



## Effective Health Care Type 2 Diabetes Mellitus in Children and Adolescents

### Results of Topic Selection Process & Next Steps

The nominator, American Academy of Family Physicians (AAFP) is interested in a new evidence review on screening and management of type 2 diabetes in children and adolescents to inform an update of their 2013 clinical practice guideline.

Because limited original research addresses the nomination, a new review is not feasible at this time. No further activity on this nomination will be undertaken by the Effective Health Care (EHC) Program.

### Topic Brief

**Topic Name:** #0770 Type 2 Diabetes Mellitus in Children and Adolescents

**Nomination Date:** 02/28/2018

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#### Authors

Jennifer Gilbert  
Rose Relevo  
Kara Winchell

**Conflict of Interest:** None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

#### Summary

- This nomination meets the selection criteria of appropriateness and importance, duplication, and impact.
- However this nomination did not meet the selection criteria of feasibility. We found only three studies relevant to the screening key question, and estimated only three studies for the treatment key questions.

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## Background

Type 2 diabetes mellitus (diabetes) is a prevalent condition in children and adolescents which has increased concomitantly with the childhood obesity epidemic. An estimated 5,000 new cases of type 2 diabetes are diagnosed each year in youth under 20.<sup>1</sup> Type 2 diabetes has continued to increase steadily in children and adolescents over the past two decades particularly among racial and ethnic minorities. For youths aged 10 to 19 years old, the unadjusted incidence rates of type 2 diabetes has increased over 7% per year from 2002 to 2012.<sup>2</sup> The longer duration of diabetes in children and adolescents creates increased risk for development of diabetes-related complications including cardiovascular disease and microvascular complications (e.g., retinopathy, neuropathy, nephropathy).<sup>3</sup> The prolonged duration of type 2 diabetes in children and adolescents affects their quality of life and leads to substantial health care costs.

Multiple professional groups have clinical guidance for children and adolescents with type 2 diabetes, but the evidence for the guidance is currently or close to being out of date.<sup>4,5</sup> The AAFP is interested in an evidence review to address the lack of consensus on the screening and treatment, particularly pharmacologic, of type 2 diabetes in children and adolescents.

### **Nominator and Stakeholder Engagement:**

After receiving the nomination, we refined the key questions and population, interventions, comparators, outcomes, and setting of interest. The original nomination from AAFP addressed screening, diagnosis and pharmacologic and non-pharmacologic treatments. After discussion with AAFP about the large breadth of the topic, they prioritized their key questions to focus on treatment and screening. We modified the key questions accordingly, and eliminated the key question on diagnosis. In addition, we added some outcomes they requested to the key questions including diabetes into adulthood.

The key questions for this nomination are:

1. What are the benefits and harms of screening for type 2 diabetes mellitus in children and adolescents?
2. For children and adolescents diagnosed with type 2 diabetes mellitus, what are the benefits and harms of pharmacologic interventions?
3. For children and adolescents diagnosed with type 2 diabetes mellitus, what are the benefits and harms of non- pharmacologic interventions?
  - a) Does the effectiveness of nonpharmacologic interventions vary by program components?
    - Intensity (e.g., program duration)
    - Delivery personnel (e.g., physician, dietician, certified diabetes educator)
4. For children and adolescents diagnosed with type 2 diabetes mellitus, what are the benefits and harms of pharmacologic interventions compared to non-pharmacologic interventions?

To define the inclusion criteria for the key questions (KQs) we specify the population, interventions, comparators, outcomes, and setting (PICOTS) of interest (Table 1).

**Table 1. Key Questions and PICOTS**

<b>Key Questions</b>	1. What are the benefits and harms of screening for type 2 diabetes mellitus in children and adolescents?	2. For children and adolescents diagnosed with type 2 diabetes mellitus, what are the benefits and harms of pharmacologic interventions?	3. For children and adolescents diagnosed with type 2 diabetes mellitus, what are the benefits and harms of non-pharmacologic interventions? a. Does the effectiveness of nonpharmacologic interventions vary by: <ul style="list-style-type: none"> <li>• Program components</li> <li>• Intensity (e.g., program duration)</li> <li>• Delivery personnel (e.g., physician, dietician, certified diabetes educator)</li> </ul>	4. For children and adolescents diagnosed with type 2 diabetes mellitus, what are the benefits and harms of pharmacologic interventions compared to non-pharmacologic interventions?
<b>Population</b>	Children and adolescents 6-18 years old suspected of having type 2 DM	Children and adolescents 6-18 years old diagnosed with type 2 DM	Children and adolescents 6-18 years old diagnosed with type 2 DM	Children and adolescents 6-18 years old diagnosed with type 2 DM

<b>Key Questions</b>	1. What are the benefits and harms of screening for type 2 diabetes mellitus in children and adolescents?	2. For children and adolescents diagnosed with type 2 diabetes mellitus, what are the benefits and harms of pharmacologic interventions?	3. For children and adolescents diagnosed with type 2 diabetes mellitus, what are the benefits and harms of non-pharmacologic interventions? a. Does the effectiveness of nonpharmacologic interventions vary by: <ul style="list-style-type: none"> <li>• Program components</li> <li>• Intensity (e.g., program duration)</li> <li>• Delivery personnel (e.g., physician, dietician, certified diabetes educator)</li> </ul>	4. For children and adolescents diagnosed with type 2 diabetes mellitus, what are the benefits and harms of pharmacologic interventions compared to non-pharmacologic interventions?
<b>Interventions</b>	<p>Screening strategy of testing overweight and obese children and adolescents with one or more risk factors<sup>6</sup>:</p> <ul style="list-style-type: none"> <li>• Type 2 DM in 1<sup>st</sup> or 2<sup>nd</sup> degree relative</li> <li>• Race/ethnicity (Native American, African American, Latino, Asian American, or Pacific Islander)</li> <li>• Insulin resistance signs (acanthosis nigrans, HTN, dyslipidemia, PCOS, or SGA birth weight)</li> <li>• Maternal history of DM or GDM</li> </ul> <p>Screening is with:</p> <ul style="list-style-type: none"> <li>• fasting plasma glucose</li> <li>• oral glucose tolerance test</li> <li>• HbA1c</li> </ul>	<p>FDA-approved medications in children/adolescents:</p> <ul style="list-style-type: none"> <li>• Metformin</li> <li>• Insulin</li> </ul> <p>Non-FDA approved medications in children/adolescents:</p> <ul style="list-style-type: none"> <li>• Thiazolidinediones (e.g., rosiglitazone, pioglitazone)</li> <li>• Insulin secretagogues [e.g., sulfonylureas (glyburide, glimepiride) and meglitinides]</li> <li>• Glucagon-like peptide-1 receptor agonists (GLP-1 receptor agonists) (e.g., exenatide, liraglutide)</li> <li>• Dipeptidyl peptidase-4 inhibitors (DPP-4 inhibitors) (e.g., sitagliptin)</li> <li>• Amylin analogues (e.g., pramlintide acetate)</li> <li>• Alpha-glucosidase inhibitors (e.g., acarbose)</li> <li>• Sodium-glucose cotransporter 2 inhibitors (SGLT2 inhibitors) (e.g., canagliflozin, dapagliflozin)</li> </ul>	<ul style="list-style-type: none"> <li>• Diet</li> <li>• Weight loss</li> <li>• Physical activity</li> <li>• Behavioral interventions</li> </ul>	Any pharmacologic intervention listed in KQ2

<b>Key Questions</b>	1. What are the benefits and harms of screening for type 2 diabetes mellitus in children and adolescents?	2. For children and adolescents diagnosed with type 2 diabetes mellitus, what are the benefits and harms of pharmacologic interventions?	3. For children and adolescents diagnosed with type 2 diabetes mellitus, what are the benefits and harms of non-pharmacologic interventions? a. Does the effectiveness of nonpharmacologic interventions vary by: <ul style="list-style-type: none"> <li>• Program components</li> <li>• Intensity (e.g., program duration)</li> <li>• Delivery personnel (e.g., physician, dietician, certified diabetes educator)</li> </ul>	4. For children and adolescents diagnosed with type 2 diabetes mellitus, what are the benefits and harms of pharmacologic interventions compared to non-pharmacologic interventions?
<b>Comparators</b>	No screening	Any medication listed above Placebo	Any non-pharmacologic intervention or combination of interventions Placebo	Any non-pharmacologic intervention or combination of interventions listed in KQ3
<b>Outcomes</b>	<p>Long-term outcomes:</p> <ul style="list-style-type: none"> <li>• Diabetes into adulthood</li> <li>• All- cause mortality</li> <li>• Cardiovascular and cerebrovascular morbidity and mortality</li> <li>• Retinopathy</li> <li>• Nephropathy</li> <li>• Neuropathy</li> <li>• Mental health outcomes</li> </ul> <p>Adverse effects to patients: (e.g., pain, infection, false-positives, false-negatives)</p> <p>Health system outcomes (e.g., cost)</p>	<p>Short-term outcomes:</p> <ul style="list-style-type: none"> <li>• Weight loss</li> <li>• Mental health outcomes</li> <li>• Quality of life</li> </ul> <p>Intermediate outcomes:</p> <ul style="list-style-type: none"> <li>• HbA1c</li> <li>• Plasma glucose</li> <li>• Insulin resistance</li> </ul> <p>Long-term outcomes:</p> <ul style="list-style-type: none"> <li>• Diabetes into adulthood</li> <li>• All- cause mortality</li> <li>• Cardiovascular and cerebrovascular morbidity and mortality</li> <li>• Retinopathy</li> <li>• Nephropathy</li> <li>• Neuropathy</li> <li>• Mental health outcomes</li> <li>• Quality of life</li> </ul> <p>Harms:</p> <ul style="list-style-type: none"> <li>• Hypoglycemia</li> <li>• Gastrointestinal side effects</li> <li>• Other harms</li> </ul>	<p>Short-term outcomes:</p> <ul style="list-style-type: none"> <li>• Weight loss</li> <li>• Mental health outcomes</li> <li>• Quality of life</li> </ul> <p>Intermediate outcomes:</p> <ul style="list-style-type: none"> <li>• HbA1c</li> <li>• Plasma glucose</li> <li>• Insulin resistance</li> </ul> <p>Long-term outcomes:</p> <ul style="list-style-type: none"> <li>• Diabetes into adulthood</li> <li>• All- cause mortality</li> <li>• Cardiovascular and cerebrovascular morbidity and mortality</li> <li>• Retinopathy</li> <li>• Nephropathy</li> <li>• Neuropathy</li> <li>• Mental health outcomes</li> <li>• Quality of life</li> </ul> <p>Harms:</p> <ul style="list-style-type: none"> <li>• Hypoglycemia</li> <li>• Other harms</li> </ul>	<p>Short-term outcomes:</p> <ul style="list-style-type: none"> <li>• Weight loss</li> <li>• Mental health outcomes</li> <li>• Quality of life</li> </ul> <p>Intermediate outcomes:</p> <ul style="list-style-type: none"> <li>• HbA1c</li> <li>• Plasma glucose</li> <li>• Insulin resistance</li> </ul> <p>Long-term outcomes:</p> <ul style="list-style-type: none"> <li>• Diabetes into adulthood</li> <li>• All- cause mortality</li> <li>• Cardiovascular and cerebrovascular morbidity and mortality</li> <li>• Retinopathy</li> <li>• Nephropathy</li> <li>• Neuropathy</li> <li>• Mental health outcomes</li> <li>• Quality of life</li> </ul> <p>Harms:</p> <ul style="list-style-type: none"> <li>• Hypoglycemia</li> <li>• Gastrointestinal side effects</li> <li>• Other harms</li> </ul>

<b>Key Questions</b>	1. What are the benefits and harms of screening for type 2 diabetes mellitus in children and adolescents?	2. For children and adolescents diagnosed with type 2 diabetes mellitus, what are the benefits and harms of pharmacologic interventions?	3. For children and adolescents diagnosed with type 2 diabetes mellitus, what are the benefits and harms of non-pharmacologic interventions? a. Does the effectiveness of nonpharmacologic interventions vary by: <ul style="list-style-type: none"> <li>• Program components</li> <li>• Intensity (e.g., program duration)</li> <li>• Delivery personnel (e.g., physician, dietician, certified diabetes educator)</li> </ul>	4. For children and adolescents diagnosed with type 2 diabetes mellitus, what are the benefits and harms of pharmacologic interventions compared to non-pharmacologic interventions?
<b>Setting</b>	Inpatient or outpatient	Inpatient or outpatient	Outpatient (excluding school-based programs)	Inpatient or outpatient-pharmacologic interventions; Outpatient (excluding school-based programs)- non-pharmacologic interventions

*Abbreviations:* DM= diabetes mellitus; HTN= hypertension; PCOS= polycystic ovary syndrome; SGA=small-for-gestational-age; GDM= gestational diabetes mellitus

## Methods

We assessed nomination #0770 *Type 2 Diabetes Mellitus in Children and Adolescents* for priority for a systematic review or other AHRQ EHC report with a hierarchical process using established selection criteria (Appendix A). Assessment of each criteria determined the need for evaluation of the next one.

1. Determine the *appropriateness* of the nominated topic for inclusion in the EHC program.
2. Establish the overall *importance* of a potential topic as representing a health or healthcare issue in the United States.
3. Determine the *desirability of new evidence review* by examining whether a new systematic review or other AHRQ product would be duplicative.
4. Assess the *potential impact* a new systematic review or other AHRQ product.
5. Assess whether the *current state of the evidence* allows for a systematic review or other AHRQ product (feasibility).
6. Determine the *potential value* of a new systematic review or other AHRQ product.

### Appropriateness and Importance

We assessed the nomination for appropriateness and importance.

### Desirability of New Review/Duplication

We searched for high-quality, completed or in-process evidence reviews published in the last three years on the key questions of the nomination. See Appendix B for sources searched.

### Impact of a New Evidence Review

The impact of a new evidence review was qualitatively assessed by analyzing the current standard of care, the existence of potential knowledge gaps, and practice variation. We considered whether it was possible for this review to influence the current state of practice through various dissemination pathways (practice recommendation, clinical guidelines, etc.).

### Feasibility of New Evidence Review

We conducted a literature search in PubMed from April 2013 to April 2018.

For KQ 1 on screening, we reviewed all identified titles and abstracts for inclusion and classified them by study design, to assess the size and scope of a potential evidence review.

Because a large number of articles were identified for KQs 2, 3, and 4 on pharmacologic and non-pharmacologic treatments, we reviewed a random sample of 200 titles and abstracts for inclusion and classified them by study design, to assess the size and scope of a potential evidence review. We then calculated the projected total number of included studies based on the proportion of studies included from the random sample.

See Appendix C for the PubMed search strategy and links to the ClinicalTrials.gov searches.

### Compilation of Findings

We constructed a table with the selection criteria and our assessments (Appendix A).

## Results

### Appropriateness and Importance

This is an appropriate and important topic. Type 2 diabetes in children and adolescents represents a significant health burden with an incidence of about 5000 new cases of diabetes mellitus diagnosed each year in youth 10 to 19 years old.<sup>2</sup> Diabetes in this population is associated with high costs to patients and health care systems.



## Desirability of New Review/Duplication

A new evidence review on Type 2 Diabetes Mellitus in Children and Adolescents would not be duplicative of an existing product. One 2016 systematic review<sup>7</sup> addresses KQ 2 on pharmacologic treatments of children and adolescents with type 2 diabetes. This review would only be partially duplicative as it only covers some of the medications interested in by the nominator. In addition the review focuses only on short-term outcomes, primarily HbA1c and adverse effects, and does not address any long-term outcomes in which the nominator has expressed interest. See Table 2, Duplication column.

## Impact of a New Evidence Review

A new systematic review on the Type 2 Diabetes Mellitus in Children and Adolescents may have a high level of impact due to practice variation and lack of current guidance for screening and treatments for children and adolescents with type 2 diabetes.

## Feasibility of a New Evidence Review

A new evidence review examining Type 2 Diabetes Mellitus in Children and Adolescents is not feasible due to the limited research identified. For screening in KQ 1, we examined all of the results and identified 3 observational studies.<sup>8-10</sup> For non-pharmacologic treatments in KQ 3, we identified only 1 RCT<sup>11</sup> based on our random sample for treatments. From this we estimated 3 relevant studies for KQ 3.

We identified four clinical trials addressing pharmacologic treatments (KQ 2)—two have been completed<sup>12, 13</sup> and two are still active.<sup>14, 15</sup> See Table 2, Feasibility column.

**Table 2.** Key questions and Results for Duplication and Feasibility

Key Question	Duplication (1/2015-12/2018)	Feasibility (4/2013-4/2018)
KQ 1 - screening	Total number of identified systematic reviews: 0	<p><u>Size/scope of review</u>            Relevant Studies Identified: 3                ○ Observational: 3<sup>8-10</sup></p> <p><u>Clinicaltrials.gov</u>            We identified no relevant clinical trials.</p>
KQ 2- pharmacologic treatment vs. pharmacologic treatment	Total number of identified systematic reviews: 1 <ul style="list-style-type: none"> <li>• Other review: 1<sup>7</sup></li> </ul>	<p><u>Size/scope of review</u>            Relevant Studies Identified: 0            Projected Total: 0</p> <p><u>Clinicaltrials.gov</u></p> <ul style="list-style-type: none"> <li>• Recruiting: 0</li> <li>• Active: 2<sup>14, 15</sup></li> <li>• Complete: 2<sup>12, 13</sup></li> </ul>
KQ 3- Non-pharmacologic treatment vs. non-pharmacologic treatment	Total number of identified systematic reviews: 0	<p><u>Size/scope of review</u>            Relevant Studies Identified: 1                ○ Type: RCT<sup>11</sup>            Projected Total: 3</p> <p><u>Clinicaltrials.gov</u>            We identified no relevant clinical trials.</p>
KQ 4- pharmacologic treatment vs. non-pharmacologic treatment	Total number of identified systematic reviews: 0	<p><u>Size/scope of review</u>            Relevant Studies Identified: 0            Projected Total: 0</p> <p><u>Clinicaltrials.gov</u>            We identified no relevant clinical trials.</p>

*Abbreviations:* AHRQ=Agency for Healthcare Research and Quality; KQ=Key Question

## Summary of Findings

- Appropriateness and importance: The topic is both appropriate and important.
- Duplication: A new review would not be duplicative of an existing product. One systematic review was identified which addressed only KQ 2 on pharmacologic treatments, but no other reviews were identified to cover the other KQs.
- Impact: A new systematic review has high potential. There is practice variation and lack of updated guidance on screening tools and treatments (pharmacologic and non-pharmacologic) for type 2 diabetes in children and adolescents.
- Feasibility: A new review is likely not feasible based on our estimation of the evidence base from a review of the results on screening (KQ 1) and a random sample of treatment results (KQs 2, 3, and 4).

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## Appendix A. Selection Criteria Summary

Selection Criteria	Assessment
<b>1. Appropriateness</b>	
1a. Does the nomination represent a health care drug, intervention, device, technology, or health care system/setting available (or soon to be available) in the U.S.?	Yes, this nomination does represent drugs and interventions available in the U.S.
1b. Is the nomination a request for a systematic review?	Yes, this is a request for a systematic review.
1c. Is the focus on effectiveness or comparative effectiveness?	Yes, this nomination focuses on comparative effectiveness.
1d. Is the nomination focus supported by a logic model or biologic plausibility? Is it consistent or coherent with what is known about the topic?	Yes, this nomination is supported by biologic plausibility and is consistent with what is known on type 2 diabetes in children and adolescents.
<b>2. Importance</b>	
2a. Represents a significant disease burden; large proportion of the population	Yes, type 2 diabetes in children and adolescents represents a significant disease burden. Approximately 5,000 new cases of type 2 diabetes mellitus (diabetes) are diagnosed each year in youth. <sup>1</sup>
2b. Is of high public interest; affects health care decision making, outcomes, or costs for a large proportion of the US population or for a vulnerable population	Yes, type 2 diabetes affects many US children, with particularly high rates among racial and ethnic minorities. <sup>2</sup>
2c. Represents important uncertainty for decision makers	Yes, this nomination represents uncertainty for clinicians and other decision makers. There is not clear guidance for screening and pharmacologic and non-pharmacologic management for type 2 diabetes in children and adolescents.
2d. Incorporates issues around both clinical benefits and potential clinical harms	Yes, this nomination addresses both benefits and harms.
2e. Represents high costs due to common use, high unit costs, or high associated costs to consumers, to patients, to health care systems, or to payers	Yes, this nomination represents high costs based on common use of medications and high disease prevalence.
<b>3. Desirability of a New Evidence Review/Duplication</b>	
3. Would not be redundant (i.e., the proposed topic is not already covered by available or soon-to-be available high-quality systematic review by AHRQ or others)	An AHRQ review would not be redundant as we identified one review which covered a part of the nomination. For KQ 2, we identified one 2016 systematic review <sup>7</sup> which examined pharmacologic treatments in patients birth to 18 years old which is partially duplicative. This review covers only some of the medications interested in by the nominator and addresses only short-term outcomes, primarily HbA1c and adverse effects, while not addressing any long-term outcomes.
<b>4. Impact of a New Evidence Review</b>	
4a. Is the standard of care unclear (guidelines not available or guidelines inconsistent, indicating an information gap that may be addressed by a new evidence review)?	Yes, standard of care for type 2 diabetes in children and adults is unclear because evidence for guidelines is now or close to being outdated.
4b. Is there practice variation (guideline inconsistent with current practice, indicating a potential implementation gap and not best addressed by a new evidence review)?	Yes, practice variation exists in screening and treatment of children and adolescents for type 2 diabetes. Regarding pharmacologic management, many medications are used off label in this population.
<b>5. Primary Research</b>	

Selection Criteria	Assessment
<p>5. Effectively utilizes existing research and knowledge by considering:</p> <ul style="list-style-type: none"> <li>- Adequacy (type and volume) of research for conducting a systematic review</li> <li>- Newly available evidence (particularly for updates or new technologies)</li> </ul>	<p>We determined that this review is likely not feasible.</p> <p><i>Size/scope of review:</i> We estimated only a total of 6 studies, 3 studies across KQ 1 and 3 studies relevant to KQ 3.</p> <p><i>ClinicalTrials.gov.:</i> We identified 4 trials, 2 completed and 2 active, not recruiting which addressed KQ 2.</p>

*Abbreviations:* AHRQ=Agency for Healthcare Research and Quality; KQ=Key Question;

## Appendix B. Search for Evidence Reviews (Duplication)

Listed are the sources searched.

Search date: 01/01/2015 to 12/31/2018

AHRQ: Evidence reports and technology assessments, USPSTF recommendations

VA Products: PBM, and HSR&D (ESP) publications, and VA/DoD EBCPG Program

Cochrane Systematic Reviews and Protocols <http://www.cochranelibrary.com/>

PubMed

PubMed Health <http://www.ncbi.nlm.nih.gov/pubmedhealth/>

HTA (CRD database): Health Technology Assessments <http://www.crd.york.ac.uk/crdweb/>

PROSPERO Database (international prospective register of systematic reviews and protocols)

<http://www.crd.york.ac.uk/prospero/>

CADTH (Canadian Agency for Drugs and Technologies in Health) <https://www.cadth.ca/>

DoPHER (Database of promoting health effectiveness reviews)

<http://eppi.ioe.ac.uk/webdatabases4/Intro.aspx?ID=9>

ECRI institute <https://www.ecri.org/Pages/default.aspx>

PsycINFO (Ovid)

## Appendix C. Search Strategy & Results (Feasibility)

Topic: Type 2 Diabetes Mellitus in Children and Adolescents Date: April 5, 2018 Database Searched: MEDLINE(PubMed)	
Concept	Search String
Type 2 Diabetes Mellitus NOT Gestational NOT Type 1	(((((("Diabetes Mellitus, Type 2"[Mesh] OR ((Diabetes[Title/Abstract] OR DM[Title/Abstract])) AND (two[Title/Abstract] OR 2[Title/Abstract] OR II[Title/Abstract])))) NOT ((("Diabetes, Gestational"[Mesh] OR "Gestational Diabetes Insipidus" [Supplementary Concept]) OR gestational[Title/Abstract]))) NOT ((("Diabetes Mellitus, Type 1"[Mesh] OR ((diabetes[Title/Abstract] OR DM[Title/Abstract])) AND (1[Title/Abstract] OR i[Title/Abstract]))))
AND	
Children and Adolescents NOT Pregnant Women or Infants	(((((((((("Pediatrics"[Mesh] OR "Pediatric Obesity"[Mesh] OR ( "Adolescent"[Mesh] OR "Adolescent Health Services"[Mesh] OR "Adolescent Medicine"[Mesh] OR "Adolescent Health"[Mesh] ) ) OR ( "Child"[Mesh] OR "Child, Preschool"[Mesh] ) ) ) ) ) OR (((youth [tiab] OR child[Title/Abstract] OR children[Title/Abstract] OR adolescent[Title/Abstract] OR adolescents[Title/Abstract] OR pediatric[Title/Abstract] OR pediatrics[Title/Abstract])))) NOT (((((((("Pregnant Women"[Mesh] OR "Pregnancy"[Mesh] OR "Infant"[Mesh]) OR ((pregnant[Title/Abstract] OR pregnancy[Title/Abstract] OR infant[Title/Abstract]))) NOT "Young Adult"[Mesh])
NOT	
Not Editorials, etc.	(((((("Letter"[Publication Type]) OR "News"[Publication Type] OR "Patient Education Handout"[Publication Type] OR "Comment"[Publication Type] OR "Editorial"[Publication Type])) OR "Newspaper Article"[Publication Type]
Not Surgery or Prevention	(((((("prevention and control" [Subheading] OR "Tertiary Prevention"[Mesh] OR "Secondary Prevention"[Mesh] OR "Primary Prevention"[Mesh] OR ( "General Surgery"[Mesh] OR "Surgical Procedures, Operative"[Mesh] OR "surgery" [Subheading] ) ) OR "Surgeons"[Mesh])) OR ((prevention[Title/Abstract] OR surgery[Title/Abstract] OR surgical[Title/Abstract] OR surgeons[Title/Abstract]))
Limit to last 5 years ; human ; English ; children and adolescents	Filters activated: published in the last 5 years, Humans, English, Child: birth-18 years.
KQ1 Screening #100 N=23	("Mass Screening"[Mesh] AND ((screen[Title/Abstract] OR screening[Title/Abstract]))

<p>SR=4  <a href="https://www.ncbi.nlm.nih.gov/sites/myncbi/r.relevo.1/collections/54690742/public/">https://www.ncbi.nlm.nih.gov/sites/myncbi/r.relevo.1/collections/54690742/public/</a>  RCT=3  <a href="https://www.ncbi.nlm.nih.gov/sites/myncbi/r.relevo.1/collections/54690747/public/">https://www.ncbi.nlm.nih.gov/sites/myncbi/r.relevo.1/collections/54690747/public/</a>  Other=16  <a href="https://www.ncbi.nlm.nih.gov/sites/myncbi/r.relevo.1/collections/54690750/public/">https://www.ncbi.nlm.nih.gov/sites/myncbi/r.relevo.1/collections/54690750/public/</a></p>	
<p>KQ 2 &amp; 4 Pharmacologic interventions (as specified)  N= 91</p>	<p>((((((("Metformin"[Mesh]) OR "Insulin"[Mesh]) OR "Thiazolidinediones"[Mesh]) OR "Glyburide"[Mesh]) OR "Glucagon-Like Peptide-1 Receptor"[Mesh])) OR ((metformin[Title/Abstract] OR insulin[Title/Abstract] OR thiazolidinediones[Title/Abstract] OR rosiglitazone[Title/Abstract] OR pioglitazone[Title/Abstract] OR secretagogues[Title/Abstract] OR sulfonylureas[Title/Abstract] OR glyburide[Title/Abstract] OR glimepiride[Title/Abstract] OR meglitinides[Title/Abstract] OR "receptor agonists"[Title/Abstract] OR exenatide[Title/Abstract] OR liraglutide[Title/Abstract]))) AND (((("Drug Therapy"[Mesh] OR "drug therapy" [Subheading]) OR ((drug[Title/Abstract] OR drugs[Title/Abstract] OR medication[Title/Abstract] OR medicine[Title/Abstract] OR pharmacolo*[Title/Abstract])))</p>
<p>SR=4  <a href="https://www.ncbi.nlm.nih.gov/sites/myncbi/r.relevo.1/collections/54690765/public/">https://www.ncbi.nlm.nih.gov/sites/myncbi/r.relevo.1/collections/54690765/public/</a>  RCT=74  <a href="https://www.ncbi.nlm.nih.gov/sites/myncbi/r.relevo.1/collections/54690780/public/">https://www.ncbi.nlm.nih.gov/sites/myncbi/r.relevo.1/collections/54690780/public/</a>  Other=13  <a href="https://www.ncbi.nlm.nih.gov/sites/myncbi/r.relevo.1/collections/54811743/public/">https://www.ncbi.nlm.nih.gov/sites/myncbi/r.relevo.1/collections/54811743/public/</a></p>	
<p>KQ 3 &amp; 4 Non-pharmacologic interventions NOT school based interventions  N=363</p>	<p>((((((("Diet"[Mesh] OR "Diet Therapy"[Mesh]) OR "Nutrition Therapy"[Mesh]) OR ( "Weight Loss"[Mesh] OR "Weight Reduction Programs"[Mesh] OR "Diet, Reducing"[Mesh] )) OR "Exercise"[Mesh]) OR ( "Behavioral Medicine"[Mesh] OR "Cognitive Therapy"[Mesh] ))) OR ((diet[Title/Abstract] OR nutrition[Title/Abstract] OR nutritional[Title/Abstract] OR weight[Title/Abstract] OR activity[Title/Abstract] OR exercise[Title/Abstract] OR behavioral[Title/Abstract] OR cognitive[Title/Abstract]))) NOT ((("School Health Services"[Mesh]) OR ((school[Title/Abstract] OR school-based[Title/Abstract])))</p>
<p>SR=18  <a href="https://www.ncbi.nlm.nih.gov/sites/myncbi/r.relevo.1/collections/54690802/public/">https://www.ncbi.nlm.nih.gov/sites/myncbi/r.relevo.1/collections/54690802/public/</a>  RCT=130  <a href="https://www.ncbi.nlm.nih.gov/sites/myncbi/r.relevo.1/collections/54690810/public/">https://www.ncbi.nlm.nih.gov/sites/myncbi/r.relevo.1/collections/54690810/public/</a>  Other=215  <a href="https://www.ncbi.nlm.nih.gov/sites/myncbi/r.relevo.1/collections/54690814/public/">https://www.ncbi.nlm.nih.gov/sites/myncbi/r.relevo.1/collections/54690814/public/</a></p>	
<p>Systematic Review</p>	<p>PubMed subsection "Systematic [sb]"</p>



Randomized Controlled Trials	Cochrane Sensitive Search Strategy for RCT's “(((((((groups[tiab])) OR (trial[tiab])) OR (randomly[tiab])) OR (drug therapy[sh])) OR (placebo[tiab])) OR (randomized[tiab])) OR (controlled clinical trial[pt])) OR (randomized controlled trial[pt])”
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**Clinicaltrials.gov**

**1 Study** found for: **screening** | Active, not recruiting, Completed Studies | Diabetes Mellitus, Type 2 | Child | Start date from 01/01/2013 to 12/31/2018

[https://clinicaltrials.gov/ct2/results?cond=Diabetes+Mellitus%2C+Type+2&term=screening&strd\\_s=01%2F01%2F2013&strd\\_e=12%2F31%2F2018&cntry=&state=&city=&dist=&Search=Search&recrs=d&recrs=e&age=0](https://clinicaltrials.gov/ct2/results?cond=Diabetes+Mellitus%2C+Type+2&term=screening&strd_s=01%2F01%2F2013&strd_e=12%2F31%2F2018&cntry=&state=&city=&dist=&Search=Search&recrs=d&recrs=e&age=0)

**8 Studies** found for: Active, not recruiting, Completed Studies | Diabetes Mellitus, Type 2 | **drug therapy** | Child | Start date from 01/01/2013 to 12/31/2018

[https://clinicaltrials.gov/ct2/results?cond=Diabetes+Mellitus%2C+Type+2&term=&type=&rslt=&recrs=d&recrs=e&age\\_v=&age=0&gndr=&intr=drug+therapy&titles=&outc=&spons=&lead=&id=&cntry=&state=&city=&dist=&locn=&strd\\_s=01%2F01%2F2013&strd\\_e=12%2F31%2F2018&prcd\\_s=&prcd\\_e=&sfpd\\_s=&sfpd\\_e=&lupd\\_s=&lupd\\_e=](https://clinicaltrials.gov/ct2/results?cond=Diabetes+Mellitus%2C+Type+2&term=&type=&rslt=&recrs=d&recrs=e&age_v=&age=0&gndr=&intr=drug+therapy&titles=&outc=&spons=&lead=&id=&cntry=&state=&city=&dist=&locn=&strd_s=01%2F01%2F2013&strd_e=12%2F31%2F2018&prcd_s=&prcd_e=&sfpd_s=&sfpd_e=&lupd_s=&lupd_e=)

**21 Studies** found for: Active, not recruiting, Completed Studies | Diabetes Mellitus, Type 2 | **behavior OR cognitive OR diet OR weight** | Child | Start date from 01/01/2013 to 12/31/2018

[https://clinicaltrials.gov/ct2/results?cond=Diabetes+Mellitus%2C+Type+2&term=&intr=behavior+OR+cognitive+OR+diet+OR+weight&strd\\_s=01%2F01%2F2013&strd\\_e=12%2F31%2F2018&cntry=&state=&city=&dist=&Search=Search&recrs=d&recrs=e&age=0](https://clinicaltrials.gov/ct2/results?cond=Diabetes+Mellitus%2C+Type+2&term=&intr=behavior+OR+cognitive+OR+diet+OR+weight&strd_s=01%2F01%2F2013&strd_e=12%2F31%2F2018&cntry=&state=&city=&dist=&Search=Search&recrs=d&recrs=e&age=0)