Delea, 2003 ²²⁸ Pharmetrics Integrated Outcomes Database	Cohort	Rosiglitazone, 1882	Non-TZD, 28103	NR (NR)	NR (NR)		Icd-9 code for CHF 2.27 (1.65-3.13) hr (95% CI)			
Manley, 2003 ²³⁹	Cohort	Rosiglitazone, 15	Rosiglitazone + pioglitazone	NR (NR)	NR (NR) NR (NR)					Anemia 34.89% baseline hct level for GP1 34.00% final hct level for GP2 (p=0.024)
Delea, 2003 ²²⁸ Pharmetrics Integrated Outcomes Database	Cohort	Pioglitazone, 1347	Non-TZD, 28103	NR (NR)	NR (NR)		Icd-9 code for CHF 1.92 (1.24-2.97) hr (95% CI)			
Inzucchi, 2005 ¹⁸⁴	Cohort	Unspecified TZD, 819	None insulin-sensitizing antihyperglycaemic, 6641	NR (NR)	NR (NR)		Medical record for CHF 402 (49.1) total for GP1 2859 (43.1) total for GP2			
Inzucchi, 2005 ¹⁸⁴	Cohort	None insulin-sensitizing antihyperglycaemic, 6641	Metformin + TZD, 139	NR (NR)	NR (NR)		Medical record for CHF 2859 (43.1) total for GP1 54 (38.8) total for GP2			

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Chalasani, 2005 ²²²	Cohort	Rosiglitazone (among those with abnormal liver function tests)	Rosiglitazone (among those without abnormal liver function tests)	NR	NR					Elevated aminotransferase levels (10 times ULN) (0.9) serious for GP1 (0.6) serious for GP2 (10) total for GP1 (6.6) total for GP2
Masoudi, 2005 ²²³	Cohort	Thiazolidinedione	Non-thiazolidinedione and non-metformin (sulfonylurea or insulin)	NR (NR)	NR (NR)		Medicare claims data for readmission for CHF as the principal diagnosis HR 1.06 (1.0-1.09) vs GP2			
Thiazolidinedione vs. Thiazolidinedione + Sulfonylurea										
McCluskey, 2004 ⁷⁶	RCT	Rosiglitazone + placebo, 15	Rosiglitazone + glimepiride, 24	4 or 8 mg (fixed)	4 or 8 mg (fixed) 2 mg (esc) 8	Fsg<36mg/dl 0 (0) withdrawn for GP1 0 (0) total for GP1 0 (0) withdrawn for GP2 1 (4.2) total for GP2				Treatment failure 2 (13.3) withdrawn for GP1 1 (4) withdrawn for GP2

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Kubo, 2002 ²⁵	Non-randomized trial	Pioglitazone, 18	Pioglitazone + gliclazide, 19	30 mg (fixed)	40 mg (fixed) 30 mg (fixed)		Edema not reported 3 (16.7) total for GP1			Elevated aminotransferase levels 0 (0) serious for GP1 0 (0) total for GP1
Metformin vs. Sulfonylurea										
Marre, 2002 ⁸⁴	RCT	Metformin, 104	Glibenclamide, 103	500 mg (esc) 2000	5 mg (esc) 20	Symptoms or labs 1 (1.0) serious for GP1 1 (1.0) total for GP1 1 (1.0) serious for GP2 8 (7.8) total for GP2		Not reported 15 (14.4) total for GP1 2 (1.9) serious for GP2 12 (11.7) total for GP2		
Amador-Licona, 2000 ⁸⁵	RCT	Metformin, 28	Glibenclamide, 23	850 mg (dose was adjusted to reach adequate metabolic control for 3 weeks)	5 mg (dose was adjusted to reach adequate metabolic control for 3 weeks)			Diarrhea + Diffuse abdominal pain 0 (0) withdrawn for GP1 4 (14.3) total for GP1		
Hermann, 1994 ⁸⁷	RCT	Metformin + diet	Glibenclamide + diet	1000 mg (esc) 3000	3.5 mg (esc) 10.5	Not reported 8 (21) serious for GP1 12 (35) serious for GP2		Nausea + diarrhea + dyspepsia, digestive 24 (63) serious for GP1 11 (32) serious for GP2		

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
1998, ¹⁵ UKPDS (10 year results)	RCT	Metformin + diet, 342	Glibenclamide + diet, 277	850 mg (esc) 2550	10 mg (esc) 20	Symptoms 1 (0.3) serious (death) for GP1 Major events (0% per year) for GP1 (2.5% per year) for GP2 Total events (4.2% per year) for GP1 (17.5% per year) for GP2				
1995, ⁹² UKPDS	RCT	Metformin + diet, 262	Glibenclamide + diet, 472	850 mg (esc) 2550	10 mg (esc) 20	Not reported (0.5% mean annual % over 3 years) serious for GP1 (6.3% mean annual % over 3 years) total for GP1 (1.3% mean annual % over 3 years) serious for GP2 (26.8% mean annual % over 3 years) total for GP2				

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Yamanouchi, 2005 ⁵⁷	RCT	Metformin + diet + exercise, 39	Glimepiride + diet + exercise, 37	750 mg (fixed)	1.0 mg (esc) 2.0 after 1 month in 8 cases. Rest on 1 mg	Not reported 0 (0) serious for GP1 0 (0) total for GP1 0 (0) serious for GP2 1 (2.7) total for GP2	Edema 0 (0) total for GP1 0 (0) total for GP2			ALT>1.5 times ULN + AST>1.5 times ULN 0 (0) total for GP1 0 (0) total for GP2
Charpentier, 2001 ⁸⁹	RCT	Metformin + placebo, 75	Glimepiride + placebo, 150	850 mg tid (fixed)	1 mg (either fixed or increased stepwise to 2,4, or 6 mg od depending on clinical symptoms of hypoglycemia)	Clinical symptoms 0 (0) serious for GP1 8 (11) total for GP1 3 (2.0) serious for GP2 20 (13) total for GP2		Diarrhea 5 (7) total for GP1 2 (1) total for GP2	Unspecified adverse events 7 (9.3) withdrawn for GP1 8 (5.3) withdrawn for GP2	
Derosa, 2004 ⁹⁰	RCT	Metformin + placebo + diet + exercise, 75	Glimepiride + placebo + diet + exercise, 73	1000 mg (esc) 3000	1 mg (esc) 4	Not reported 0 (0) serious for GP1 0 (0) total for GP1 0 (0) serious for GP2 0 (0) total for GP2		Nausea + diarrhea 2 (2.4) withdrawn for GP1		
Goldstein, 2003 ⁸²	RCT	Metformin, 75	Glipizide, 84	500 mg (titrated to patient glucose response) 2000 mg	30 mg (titrated to patient glucose response) 30 mg			Diarrhea 13 (17.3) total for GP1 11 (13.1) total for GP1		Lactic acidosis 0 (0) serious for GP1 0 (0) serious for GP2

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Garber, 2002 ⁷⁹	RCT	Metformin, 159	Glyburide (micronase), 160	500 mg (increase by 1 tablet at weeks 4, 6, 8 if patients meet criteria) 2000	2.5 mg (increase by 1 tablet at weeks 4, 6, 8 if patients meet criteria) 10	FASTing plasma glucose <50 0 (0) total for GP1 (6.3) total for GP2		Nausea + vomiting + diarrhea + dyspepsia 43 IR for GP1 24 IR for GP2	Discontinuation due to adverse events 6.3 IR for GP1 6.9 IR for GP2	
Garber, 2003 ⁸⁰	RCT	Metformin, 164	Glyburide (no trade drug specified), 151	500 mg (adjusted to patient response) 2000 mg	2.5 (adjusted to patient response) 10 mg	Symptoms suggesting hypoglycemia 29 (17.7) total for GP1 98 (57.6) total for GP2 Fingerstick blood glucose 1 (0.6) total for GP1 16 (10.6) total for GP2		Adominal pain 10 (6.1) total for GP1 6 (4) total for GP2 nausea + vomiting 17 (10.4) total for GP1 10 (6.6) total for GP2 diarrhea 30 (18.3) total for GP1 8 (5.3) total for GP2		

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Blonde, 2002 ⁶¹	RCT	Metformin, 153	Glyburide (no trade drug specified), 164	500 mg (esc) 2000 mg	10 mg (fixed)	Fsg<=60mg/dl + symptomatic 1 (<1) total for GP1 3 (1.8) total for GP2		Dyspepsia, heartburn 7 (4.6) total for GP1 5 (3) total for GP2 Nausea + vomiting 19 (12.4) total for GP1 9 (5.5) total for GP2 Flatulence 3 (2) total for GP1 0 (0) total for GP2	Withdrew due to unspecified adverse event 8 (5) withdrawn for GP1 5 (3) withdrawn for GP2	Lactic acidosis 0 (0) total for GP1 0 (0) total for GP2
DeFronzo, 1995 ⁸⁸	RCT	Metformin + placebo, 210	Glyburide (no trade drug specified) + placebo, 209	500 mg (esc) 2500	10 mg /day in two divided doses (esc) 20mg per day in 2 divided doses	Not reported 4 (2) total for GP1 6 (3) total for GP2		Nausea + diarrhea 3 (1.4) total for GP1 2 (1.0) total for GP2		Unspecified adverse events 4 (2) serious for GP1 6 (3) serious for GP2 treatment failure + symptomatic diabetes 21 (10) serious for GP1 6 (3) serious for GP2

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Lawrence, 2004 ⁵⁴	RCT	Metformin, 21	Gliclazide, 22	500 mg (esc) 1 g tid	80 mg (esc) 160 mg bid		Ankle edema 0 (0) withdrawn for GP1 0 (0) withdrawn for GP2			
Noury, 1991 ⁸⁶	RCT	Metformin, 30	Gliclazide, 27	1700 mg (fixed)	80 mg (esc) 240			Nausea 1 (3.3) total for GP1 0 (0) total for GP2		
Turner, 1998 ⁹³ UKPDS	RCT	Metformin + diet, 49	Glyburide (diabeta) or chlorpropamide + diet, 124	NR (esc) 2550mg Sulfonylurea could be added to the regimen if still hyperglycemic (esc) 20 If still hyperglycemic, insulin could be added	NR (esc) 20mg for glyburide 500mg for chlorpropamide Metformin could be added if had hyperglycemia (esc) 2550mg If still hyperglycemic, insulin could be added	Major hypoglycemic episodes 0 annual proportion in GP1 with event 2.5 (0-6.7) annual proportion (range) in GP2 Any minor or major event 7 (0-12) annual proportion (range) in GP1 21 (18-27) annual proportion (range) in GP2				

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Nichols, 2005 ²³⁰ Kaiser Permanente database	Cohort	Metformin	Unspecified sulfonylurea	NR (NR)	NR (NR)		Medical record for CHF + icd-9 code for CHF + clinical diagnosis + first record 10.5 (6.7-16.2) IR & 95% CI for GP1 13.8 (11.4-16.6) IR & 95% CI for GP2			
Maru, 2005 ²³² UK General Practice Research Database	Cohort	Metformin, 4579	Unspecified sulfonylurea, 11350	NR (NR)	NR (NR)		Chf/clinical diagnosis + validated a small sample via questionnaires to GP to confirm the diagnosis + oxmis and read codes similar to icd-9 codes 18.8/1000 person-years IR for GP1 26.6/1000 person-years IR for GP2			

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Bytzer, 2001 ²¹⁶	Cross-sectional	Metformin, 211	Unspecified sulfonylurea, 206	NR (NR)	NR (NR)	F-351		1. Dysmotility-like dyspepsia 25 (11.9) total for GP1 19 (9.2) total for GP2 2. Frequent abdominal pain 18 (8.5) total for GP1 10 (4.9) total for GP2 3. steatorrhea-like stools 31 (14.6) total for GP1 33 (15.8) total for GP2 4. Gastro-aesophageal reflux 29 (13.7) total for GP1 25 (12.1) total for GP2 5. Constipation 44 (20.9) total for GP1 51 (24.8) total for GP2 6. Fecal incontinence 22 (10.4) total for GP1 11 (5.3) total for GP2 bowel related pain 28 (13.3) total for GP1 24 (11.7) total for GP2		

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Dandona, 1983 ²¹⁵	Cross-sectional	Metformin, 54	Unspecified sulfonylurea, 53	NR (NR)	NR (NR)			Diarrhea 11 (20) serious for GP1 11 (20) total for GP1 3 (6) serious for GP2 3 (6) total for GP2		
Frenchman, 2003 ²⁰⁰	Cohort	Metformin + second medication was added in 47.6% of patients: 9 sulfonylureas, and 1 insulin, 48	Unspecified sulfonylurea + second medication added in 17.7% of patients: 9 metformin, 2 insulin, 2 rosiglitazone, and 1 pioglitazone, 121	NR (NR)	NR (NR)	Low fpg (unspecified) 2 (4.2) total for GP1 18 (14.9) total for GP2	Edema 2 (4.2) total for GP1 3 (2.5) total for GP2	Nausea + vomiting + diarrhea 1 (2.1) withdrawn for GP1 5 (10.4) total for GP1 0 (0) withdrawn for GP2 3 (2.5) total for GP2		total adverse events 21 (43.8) total for GP1 29 (24) total for GP2 Decreased dose due to unspecified adverse event 6 (12.5) total for GP1 6 (5) total for GP2

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Leese, 2003 ²⁰¹ DARTS/MEMO	Cohort	Metformin or diet	Unspecified sulfonylurea	NR	NR	Blood glucose <3.5 mmol/l requiring glucagon or iv dextrose or confirmation by paramedics by rapid recovery with treatment 0.9/100 patient-years (0.6-1.3) IR & 95%CI for GP2 0.05/100 patient-years (0.01-0.2) IR & 95%CI for GP2				
Metformin vs. Meglitinide										
Horton, 2000 ⁹⁶	RCT	Metformin, 178	Nateglinide, 179	500 mg (fixed)	120 mg tid (fixed)	Plasma glucose measurement <=3.3 mmol or suggestive cases 19 (10.1) total for GP1 1 (0.6) withdrawn for GP2 23 (12.8) total for GP2		Nausea + diarrhea 6 (3.4) withdrawn for GP1 1 (0.6) withdrawn for GP2		

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Derosa, 2003 ⁹⁷	RCT	Metformin + diet + exercise, 56	Repaglinide + diet + exercise, 56	500 mg bid (1500-2500 during 8 week titration period, then fixed) 2500 mg/day	0.5 mg bid (2-4 mg per day during 8 week titration period, then fixed) 4 tid	Not reported 0 (0) withdrawn for GP1 0 (0) serious for GP1 0 (0) total for GP1 0 (0) withdrawn for GP2 0 (0) serious for GP2 0 (0) total for GP2		Nausea + diarrhea 2 (3.6) withdrawn for GP1 0 (0) withdrawn for GP2		
Metformin vs. Alpha-Glucosidase Inhibitor										
Willms, 1999 ⁹⁹	RCT	Metformin, 27	Acarbose, 31	850 mg bid (fixed)	100 mg tid (fixed)	Not reported 5 (18.5) total for GP1 3 (9.7) total for GP2		Not reported 37 total number of occurrences for GP1 42 total number of occurrences for GP2	Withdrawn due to unspecified adverse event 4 (14.8) withdrawn for GP1 18 (58.1) withdrawn for GP2	
Metformin vs. Metformin + Sulfonylurea										
Marre, 2002 ⁹⁴	RCT	Metformin, 104	Metformin + glibenclamide, 101	500 mg (esc) 2000	500 mg (esc) 2000 2.5 mg (esc) 10	Symptoms or labs 1 (1.0) serious for GP1 1 (1.0) total for GP1 0 (0) serious for GP2 11(10.9) total for GP2		Not reported 15 (14.4) total for GP1 7 (6.9) total for GP2		

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Marre, 2002 ⁸⁴	RCT	Metformin, 104	Metformin + glibenclamide, 103	500 mg (esc) 2000	500 mg (esc) 2000 5 mg (esc) 20	Symptoms or labs 1 (1.0) serious for GP1 1 (1.0) total for GP1 2 (1.9) serious for GP2 14 (13.6) total for GP2		Not reported 15 (14.4) total for GP1 19 (18.4) total for GP2		
Tosi, 2003 ⁸⁵	RCT, cross-over	Metformin, 19	Metformin + glibenclamide, 39	500 mg (esc) 3000	400 mg (esc) 2400 2.5 mg (esc) 15	Not reported 2 (10.5) withdrawn for GP1 1 (5) total for GP1		Diarrhea + constipation + discomfort, abdominal pain, and anorexia 2 (10.5) total for GP1 1 (2.6) withdrawn for GP2 1 (2.6) total for GP2		Leukopenia 1 (2.6) total for GP2
Hermann, 1994 ⁸⁷	RCT	Metformin + diet	Metformin + glibenclamide + diet	1000 mg (esc) 3000	500 mg (esc) 3000 1.75 mg (esc) 14.0	Not reported 8 (21) serious for GP1 24 (33) serious for GP2		Nausea + diarrhea + dyspepsia, digestive 24 (63) serious for GP1 25 (35) serious for GP2		

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Charpentier, 2001 ⁸⁹	RCT	Metformin + placebo, 75	Metformin + glimepiride, 147	850 mg tid (fixed)	850 mg tid (fixed) 1 mg (either fixed or increased stepwise to 2,4, or 6 mg od depending on clinical symptoms of hypoglycemia)	Clinical symptoms 0 (0) serious for GP1 8 (11) total for GP1 2 (1.4) serious for GP2 32 (22) total for GP2		Diarrhea 5 (7) total for GP1 4 (3) total for GP2	Unspecified adverse events 7 (9.3) withdrawn for GP1 6 (4.1) withdrawn for GP2	

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Feinglos, 2005 ¹⁰⁴	RCT	Metformin + placebo, 56	Metformin + glipizide, 56	> or = 1000/day mg (fixed)	> or = 1000/day mg (fixed) 2.5 mg (fixed)	Finger stick glucose <60 mg/dl w/ symptoms or finger stick glucose <50 mg/dl w/o symptoms or fpg<55 mg/dl w/o symptoms 0 (0) withdrawn for GP1 0 (0) serious for GP1 2 (3.3) total for GP1 0 (0) withdrawn for GP2 0 (0) serious for GP2 9 (14.8) total for GP2				
Goldstein, 2003 ⁸²	RCT	Metformin, 75	Metformin + glipizide, 87	500 mg (tirated to patient glucose response) 2000 mg	500/5 mg (tirated to patient glucose response) 2000/20 mg			Diarrhea 13 (17.3) total for GP1 16 (18.4) total for GP1		Lactic acidosis 0 (0) serious for GP1 0 (0) serious for GP2
Garber, 2002 ⁷⁹	RCT	Metformin, 159	Metformin + glyburide (micronase), 158	500 mg (increase by 1 tablet at weeks 4, 6, 8 if patients meet some criteria) 2000	250/1.25 mg (increase by 1 tablet at weeks 4, 6, 8 if patients meet some criteria)	Not reported 18 (11.4) total for GP2		Nausea + vomiting + diarrhea + dyspepsia 43 IR for GP1 32 IR for GP2	Discontinuation due to adverse events 6.3 IR for GP1 3.8 IR for GP2	

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Garber, 2002 ⁷⁹	RCT	Metformin, 159	Metformin + glyburide (micronase), 162	500 mg (increase by 1 tablet at weeks 4, 6, 8 if patients meet some criteria) 2000	500/2.5 mg (increase by 1 tablet at weeks 4, 6, 8 if patients meet some criteria)	Not reported 61 (37.7) total for GP2		Nausea + vomiting + diarrhea + dyspepsia 43 IR for GP1 38 IR for GP2	Discontinuation due to adverse events 6.3 IR for GP1 11.1 IR for GP2	
Blonde, 2002 ⁸¹	RCT	Metformin, 153	Metformin + glyburide (no trade drug specified), 160	500 mg (esc) 2000 mg	500/2.5 mg (esc) 2000/10	Fsg<=60mg/dl + symptomatic 1 (<1) total for GP1 22 (6.8) total for both metformin + Glyburide groups		Dyspepsia, heartburn 7 (4.6) total for GP1 8 (5) total for GP2 Nausea + vomiting 19 (12.4) total for GP1 16 (10) total for GP2 flatulence 3 (2) total for GP1 10 (6.3) total for GP2	Withdrew due to unspecified adverse event 8 (5) withdrawn for GP1 5 (3.4) withdrawn for both metformin + Glyburide groups	Lactic acidosis 0 (0) total for GP1 0 (0) total for GP2

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Blonde, 2002 ⁶¹	RCT	Metformin, 153	Metformin + glyburide (no trade drug specified), 162	500 mg (esc) 2000 mg	500/5 mg (esc) 2000/20	Fsg<=60mg/dl + symptomatic 1 (<1) total for GP1 22 (6.8) total for both metformin + Glyburide groups		Dyspepsia, heartburn 7 (4.6) total for GP1 6 (3.7) total for GP2 Nausea + vomiting 19 (12.4) total for GP1 11 (6.8) total for GP2 Flatulence 3 (2) total for GP1 4 (2.5) total for GP2	Withdrew due to unspecified adverse event 8 (5) withdrawn for GP1 5 (3.4) withdrawn for both metformin + Glyburide groups	Lactic acidosis 0 (0) total for GP1 0 (0) total for GP2

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Garber, 2003 ⁸⁰	RCT	Metformin, 164	Metformin + glyburide (no trade drug specified), 171	500 mg (adjusted to patient response) 2000 mg	250 mg (adjusted to patient response) 1000 mg 1.25 mg (esc) 5 mg	Symptoms suggesting hypoglycemia 29 (17.7) total for GP1 59 (39.1) total for GP2 Fingerstick blood glucose 1 (0.6) total for GP1 19 (11.2) total for GP2		Abdominal pain 10 (6.1) total for GP1 7 (4.1) total for GP2 nausea + vomiting 17 (10.4) total for GP1 8 (4.7) total for GP2 diarrhea 30 (18.3) total for GP1 13 (7.6) total for GP2		
DeFronzo, 1995 ⁸⁸	RCT	Metformin + placebo, 210	Metformin + glyburide (no trade drug specified), 213	500 mg (esc) 2500	500 mg (esc) 2500 10 mg (esc) 20	Not reported 4 (2) total for GP1 38 (18) total for GP2		Nausea + diarrhea 3 (1.4) total for GP1 2 (0.9) total for GP2		unspecified adverse events 4 (2) serious for GP1 4 (2) serious for GP2 treatment failure + symptomatic diabetes 21 (10) serious for GP1 1 (0.5) serious for GP2

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

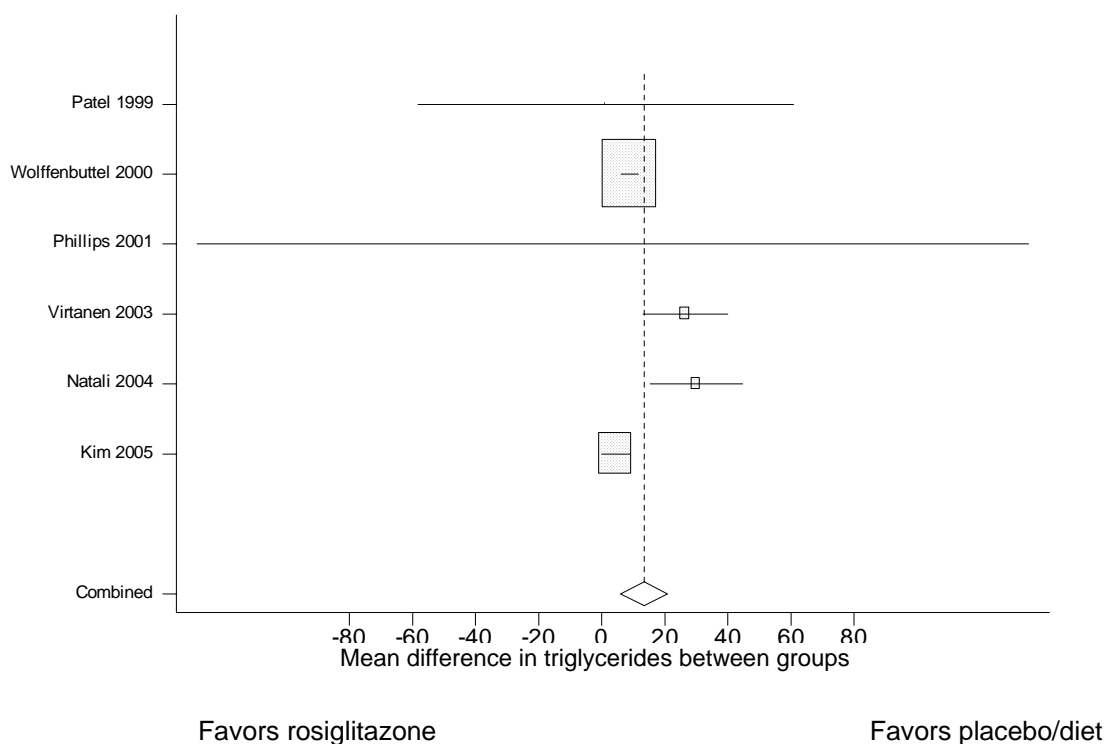
Author, year Study group	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Dandona, 1983 ²¹⁵	Cross-sectional	Metformin, 54	Metformin + sulfonylurea, 45	NR (NR)	NR (NR)			Diarrhea 11 (20) serious for GP1 11 (20) total for GP1 9 (20) serious for GP2 9 (20) total for GP2		
Nichols, 2005 ²³⁰ Kaiser Permanente database	Cohort	Metformin	Metformin + unspecified sulfonylurea	NR (NR)	NR (NR) NR (NR)		Medical record for CHF + icd-9 code for CHF + clinical diagnosis + first record 10.5 (6.7-16.2) IR & 95% CI for GP1 13.4 (11.6-15.5) IR & 95% CI for GP2			
Metformin vs. Thiazolidinedione + Metformin										
Bailey, 2005 ¹⁰¹	RCT	Metformin, 280	Rosiglitazone + metformin, 288	2500 mg (esc) 3000	4/2000 mg (esc) 8/2000	Unspecified 0 (0) withdrawn for GP1 0 (0) serious for GP1 1 (0.4) total for GP1 0 (0) withdrawn for GP2 0 (0) serious for GP2 3 (1) total for GP2	Edema not reported 3 (1) total for GP1 8 (3) total for GP2	NR but included diarrhea and abdominal pain 15 (5.4) withdrawn for GP1 9 (3.2) withdrawn for GP2	Withdrawn due to unspecified adverse events 22 (7.9) withdrawn for GP1 12 (4.2) withdrawn for GP2	ALT>3x ULN + AST>3x ULN 3 (1) total for GP1 1 (<1) total for GP2

Appendix F: Evidence Table 35. Comparative effectiveness of oral diabetes medications on adverse events

Author, year	Study design	Comp GP 1, N	Comp GP 2, N	GP 1, initial dose in mg (fixed or esc) max dose	GP 2, initial dose in mg (fixed or esc) max dose	Hypoglycemia Specific outcome N (%)	Congestive heart failure/Edema Specific outcome N (%)	GI problems Specific outcome N (%)	Withdrawn due to unspecified adverse event N (%)	Other Specific outcome N (%)
Study group										

APPENDIX G

Figure 5b. Meta-analysis of post-treatment difference in triglycerides between rosiglitazone and placebo/diet in patients with type 2 diabetes

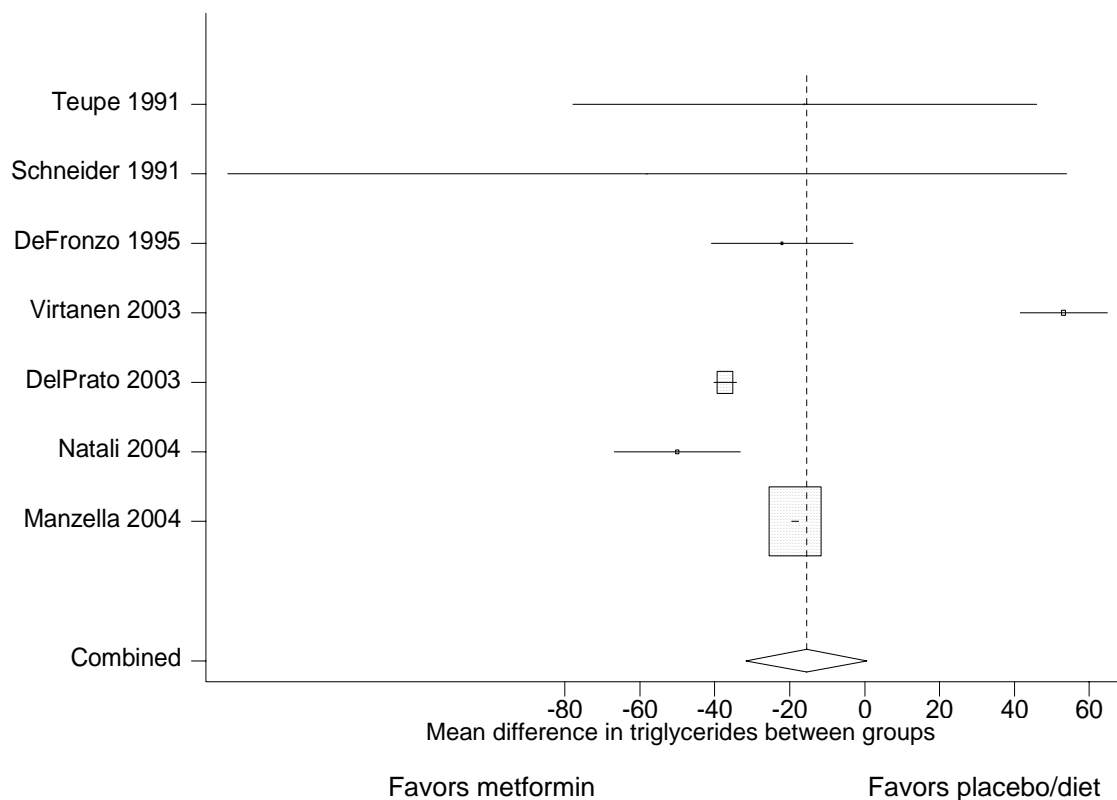


Boxes indicate individual study point estimates. Box size denotes the weight of the study, with larger boxes contributing more to the pooled point estimate. Horizontal lines going through each box represent the 95% confidence interval for each individual study. The diamond at the bottom of the graph indicates the 95% confidence interval for the random effects pooled point estimate.

Test for heterogeneity: $Q = 18.600$ on 5 degrees of freedom ($p = 0.002$)

I-squared statistic = 73 (95% confidence interval: 38 to 88)

Figure 5c. Meta-analysis of post-treatment difference in triglycerides between metformin and placebo/diet in patients with type 2 diabetes

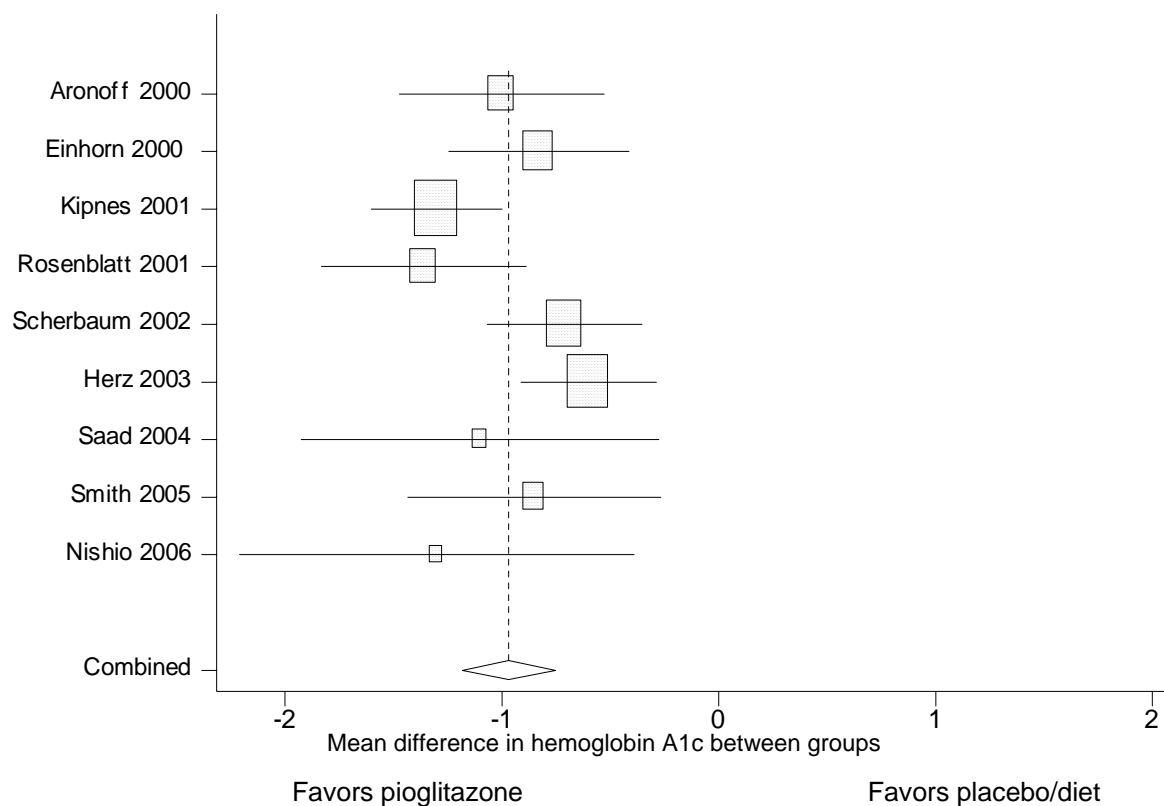


Boxes indicate individual study point estimates. Box size denotes the weight of the study, with larger boxes contributing more to the pooled point estimate. Horizontal lines going through each box represent the 95% confidence interval for each individual study. The diamond at the bottom of the graph indicates the 95% confidence interval for the random effects pooled point estimate.

Test for heterogeneity: $Q = 303.903$ on 6 degrees of freedom ($p = 0.000$)

I-squared statistic = 98 (95% confidence interval: 97 to 99)

Figure 1a. Meta-analysis of post-treatment difference in hemoglobin A1c between pioglitazone and placebo/diet in patients with type 2 diabetes

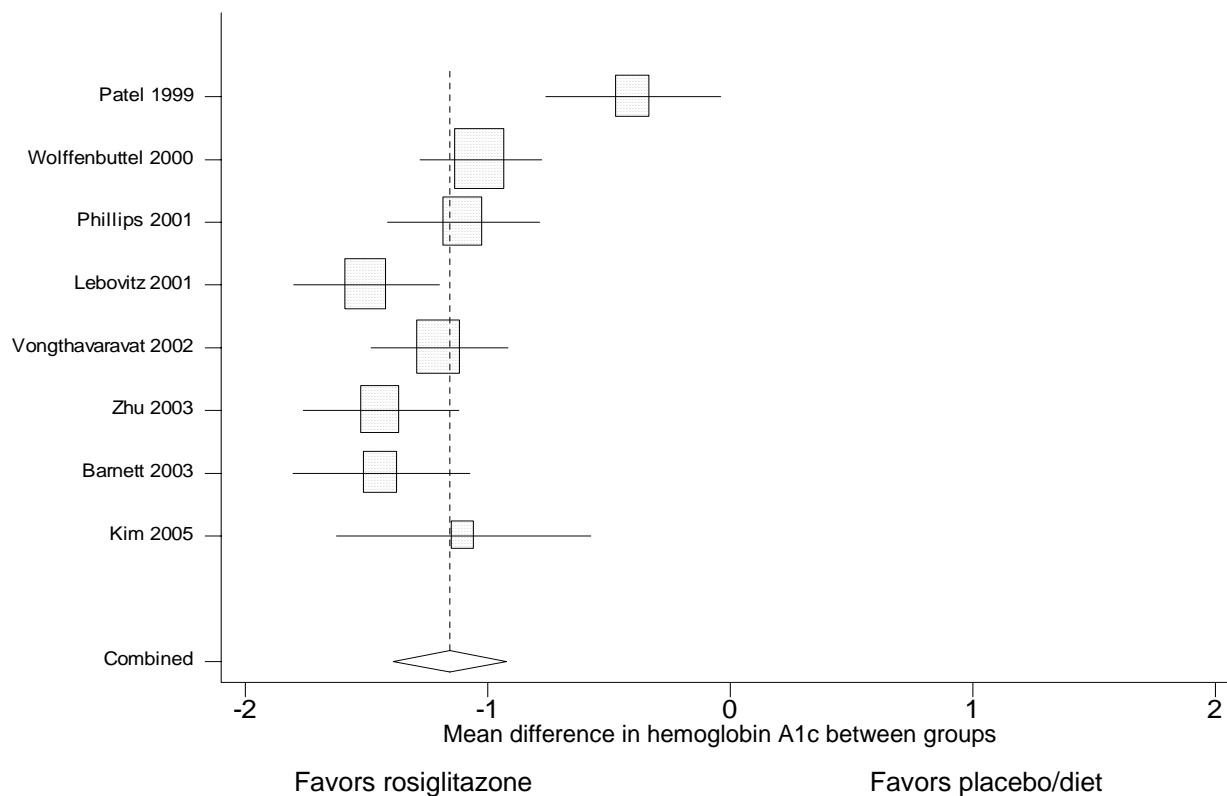


Boxes indicate individual study point estimates. Box size denotes the weight of the study, with larger boxes contributing more to the pooled point estimate. Horizontal lines going through each box represent the 95% confidence interval for each individual study. The diamond at the bottom of the graph indicates the 95% confidence interval for the random effects pooled point estimate.

Test for heterogeneity: $Q = 15.885$ on 8 degrees of freedom ($p = 0.044$)

I-squared statistic = 50 (95% confidence interval: 0 to 77)

Figure 1b. Meta-analysis of post-treatment difference in hemoglobin A1c between rosiglitazone and placebo/diet in patients with type 2 diabetes



Boxes indicate individual study point estimates. Box size denotes the weight of the study, with larger boxes contributing more to the pooled point estimate. Horizontal lines going through each box represent the 95% confidence interval for each individual study. The diamond at the bottom of the graph indicates the 95% confidence interval for the random effects pooled point estimate.

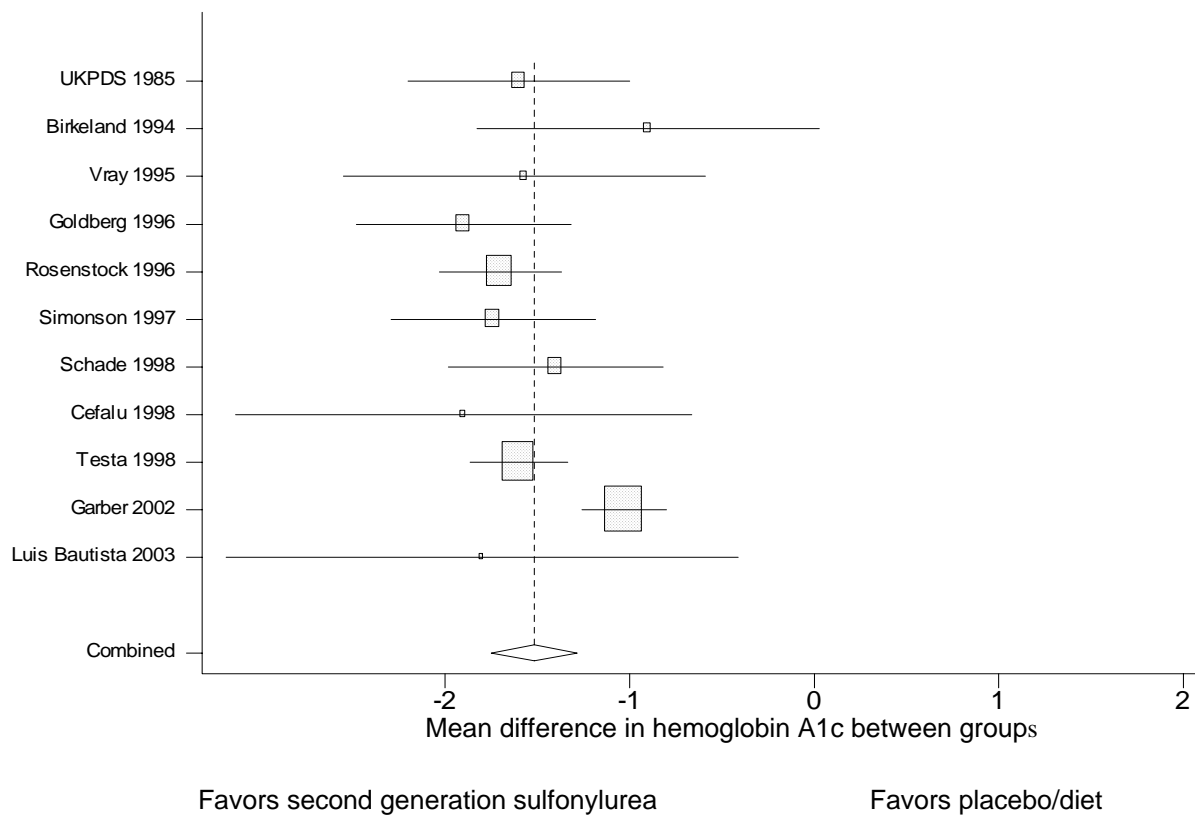
Test for heterogeneity: $Q = 28.514$ on 7 degrees of freedom ($p = 0.000$)

I-squared statistic = 75 (95% confidence interval: 51 to 88)

*Removed study by Hallsten since baseline HbA1c of 6.8% much lower than other studies; therefore, see less of a between-group difference.[5130]

**Dosing was significant in metaregression with higher doses having larger between-group differences.

Figure 1d. Meta-analysis of post-treatment difference in hemoglobin A1c between second generation sulfonylureas and placebo/diet in patients with type 2 diabetes



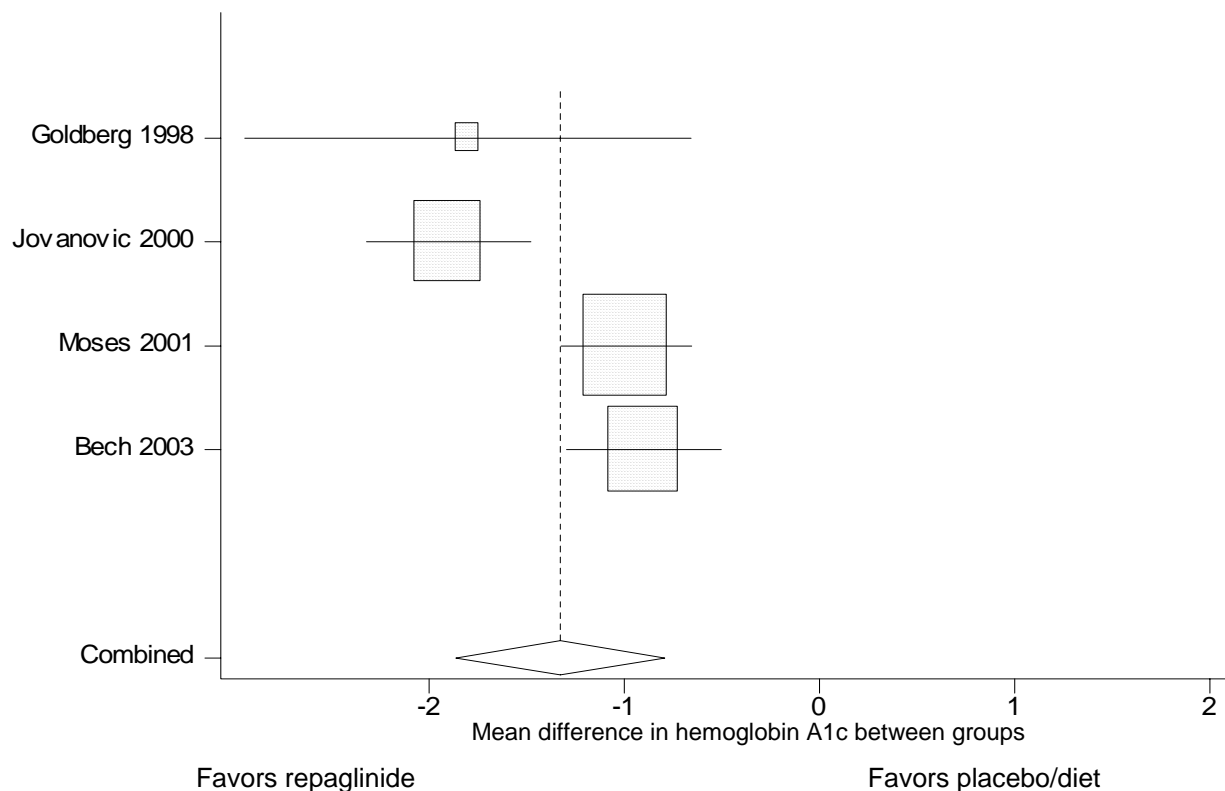
Boxes indicate individual study point estimates. Box size denotes the weight of the study, with larger boxes contributing more to the pooled point estimate. Horizontal lines going through each box represent the 95% confidence interval for each individual study. The diamond at the bottom of the graph indicates the 95% confidence interval for the random effects pooled point estimate.

Test for heterogeneity: $Q = 22.110$ on 10 degrees of freedom ($p = 0.015$)

I-squared statistic = 55 (95% confidence interval: 11 to 77)

* Dose was significant in metaregression with higher doses having larger between-group differences.

Figure 1e. Meta-analysis of post-treatment difference in hemoglobin A1c between repaglinide and placebo/diet in patients with type 2 diabetes



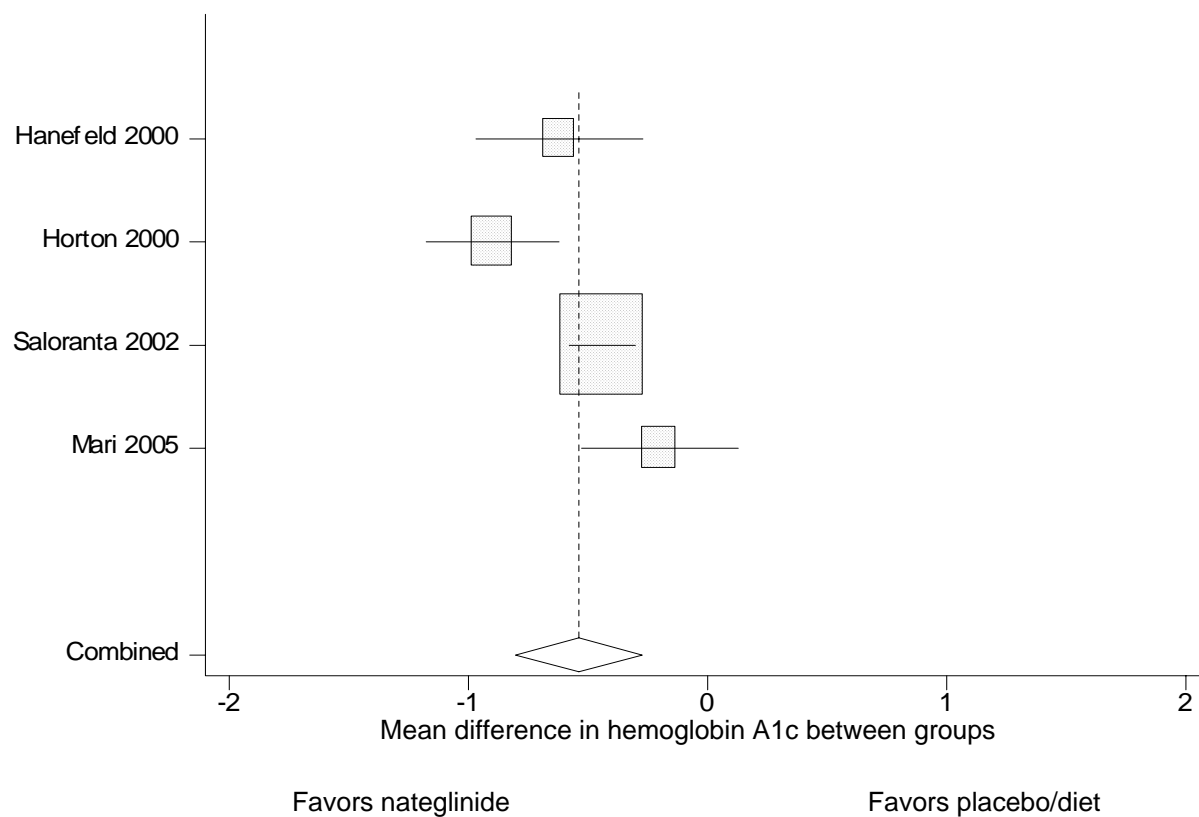
Boxes indicate individual study point estimates. Box size denotes the weight of the study, with larger boxes contributing more to the pooled point estimate. Horizontal lines going through each box represent the 95% confidence interval for each individual study. The diamond at the bottom of the graph indicates the 95% confidence interval for the random effects pooled point estimate.

Test for heterogeneity: $Q = 15.352$ on 3 degrees of freedom ($p = 0.002$)

I-squared statistic = 80 (95% confidence interval: 49 to 93)

*Dosing was significant in metaregression with higher doses having larger between-group differences.

Figure 1f. Meta-analysis of post-treatment difference in hemoglobin A1c between nateglinide and placebo/diet in patients with type 2 diabetes



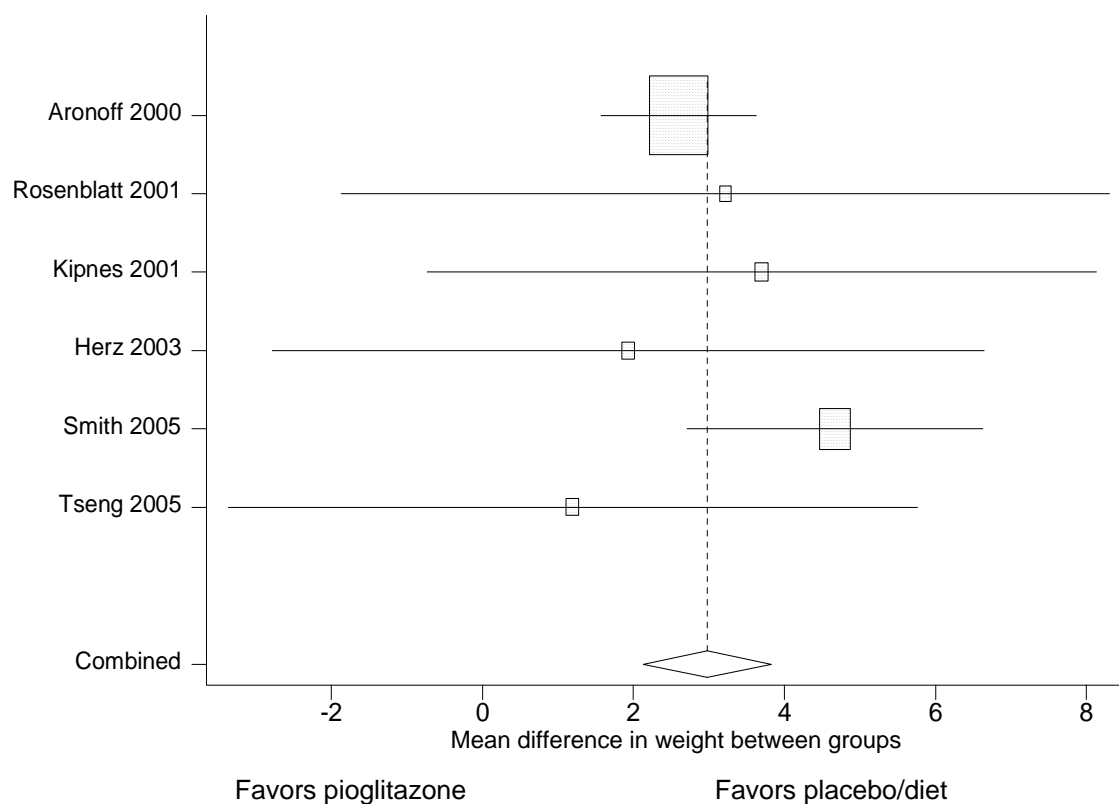
Boxes indicate individual study point estimates. Box size denotes the weight of the study, with larger boxes contributing more to the pooled point estimate. Horizontal lines going through each box represent the 95% confidence interval for each individual study. The diamond at the bottom of the graph indicates the 95% confidence interval for the random effects pooled point estimate.

Test for heterogeneity: $Q = 12.390$ on 3 degrees of freedom ($p = 0.006$)

I-squared statistic = 76 (95% confidence interval: 33 to 91)

If we stratify by baseline HbA1c, heterogeneity disappears. We did not stratify due to the small number of trials.

Figure 2a. Meta-analysis of post-treatment difference in weight between pioglitazone and placebo/diet in patients with type 2 diabetes.

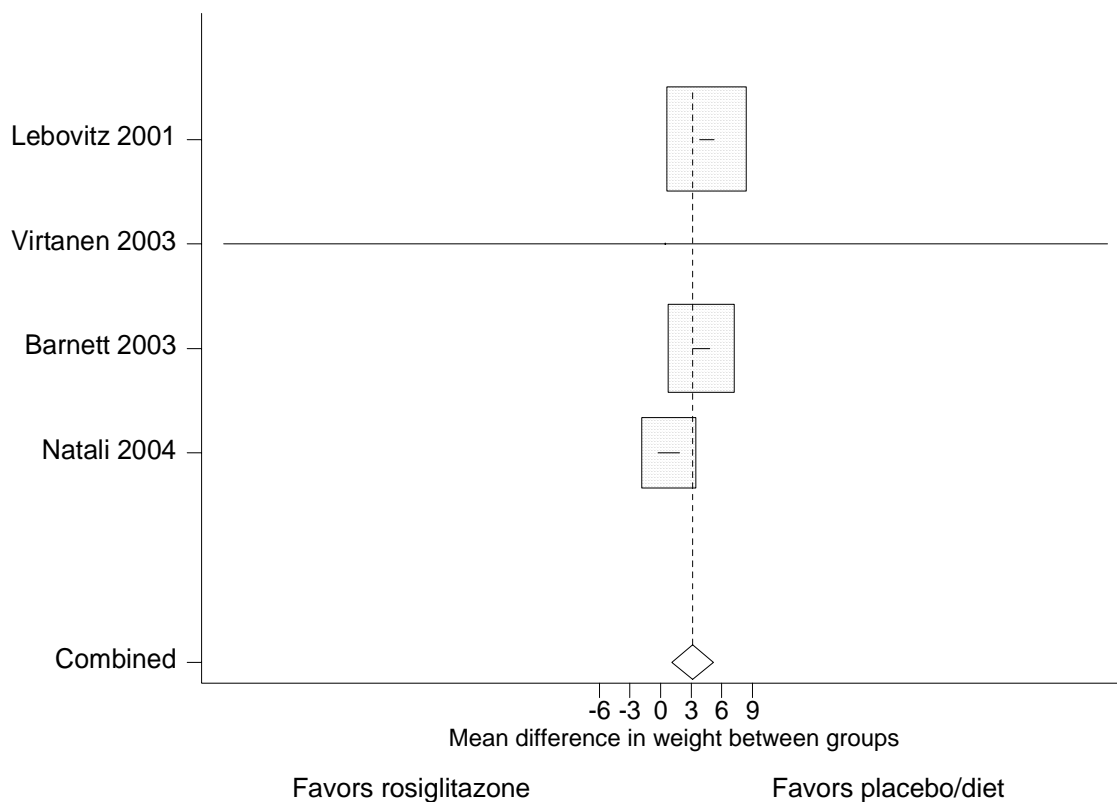


Boxes indicate individual study point estimates. Box size denotes the weight of the study, with larger boxes contributing more to the pooled point estimate. Horizontal lines going through each box represent the 95% confidence interval for each individual study. The diamond at the bottom of the graph indicates the 95% confidence interval for the random effects pooled point estimate.

Test for heterogeneity: $Q = 4.274$ on 5 degrees of freedom ($p = 0.511$)

I-squared statistic = 0 (95% confidence interval: 0 to 75)

Figure 2b. Meta-analysis of post-treatment difference in weight between rosiglitazone and placebo/diet in patients with type 2 diabetes.

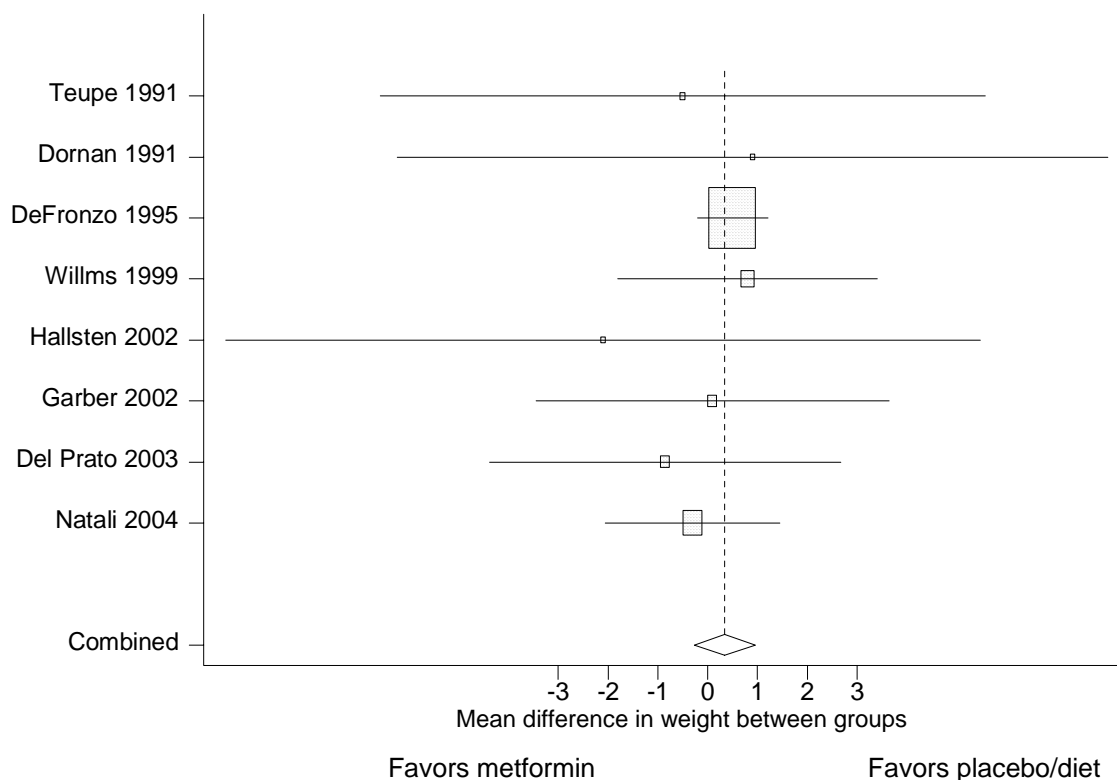


Boxes indicate individual study point estimates. Box size denotes the weight of the study, with larger boxes contributing more to the pooled point estimate. Horizontal lines going through each box represent the 95% confidence interval for each individual study. The diamond at the bottom of the graph indicates the 95% confidence interval for the random effects pooled point estimate.

Test for heterogeneity: $Q = 35.192$ on 3 degrees of freedom ($p = 0.000$)

I-squared statistic = 91 (95% confidence interval: 81 to 96)

Figure 2c. Meta-analysis of post-treatment difference in weight between metformin and placebo/diet in patients with type 2 diabetes.

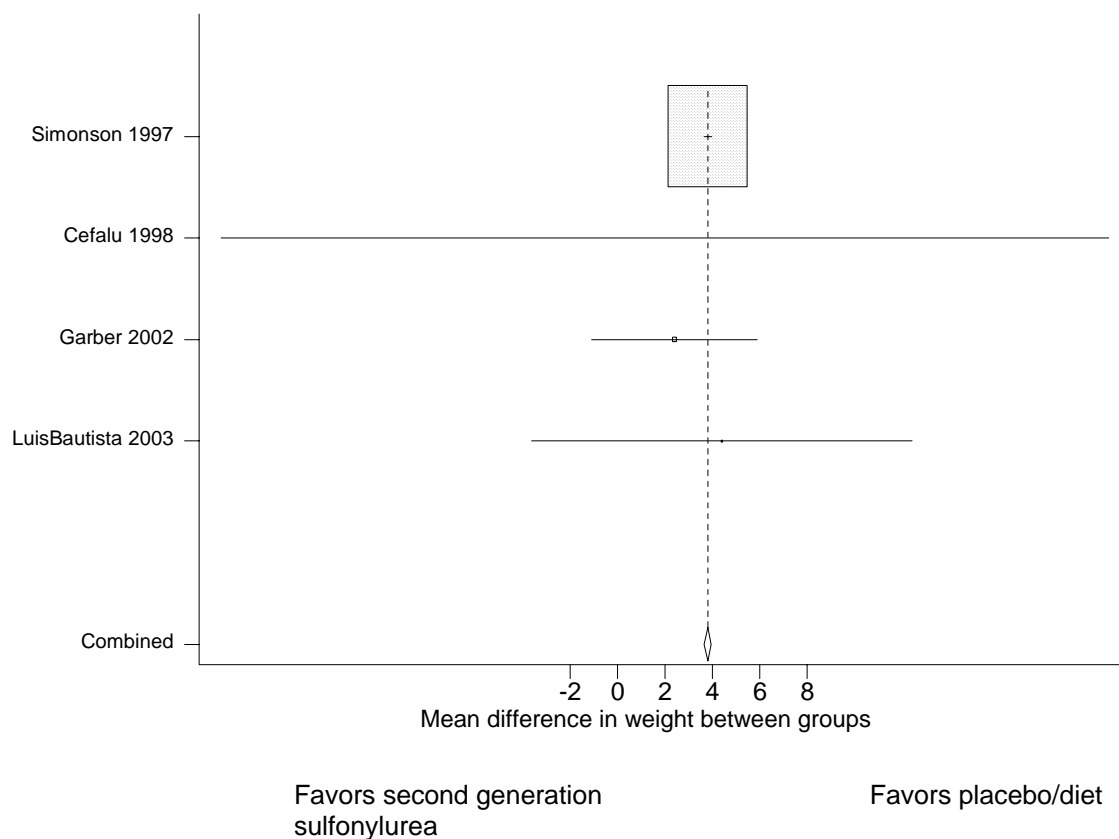


Boxes indicate individual study point estimates. Box size denotes the weight of the study, with larger boxes contributing more to the pooled point estimate. Horizontal lines going through each box represent the 95% confidence interval for each individual study. The diamond at the bottom of the graph indicates the 95% confidence interval for the random effects pooled point estimate.

Test for heterogeneity: $Q = 1.778$ on 7 degrees of freedom ($p = 0.971$)

I-squared statistic = 0 (95% confidence interval: 0 to 68)

Figure 2d. Meta-analysis of post-treatment difference in weight between second generation sulfonylurea and placebo/diet in patients with type 2 diabetes.

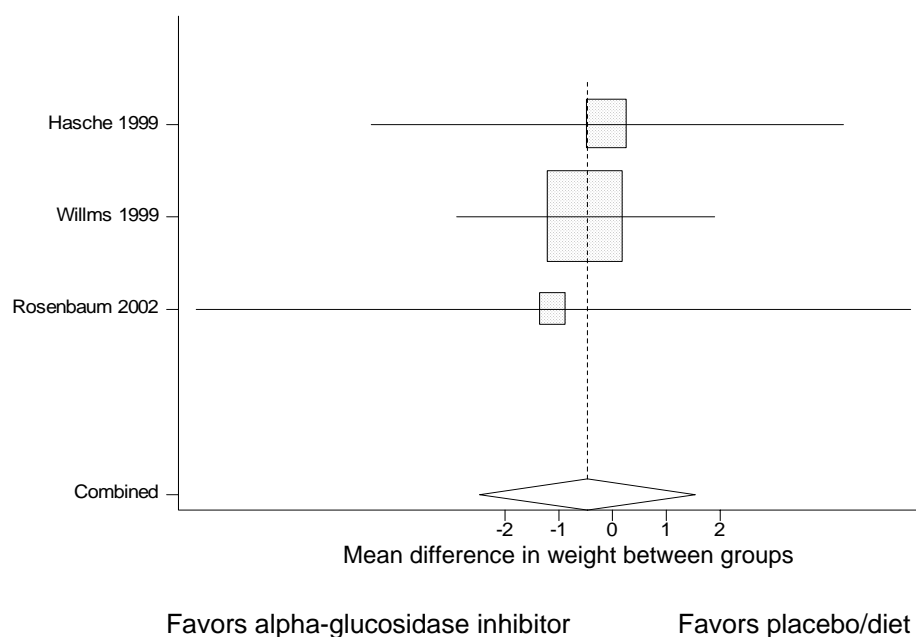


Boxes indicate individual study point estimates. Box size denotes the weight of the study, with larger boxes contributing more to the pooled point estimate. Horizontal lines going through each box represent the 95% confidence interval for each individual study. The diamond at the bottom of the graph indicates the 95% confidence interval for the random effects pooled point estimate.

Test for heterogeneity: $Q = 0.675$ on 3 degrees of freedom ($p = 0.879$)

I-squared statistic = 0 (95% confidence interval: 0 to 85)

Figure 2e. Meta-analysis of post-treatment difference in weight between alpha-glucosidase inhibitors and placebo/diet in patients with type 2 diabetes.

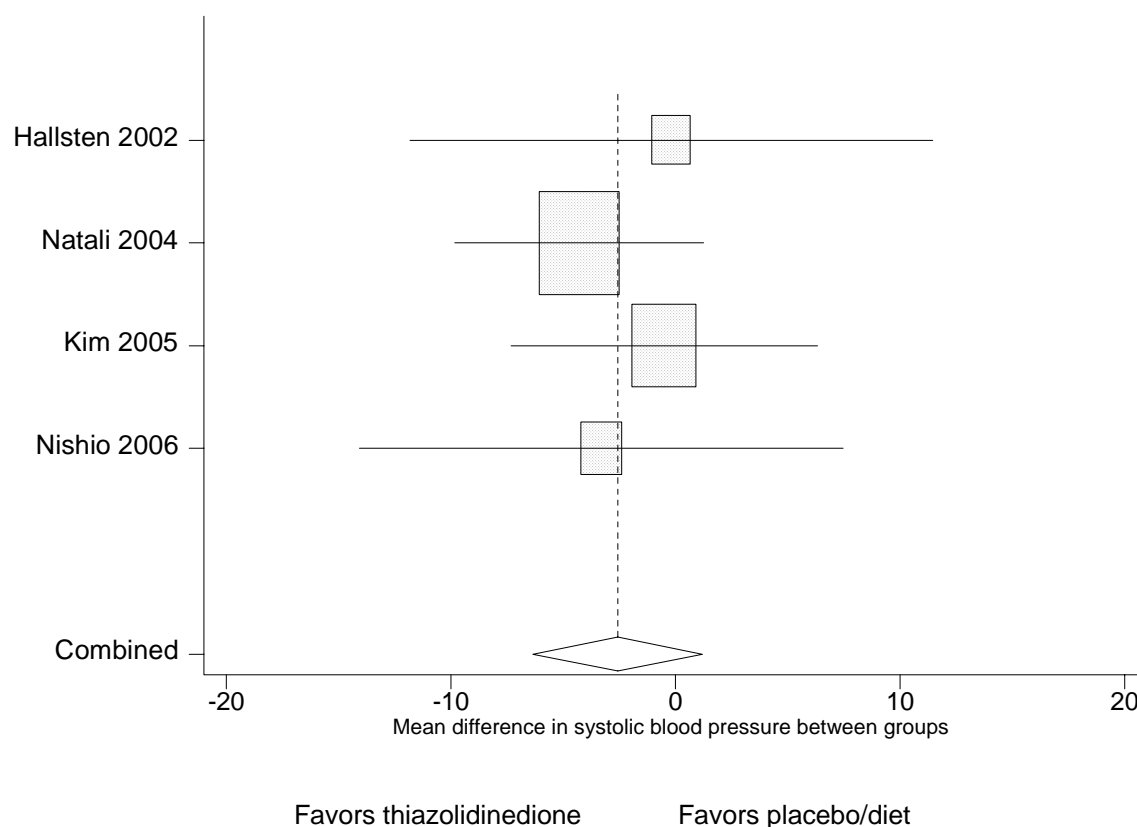


Boxes indicate individual study point estimates. Box size denotes the weight of the study, with larger boxes contributing more to the pooled point estimate. Horizontal lines going through each box represent the 95% confidence interval for each individual study. The diamond at the bottom of the graph indicates the 95% confidence interval for the random effects pooled point estimate.

Test for heterogeneity: $Q = 0.062$ on 2 degrees of freedom ($p = 0.969$)

I-squared statistic = 0 (95% confidence interval: 0 to 90)

Figure 3a. Meta-analysis of post-treatment difference in systolic blood pressure effect between thiazolidinediones and placebo/diet in patients with type 2 diabetes

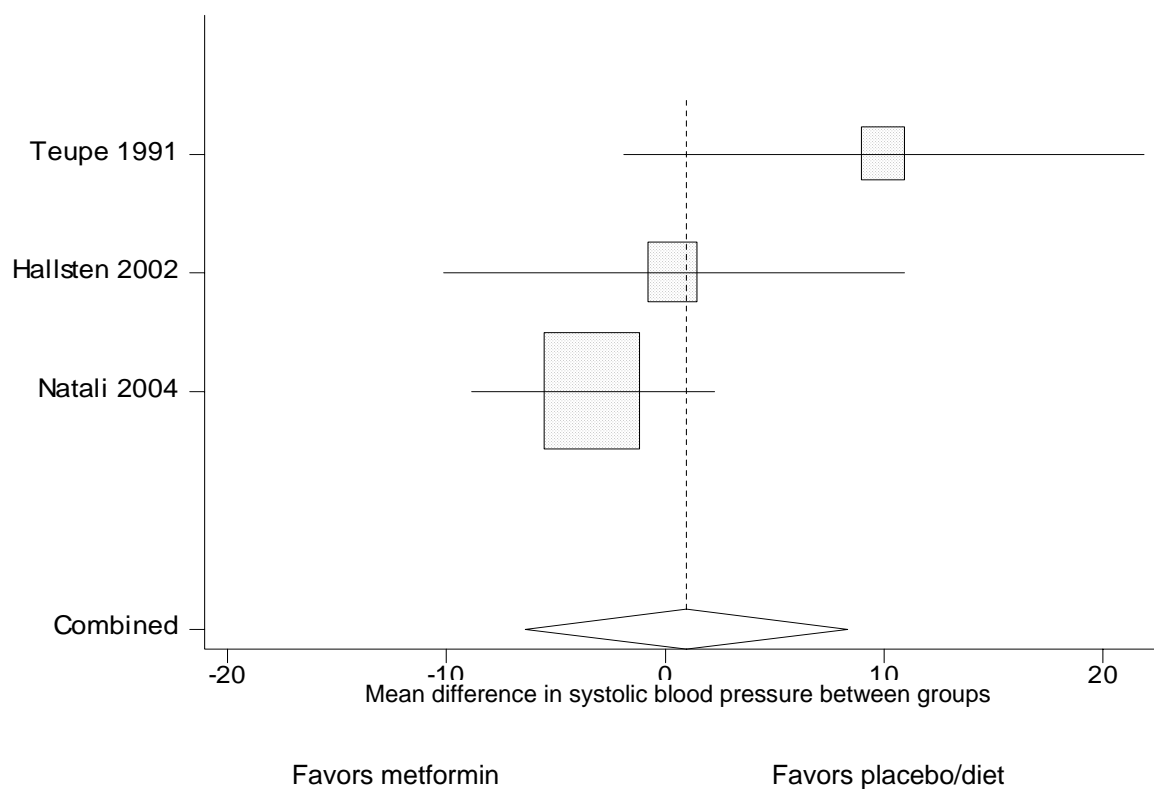


Boxes indicate individual study point estimates. Box size denotes the weight of the study, with larger boxes contributing more to the pooled point estimate. Horizontal lines going through each box represent the 95% confidence interval for each individual study. The diamond at the bottom of the graph indicates the 95% confidence interval for the random effects pooled point estimate.

Test for heterogeneity: $Q = 0.905$ on 3 degrees of freedom ($p = 0.824$)

I-squared statistic = 0 (95% confidence interval: 0 to 85); p -value = 0.82

Figure 3b. Meta-analysis of post-treatment difference in systolic blood pressure effect between metformin and placebo/diet in patients with type 2 diabetes

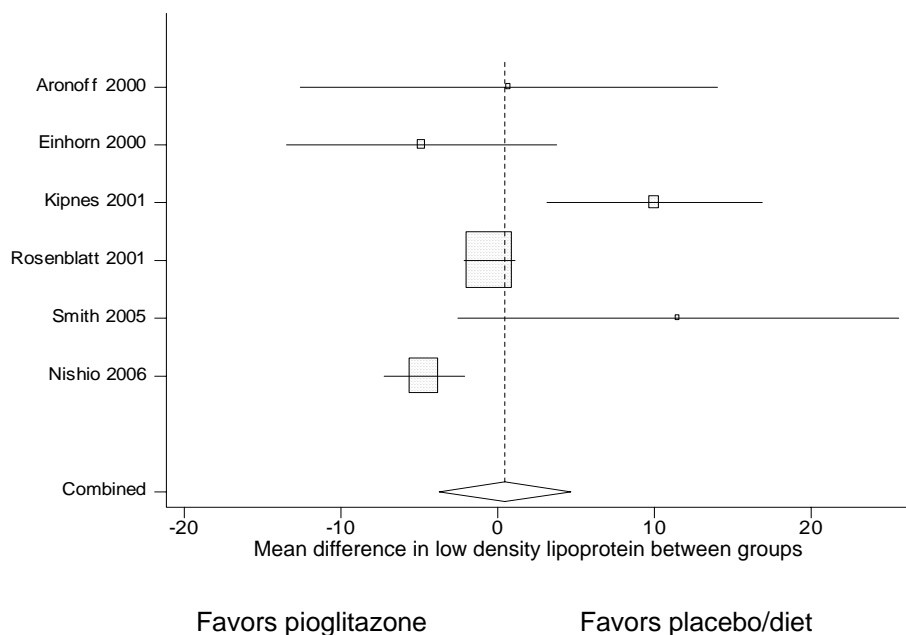


Boxes indicate individual study point estimates. Box size denotes the weight of the study, with larger boxes contributing more to the pooled point estimate. Horizontal lines going through each box represent the 95% confidence interval for each individual study. The diamond at the bottom of the graph indicates the 95% confidence interval for the random effects pooled point estimate.

Test for heterogeneity: $Q = 4.0$ on 2 degrees of freedom ($p = 0.138$)

I-squared statistic = 50 (95% confidence interval: 0 to 86); p -value = 0.13

Figure 4a. Meta-analysis of post-treatment difference in low density lipoprotein effect between pioglitazone and placebo/diet in patients with type 2 diabetes

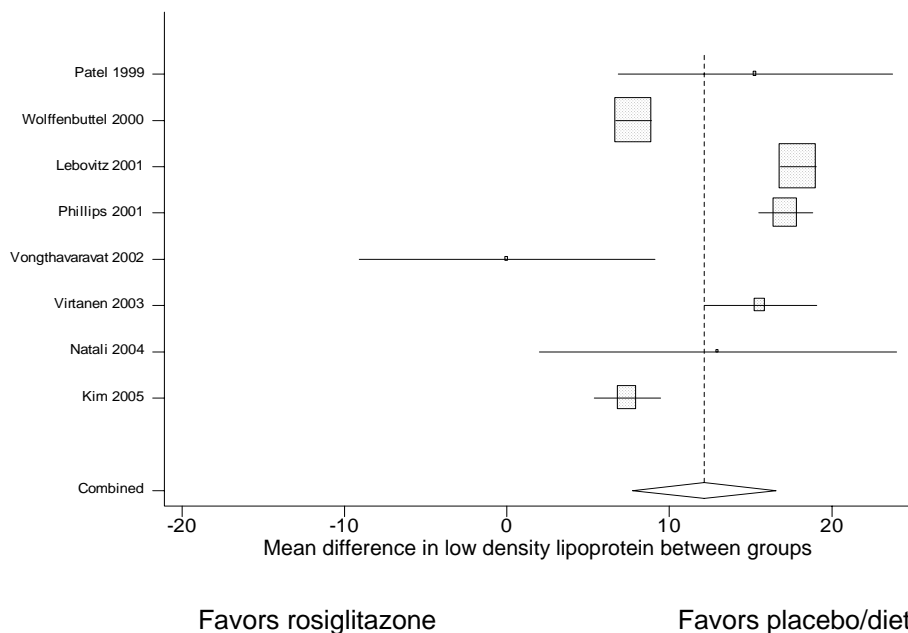


Boxes indicate individual study point estimates. Box size denotes the weight of the study, with larger boxes contributing more to the pooled point estimate. Horizontal lines going through each box represent the 95% confidence interval for each individual study. The diamond at the bottom of the graph indicates the 95% confidence interval for the random effects pooled point estimate.

Test for heterogeneity: $Q = 21.887$ on 5 degrees of freedom ($p = 0.001$)

I-squared statistic = 77 (95% confidence interval: 44 to 90)

Figure 4b. Meta-analysis of post-treatment difference in low density lipoprotein effect between rosiglitazone and placebo/diet in patients with type 2 diabetes



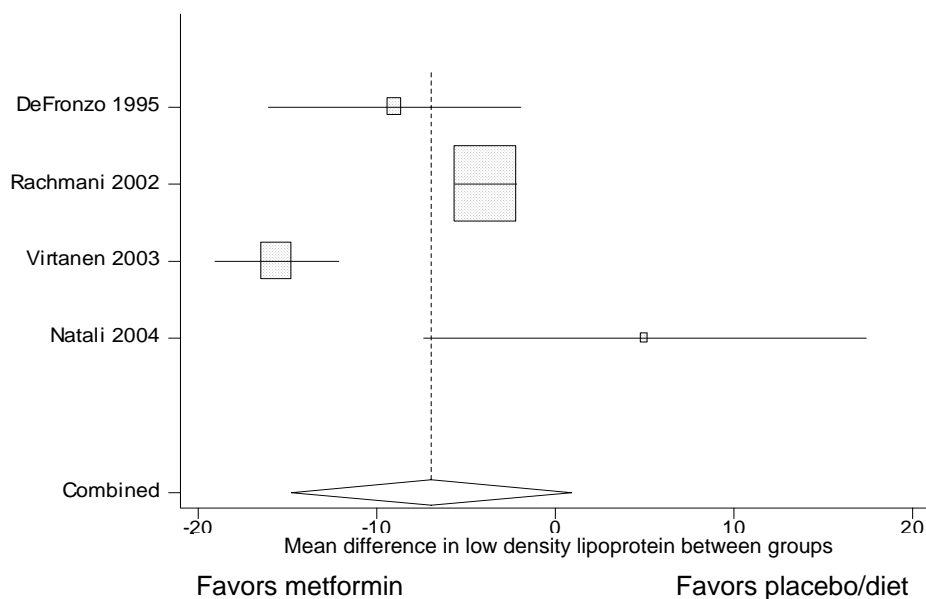
Boxes indicate individual study point estimates. Box size denotes the weight of the study, with larger boxes contributing more to the pooled point estimate. Horizontal lines going through each box represent the 95% confidence interval for each individual study. The diamond at the bottom of the graph indicates the 95% confidence interval for the random effects pooled point estimate.

Test for heterogeneity: $Q = 229.474$ on 7 degrees of freedom ($p = 0.000$)

I-squared statistic = 97 (95% confidence interval: 96 to 98)

Dose was a significant source of heterogeneity in metaregression, with higher doses showing larger between-group differences.

Figure 4c. Meta-analysis of post-treatment difference in low density lipoprotein effect between metformin and placebo/diet in patients with type 2 diabetes



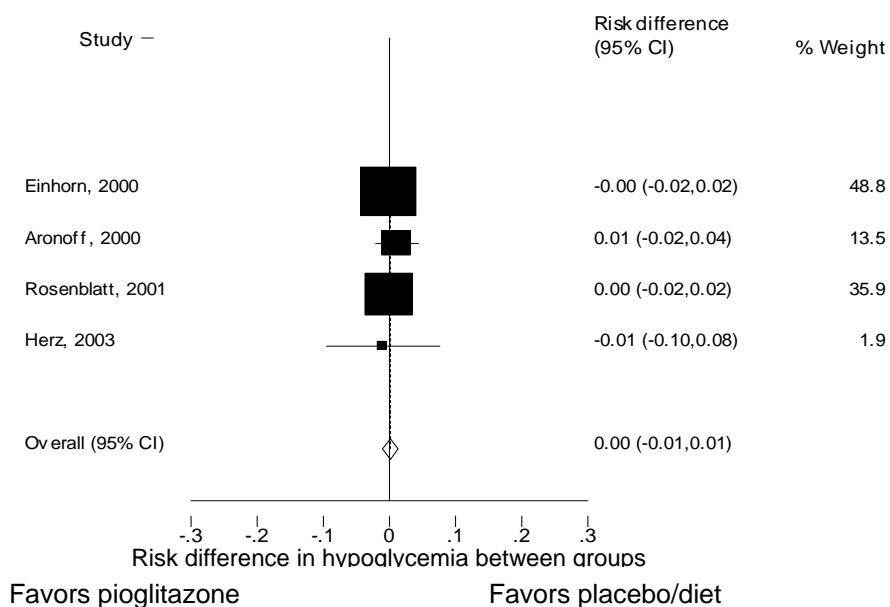
Boxes indicate individual study point estimates. Box size denotes the weight of the study, with larger boxes contributing more to the pooled point estimate. Horizontal lines going through each box represent the 95% confidence interval for each individual study. The diamond at the bottom of the graph indicates the 95% confidence interval for the random effects pooled point estimate.

Test for heterogeneity: $Q = 38.842$ on 3 degrees of freedom ($p = 0.000$)

I-squared statistic = 92 (95% confidence interval: 83 to 96)

*The study by Natali et al significantly influenced the results. By removing it, the 95% CI changed so that it did not cross zero showing metformin decreased LDL compared with placebo.

Figure 6a. Incidence of subjects with hypoglycemia in randomized controlled trials comparing pioglitazone with placebo/diet

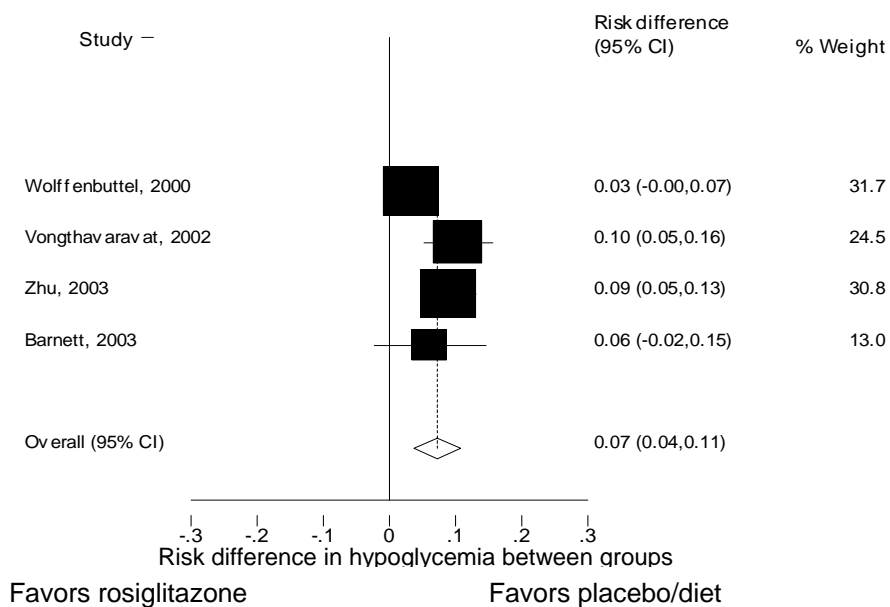


Boxes indicate individual study point estimates. Box size denotes the weight of the study, with larger boxes contributing more to the pooled point estimate. Horizontal lines going through each box represent the 95% confidence interval for each individual study. The diamond at the bottom of the graph indicates the 95% confidence interval for the random effects pooled point estimate. CI= confidence interval.

Heterogeneity chi-squared = 0.56 (d.f. = 3) p = 0.905

I-squared statistic = 0 (95% confidence interval: 0 to 85)

Figure 6b. Incidence of subjects with hypoglycemia in randomized controlled trials comparing rosiglitazone with placebo/diet

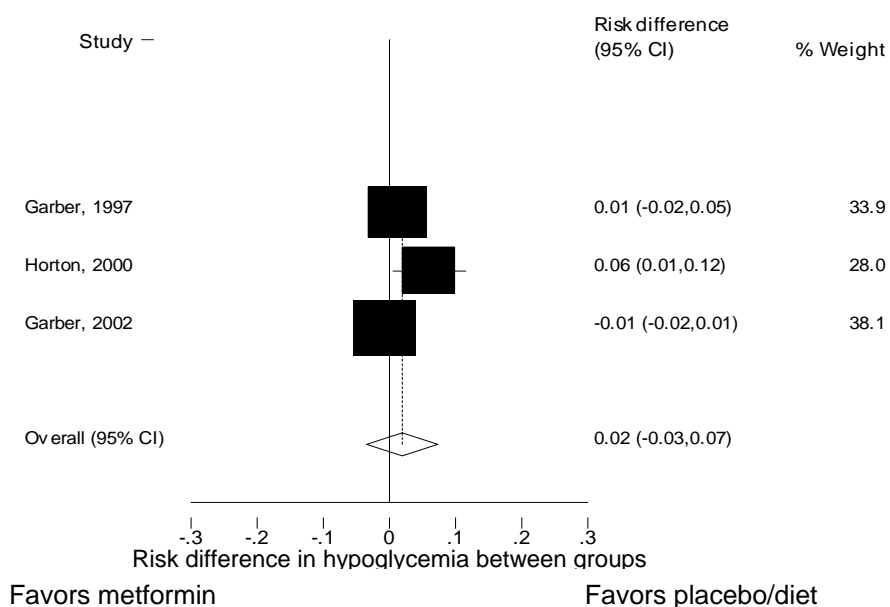


Boxes indicate individual study point estimates. Box size denotes the weight of the study, with larger boxes contributing more to the pooled point estimate. Horizontal lines going through each box represent the 95% confidence interval for each individual study. The diamond at the bottom of the graph indicates the 95% confidence interval for the random effects pooled point estimate. CI= confidence interval.

Heterogeneity chi-squared = 6.12 (d.f. = 3) p = 0.106

I-squared statistic = 51 (95% confidence interval: 0 to 84)

Figure 6c. Incidence of subjects with hypoglycemia in randomized controlled trials comparing metformin with placebo/diet

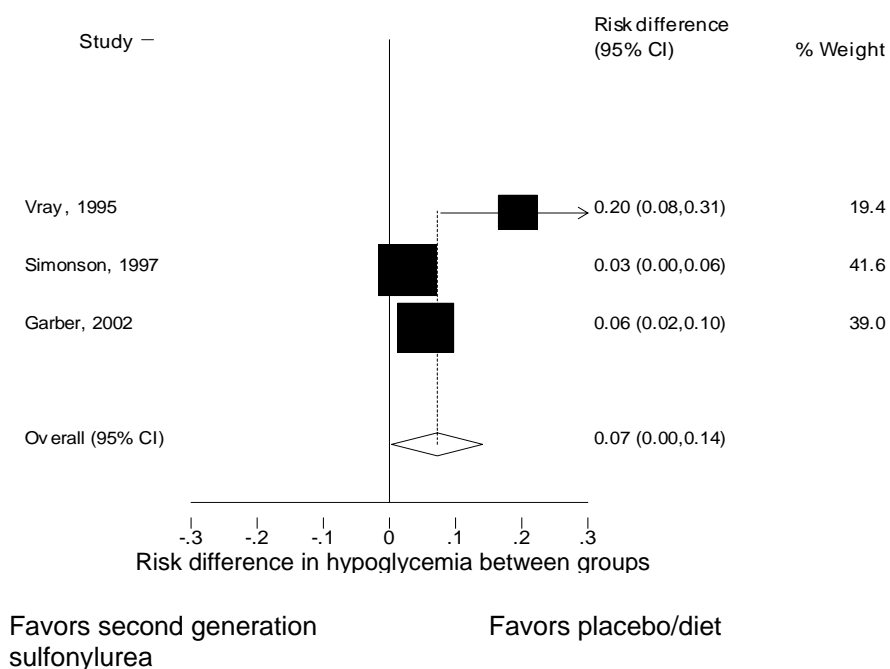


Boxes indicate individual study point estimates. Box size denotes the weight of the study, with larger boxes contributing more to the pooled point estimate. Horizontal lines going through each box represent the 95% confidence interval for each individual study. The diamond at the bottom of the graph indicates the 95% confidence interval for the random effects pooled point estimate. CI= confidence interval.

Heterogeneity chi-squared = 15.29 (d.f. = 2) p = 0.000

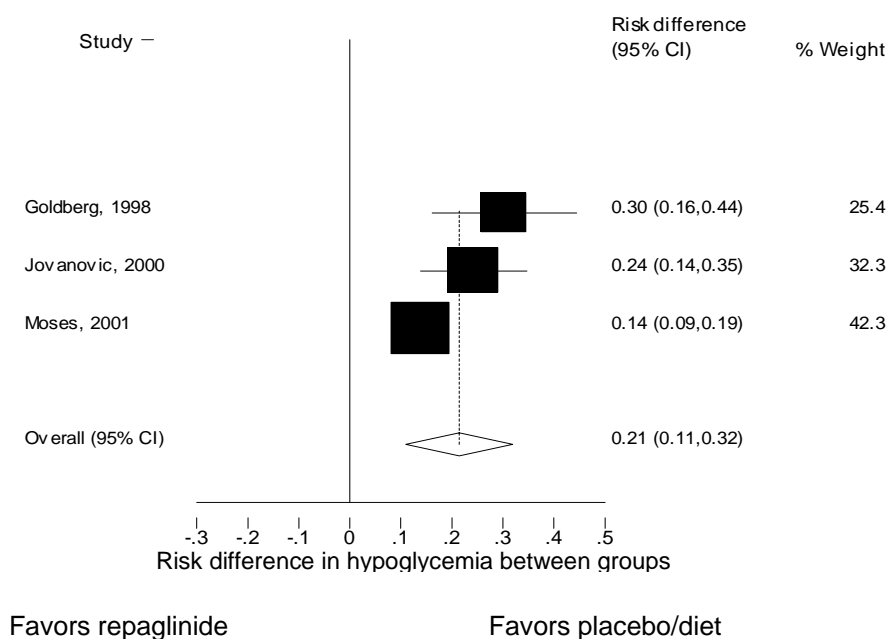
I-squared statistic = 87 (95% confidence interval: 63 to 95)

Figure 6d. Incidence of subjects with hypoglycemia in randomized controlled trials comparing second generation sulfonylureas with placebo/diet



Boxes indicate individual study point estimates. Box size denotes the weight of the study, with larger boxes contributing more to the pooled point estimate. Horizontal lines going through each box represent the 95% confidence interval for each individual study. The diamond at the bottom of the graph indicates the 95% confidence interval for the random effects pooled point estimate. CI= confidence interval.
Heterogeneity chi-squared = 12.23 (d.f. = 2) p = 0.002
I-squared statistic = 84 (95% confidence interval: 51 to 95)

Figure 6e. Incidence of subjects with hypoglycemia in randomized controlled trials comparing repaglinide with placebo/diet



Boxes indicate individual study point estimates. Box size denotes the weight of the study, with larger boxes contributing more to the pooled point estimate. Horizontal lines going through each box represent the 95% confidence interval for each individual study. The diamond at the bottom of the graph indicates the 95% confidence interval for the random effects pooled point estimate. CI= confidence interval.
Heterogeneity chi-squared = 7.04 (d.f. = 2) p = 0.030
I-squared statistic = 72 (95% confidence interval: 4 to 92)

APPENDIX H

- Amador-Licona, 2000⁸⁵
Aronoff, 2000¹⁶⁵
Baba, 1983¹³³
Bailey, 2005¹⁰¹
Bakris, 2003⁶⁶
Baksi, 2004¹²⁶
Barnett, 2003¹⁷²
Bech, 2003¹⁹⁷
Betteridge, 2005¹⁵⁷
Birkeland, 1994¹¹⁰
Blonde, 2002⁸¹
Campbell, 1994⁸³
Cefalu, 1998²⁶¹
Charbonnel, 2005⁶³
Charpentier, 2001⁸⁹
DeFronzo, 1995⁸⁸
Del, Prato, 2003¹⁴⁹
Derosa, 2003¹¹⁸
Derosa, 2004⁹⁰
Dills, 1996¹⁰⁷
Dornan, 1991²⁶⁰
Draeger, 1996¹¹²
Einhorn, 2000¹⁶⁰
Erle, 1999¹²⁷
Feinglos, 2005¹⁰⁴
Fonseca, 2000¹⁰³
Forst, 2005¹⁴⁵
Garber, 1997²¹⁷
Garber, 2002⁷⁹
Garber, 2003⁸⁰
Goldberg, 1996¹³⁴
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Goldstein, 2003⁸²
Gomez-Perez, 2002¹⁰²
Grant, 1996¹⁵⁴
Gregorio, 1999¹²⁹
Hallsten, 2002⁵⁸
Hanefeld, 2004⁶⁰
Harrower, 1985¹¹³
Hasche, 1999¹³⁸
Hermann, 1991⁹⁴
Hermann, 1991¹⁵⁹
Hermann, 1994⁸⁷
Herz, 2003¹⁶³
Horton, 2000⁹⁶
Inukai, 2005¹¹¹
Jovanovic, 2000¹⁹⁴
Kardas, 2005¹¹⁴
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Kilo, 1988¹⁴⁷
Kim, 2005¹⁵²
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Landgraf, 1999¹²¹
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Lebovitz, 2001¹⁶⁹
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Leonhardt, 1991²⁶³
Luis Bautista, 2003¹⁹³
Madsbad, 2001¹¹⁹
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Matthews, 2005⁷⁰
Moses, 2001²¹⁸
Nakamura, 2000⁶⁴
Natali, 2004¹⁴⁴
Nishio, 2006¹⁵¹
Noury, 1991⁸⁶
Patel, 1999¹⁶⁷
Pavo, 2003⁵⁹
Pfutzner, 2005⁶⁸
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Phillips, 2001¹⁶⁸
Rachmani, 2002¹⁵⁰
Ramachandran, 2004⁵⁵
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Saad, 2004¹⁶⁴
Saloranta, 2002²⁴¹
Schade, 1998¹³⁵
Scherbaum, 2002¹⁴¹
Scherthaner, 2004⁵⁶
Schneider, 1991¹⁷³
Simonson, 1997¹³⁶
Smith, 2005¹⁶¹
St John Sutto, 2002⁶⁷
Tan, 2004⁶⁵
Tan, 2004a⁶⁹
Testa, 1998¹⁹⁸
Teupe, 1991¹⁵⁵
Tosi, 2003⁹⁵
Tseng, 2005¹⁴⁰
UKPDS, 1985⁹¹
Vakkilainen, 2002¹²²
Virtanen, 2003¹⁴³
Vongthavaravat, 2002¹⁷⁰

Vray, 1995¹³⁷
Weissman, 2005¹⁰⁰
Willms, 1999⁹⁹
Wolever, 2000⁹⁸
Wolffenbuttel, 1993¹²⁰

Wolffenbuttel, 1999¹¹⁷
Wolffenbuttel, 2000¹⁷¹
Yamanouchi, 2005⁵⁷
Yanagawa, 2004⁶²
Zhu, 2003¹⁸⁸