

AHRQ Systematic Review Surveillance Program

CER #57: Methods for Insulin Delivery and Glucose Monitoring: Comparative Effectiveness

Original Release Date: July 2012

Surveillance Report: February 2016

Summary of Key Findings from Surveillance Report:

- Key Question 1: Original review conclusions are likely current.
- Key Question 2: The original review's conclusion of no evidence examining the effectiveness of real time continuous glucose monitoring (rt-CGM) versus self-monitoring of blood glucose (SMBG) in pregnant women with existing type 1 diabetes may be out of date. One RCT comparing rt-CGM to SMBG during labor and delivery on neonatal hypoglycemia in women with existing type 1 diabetes that found no difference between groups. In addition, while the original review found that sensor augmented pump therapy (SAP) was more effective than multiple daily injections with self-monitoring of blood glucose (MDI/SMBG) at lowering HbA_{1c}, it included no studies examining differences in patient subpopulations. We identified one article which found that among patients with type 1 diabetes, those with a higher baseline HbA_{1c}, who were ≥ 17 at the time of diagnosis, and who were ≥ 36 at the time of randomization experienced greater benefit with use of SAP.
- **Signal Assessment:** The signals examined in this surveillance assessment suggest that the original systematic review may not be current.

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Conflict of Interest:

None of the investigators has any affiliations or financial involvement that conflicts with the material presented in this report.

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Introduction

The purpose of the surveillance process for the EPC Program is to decide if the findings of a systematic review are current. Approximately 25 systematic reviews are selected for surveillance annually based on popularity, use in obtaining continuing medical education certificates, potential impact for changing the field, and use in clinical practice guidelines.

Comparative Effectiveness Review (CER) #57 titled “Methods for Insulin Delivery and Glucose Monitoring: Comparative Effectiveness” was originally released in July, 2012.¹

The key questions for the original review are as follows:

Key Question 1. In patients receiving intensive insulin therapy, does mode of delivery (continuous subcutaneous insulin infusion [CSII] vs. multiple daily injections [MDI]) have a differential effect on process measures, intermediate outcomes, and clinical outcomes in patients with diabetes mellitus?

Do these effects differ by:

- a. Type 1 or type 2 diabetes status?
- b. Age: very young children, adolescents, and adults, including older adults (age >65 years)?
- c. Pregnancy status: pre-existing type 1 or type 2 diabetes?

Key Question 2. In patients using intensive insulin therapy (MDI or CSII), does the type of glucose monitoring (real time continuous glucose monitoring [rt-CGM] vs. self-monitoring of blood glucose [SMBG]) have a differential effect on process measures, intermediate outcomes, and clinical outcomes in patients with diabetes mellitus (i.e., what is the incremental benefit of rt-CGM in patients already using intensive insulin therapy)?

Do these effects differ by:

- a. Type 1 or type 2 diabetes status?
- b. Age: very young children, adolescents, and adults, including older adults (age >65 years)?
- c. Pregnancy status: pre-existing type 1 or type 2 diabetes?
- d. Intensive insulin delivery: MDI or CSII?

Our surveillance assessment began in July 2015. We conducted an electronic search for literature published since the end date of the original review. After completing a scan of this literature to identify evidence potentially related to the key questions in this review, we contacted experts involved in the original review to request their opinions as to whether the conclusions had changed.

Methods

Literature Searches

We conducted a literature search of PubMed covering January 2011 to July 2015 using the identical search strategy used for the original systematic review¹ and searching for studies published since the end date of the original review.

The search was conducted to assess the currency of conclusions. This process included selecting journals from among the top 10 journals from relevant specialty subject areas (Appendix A) and among those most highly represented among the references for the original systematic review (Appendix B). The included journals were six high-profile general medical interest journals (Annals of Internal Medicine, British Medical Journal, Cochrane Database of Systematic Reviews, Journal of the American Medical Association, Lancet, and New England Journal of Medicine), and five specialty journals (Diabetes Care,

Diabetic Medicine, Diabetes and Metabolism, Diabetes Technology and Therapeutics, and Pediatrics Diabetes). The search strategy is reported in Appendix C.

Study Selection

Using the same inclusion and exclusion criteria as the original systematic review (see Appendix D), one investigator reviewed the titles and abstracts of the 11 high-impact journal search results (Appendix E).

Expert Opinion

We shared the conclusions of the original systematic review and most recent surveillance assessment, findings from the literature analysis, and the newly identified studies with eight experts in the field (original peer reviewers, technical expert panel members [TEP]) to request their assessment of the currency of report conclusions and their recommendations of any relevant new studies. Two subject matter experts responded to our request. Appendix F shows the form experts were asked to complete.

Horizon Scanning

The AHRQ Healthcare Horizon Scanning System identifies emerging health care technologies and innovations with the potential to impact health care for AHRQ's 14 priority conditions.² We reviewed the Diabetes Mellitus section² to identify new potentially high-impact interventions related to the key questions in this systematic review. Potentially high impact interventions were considered in the final assessment of the need to update.

FDA Class I Device Recalls

We searched the FDA MedWatch online database website for Class I device recalls relevant to the key questions in this systematic review.

Check for Qualitative Signals

The authors of the original systematic review conducted qualitative and quantitative synthesis of data on the comparative effectiveness of mode of insulin delivery and type of glucose monitoring on process measures, intermediate outcomes, and clinical outcomes in patients with diabetes mellitus. We compared the conclusions of the included abstracts to the conclusions of the original systematic review and assessed expert opinions to identify qualitative signals about the currency of conclusions.

Compilation of Findings and Conclusions

For this assessment we constructed a summary table (Appendix G) that includes the key questions and conclusions from the original systematic review, findings of the new literature search, FDA class I device recalls, and the expert assessments that pertained to each key question. We categorized the currency of conclusions using a 3-category scheme:

- Original conclusion is still valid and this portion of the systematic review is likely current
- Original conclusion is possibly out of date and this portion of the systematic review may not be current
- Original conclusion is out of date.

We considered the following factors when making our assessments:

- If we found no new evidence or only confirmatory evidence and all responding experts assessed the systematic review conclusion as still valid, we classified the systematic review conclusion as likely current.

- If we found some new evidence that might change the systematic review conclusion, and /or a minority of responding experts assessed the systematic review conclusion as having new evidence that might change the conclusion, then we classified the systematic review conclusion as possibly not current.
- If we found new evidence that rendered the systematic review conclusion out of date or no longer applicable, we classified the systematic review conclusion as out of date. Recognizing that our literature searches were limited, we reserved this category only for situations where a limited search would produce prima facie evidence that a conclusion was out of date, such as the withdrawal of a drug or surgical device from the market, a black box warning from FDA, etc.

Signal Assessment for Currency of the Systematic Review

We used the following considerations in our assessment of currency of the systematic review:

- **Strong signal:** A report is considered to have a strong signal if new evidence is identified that clearly renders conclusions from the original systematic review out of date, such as the addition or removal of a drug or device from the market or a new FDA boxed warning.
- **Medium signal:** A report is considered to have a medium signal when new evidence is identified which may change the conclusions from the original systematic review. This may occur when abstract review and expert assessment indicates that some conclusions from the original systematic review may not be current, or when it is unclear from abstract review how new evidence may impact the findings from the original systematic review.
- **Weak signal:** A report is considered to have a weak signal if no new evidence is identified that would change the conclusions from the original systematic review. This may occur when no new evidence is identified, or when some new evidence is identified but it is clear from abstract review and expert assessment that the new evidence is unlikely to change the conclusions of the original systematic review.

Results

Literature Search

The literature search identified 569 unique titles from the 11 selected high profile general medical and specialty journals. A random selection of 200 articles from the 11 selected high profile general medical and specialty journals is provided in Appendix E. Upon abstract review, 198 of the randomly selected articles were rejected because they did not meet the original systematic review inclusion criteria (see Appendix D). The remaining 2 articles³⁻⁴ were examined for potential to change the results of the original review.

Horizon Scanning

None of the interventions in the horizon scanning report for Priority Area 07: Diabetes Mellitus overlapped with the key questions in the original systematic review.¹ Thus, we did not identify new interventions with high-impact potential for this topic.

FDA Device Recalls

Since the original systematic review was published, one Class I device recall related to a device included in the original review was issued by the FDA. The Animas 2020 Insulin Infusion Pump, a CSII, was recalled in April of 2013. The manufacturer identified a component issue affecting a small supply of this product. This component issue may trigger pumps to sound a false alarm indicating there has been a loss of prime, an occlusion, or no cartridge has been detected.

Expert Opinion

We shared the conclusions of the original systematic review with eight experts in the field (six original peer reviewers, and two TEP members) to request their assessment of the currency of review conclusions and their recommendations of any relevant new studies. Two subject matter experts responded.

One expert noted that results of large cross sectional studies differ from the findings of RCTs in pediatric populations, and identified two⁵⁻⁶ studies. Both studies were excluded due to study design. The second reviewer identified three⁷⁻⁹ studies related to Key Question 1. All three studies were excluded based on comparator criteria.

Reviewers felt that the original review's conclusions were up to date, but should provide more information on the limitations of the available literature. One expert noted that Key Question 1 conclusions may not apply to infants, toddlers, and children with neonatal diabetes mellitus due to limited data in these populations. This reviewer also felt that conclusions on adolescents should be interpreted with caution due to different ages among those in MDI vs. CSII treatment groups. One expert noted that CSII technology had changed since the original review was published in 2012 but knew of no relevant studies.

Identifying Qualitative Signals

Appendix G shows the original key questions, the conclusions of the original report and the most recent surveillance report, the results of the literature search, the experts' assessments, FDA device recalls, and the conclusions of the Scientific Resource Center (SRC) regarding the currency of the original review.

For Key Question 1, we identified no new studies comparing CSII to MDI alone. However, one reviewer noted that since 2012, suspend pumps have been added to CSII technology, potentially impacting the effect of CSII on hypoglycemia. No studies were identified or provided.

For Key Question 2, we identified one RCT⁴ comparing rt-CMG to SMBG during labor and delivery on neonatal hypoglycemia in women with existing type 1 diabetes. Results indicate no difference between groups. No studies comparing rt-CMG to SMBG among pregnant women with existing type 1 diabetes were identified in the original review.

While the original review found that sensor augmented pumps (SAP), a technology that combines CSII with rt-CGM, were more effective than MDI with SMBG at lowering HbA_{1c} in type 1 diabetes patients, it included no comparisons by subgroup. We identified one article³ that examined subgroup differences based on data¹⁰ from the STAR 3 RCT. The original systematic review included a number of articles from STAR 3 RCT¹⁰, which found that among a population of type 1 diabetes patients, those receiving SAP had lower levels of HbA_{1c} compared to those receiving MDI/SMBG at 1 year (7.5% to 8.1%, p<0.001), and that a greater proportion of SAP patients reached target levels of HbA_{1c} compared to MDI/SMBG patients. One new article³ reported greater benefits associated with SAP for patients with a higher baseline HbA_{1c}, and for patients who were 17 or older at the time of diagnosis, and for those who were 36 or older at the time of randomization.

Signal Assessment

The SRC conclusions based on the results of the prior surveillance assessment, literature published since the original report, FDA device recalls, horizon scanning, and expert assessment is that:

- Key Question 1: The original review conclusions are likely current.
- Key Question 2: The original review's conclusion of no evidence examining the effectiveness of real time continuous glucose monitoring (rt-CGM) versus self-monitoring of blood glucose

(SMBG) in pregnant women with existing type 1 diabetes may be out of date. One RCT comparing rt-CGM to SMBG during labor and delivery on neonatal hypoglycemia in women with existing type 1 diabetes that found no difference between groups. In addition, while the original review found that the sensor augmented pump therapy (SAP) was more effective than multiple daily injections with self-monitoring of blood glucose (MDI with SMBG) at lowering HbA_{1c}, it included no studies examining differences in patient subpopulations. We identified one article which found that among patients with type 1 diabetes, those with a higher baseline HbA_{1c}, who were ≥ 17 at the time of diagnosis, and who were ≥ 36 at the time of randomization experienced greater benefit with use of SAP.

The signal for this report is medium suggesting that some of the conclusions in the original systematic review may not be current.

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Appendices

Appendix A: Top 10 Journals

Appendix B: Most Cited Journals from Original Systematic Review

Appendix C: Original Search Strategy

Appendix D: Inclusion and Exclusion Criteria from Original Systematic Review

Appendix E: Literature Search Results

Appendix F: Questionnaire Sent to Expert Reviewers

Appendix G: Summary Table

Appendix A. Top 10 Journals

In the Journal Citation Reports database, the science and social science sections were searched by subject area discipline(s) for each surveillance reports topic area. For each subject area discipline, the list was constructed by selecting the top 10 journals from the 5 year citation impact factor average list. Selected citations were downloaded in .csv format.

Endocrinology and Metabolism:	Top 10 General Medical:
1. Endocrine Reviews	1. Annals of Internal Medicine
2. Cell Metabolism	2. Archives of Internal Medicine
3. Nature Reviews: Endocrinology	3. BMC Medicine
4. Frontiers in Neuroendocrinology	4. The BMJ
5. The Lancet Diabetes & Endocrinology	5. Journal of Cachexia, Sarcopenia and Muscle
6. Trends in Endocrinology & Metabolism	6. JAMA Internal Medicine
7. Diabetes Care	7. JAMA
8. Obesity Reviews	8. The Lancet
9. Diabetes	9. New England Journal of Medicine
10. Antioxidants & Redox Signaling	10. PLOS Medicine

Appendix B. Most Cited Journals from Original Systematic Review

Rank	Journal	# of Citations
1	Diabetes Care	14
2	Diabetes Technology & Therapeutics	5
3	Diabetic Medicine	4
4	Diabetes & Metabolism	3
4	Pediatrics Diabetes	3
6	Diabetologia	2
6	Journal of Pediatric Endocrinology & Metabolism	2
6	New England Journal of Medicine	2

Appendix C. Search Strategy

MEDLINE searched via PubMed on July 7, 2015	
<p>(((((("Diabetes Mellitus"[mh] OR Diabet*[tiab] OR hyperglycem*[tiab] OR hyperglycaem*[tiab]) AND ("Insulin Infusion Systems"[mh] OR "continuous subcutaneous insulin"[tiab] OR CSII[tiab] OR "insulin pump"[tiab] OR "insulin pumps"[tiab] OR "pump therapy"[tiab] OR "pump treatment"[tiab] OR "artificial pancreas"[tiab] OR ("Monitoring, Ambulatory"[mh] AND (glucose[tiab] OR insulin[tiab] OR glycem*[tiab] OR glycaem*[tiab])) OR "CGM"[tiab] OR ("continuous glucose"[tiab] AND (monitor*[tiab] OR sensing[tiab] OR sensor*[tiab])))) NOT (animal[mh] NOT human [mh])))</p>	Original Search
<p>AND ((((((("Annals of internal medicine"[Journal]) OR "BMJ (Clinical research ed.)"[Journal]) OR "The Cochrane database of systematic reviews"[Journal]) OR "JAMA"[Journal]) OR "Lancet (London, England)"[Journal]) OR "The New England journal of medicine"[Journal]))</p>	Journal Limits : general medicine
<p>))) OR (((("Diabetes care"[Journal]) OR "Diabetic medicine : a journal of the British Diabetic Association"[Journal]) OR "Diabetes technology & therapeutics"[Journal]) OR "Diabetes & metabolism"[Journal]) OR "Pediatric diabetes"[Journal]))</p>	Journal Limits : specialty journals
<p>AND ("2011/01/01"[Date - Publication] : "3000"[Date - Publication])</p>	Date Limits

Appendix D. Inclusion and Exclusion Criteria from Original Systematic Review

Population and condition of interest

- All studies included human subjects exclusively.
- We included studies of adults, adolescents, and children with a formal diagnosis of diabetes mellitus and pregnant women with pre-existing diabetes.
- Acceptable diagnoses included type 1 diabetes and type 2 diabetes. We considered patients with latent autoimmune or pancreatotomy to have type 1 diabetes. We considered patients with steroid induced or transplant-induced diabetes to have type 2 diabetes.
- We excluded pregnant women with gestational diabetes. We excluded patients with maturity onset diabetes of the young, as the diagnosis is difficult to make without genetic testing and intensive insulin therapy is often not required.

Interventions

- We included studies that evaluated CSII and rt-CGM (see Appendix C for list of devices).
- We excluded implantable insulin pumps as they are no longer used clinically and retrospective CGM devices, as the current clinical practice is to use rt-CGM.
- We excluded studies in which regular insulin was used in the insulin pump as this is not consistent with current clinical practice.
- We excluded studies evaluating the GlucoWatch CGM, as it is no longer used in the US.

Comparisons of interest

- We included studies that compared CSII with MDI (i.e., at least 3 injections per day).
- We included studies using long and rapid-acting analog and/or NPH and regular insulin in the MDI arms because both regimens are still used in clinical practice.
- We included studies that compared rt-CGM with SMBG (i.e., at least 3 fingersticks per day).
- We excluded studies of premixed insulin, because patients who use a premixed insulin are rarely considered for intensive insulin therapy with CSII.
- We excluded studies that do not have a concurrent comparison group.

Outcomes

- Process measures
 - Ratio of basal to bolus insulin*
 - Frequency of adjusting insulin therapy
 - Adherence to insulin therapy/sensor use
 - Frequency of professional or allied health visits
 - Intermediate outcomes
 - HbA1c
 - Hyperglycemia
 - Weight gain
 - Hypoglycemia frequency
- Clinical outcomes
 - Objective assessments of microvascular outcomes (nephropathy, retinopathy, and neuropathy) and macrovascular outcomes (coronary heart disease, cerebrovascular disease, and peripheral arterial disease)
 - Severe hypoglycemia
 - Quality of life (validated measures)
 - Mortality

- Fetal outcomes (gestational age, birth weight, frequency of neonatal hypoglycemia, birth trauma, major and minor anomalies, admission to a neonatal intensive care unit)
- Maternal pregnancy outcomes (cesarean section rates)

Type of study

- We excluded articles with no original data (reviews, editorials, and commentaries) or studies published in abstract form only.
- We excluded case reports, case series, and cross-sectional studies.
- We included both RCTs and observational studies that evaluated microvascular, macrovascular, maternal, or fetal outcomes. For all other outcomes, we included only RCTs.
- We did not place any restrictions on sample size or language.
- Because we excluded studies of outdated technologies, we excluded studies published before 1994, the 1st year that insulin analogues were used.

Timing and setting

- We excluded studies in which patients used an insulin delivery or glucose monitoring device for less than 24 hours.
- We excluded studies that were not conducted in an outpatient setting.

Appendix E. Literature Search Results

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Appendix F. Questionnaire Sent to Expert Reviewers

AHRQ Comparative Effectiveness Review Surveillance Program

Reviewer Form

Title of Original Review: Methods for Insulin Delivery and Glucose Monitoring: Comparative Effectiveness

[Link to Report](#)

Name of Reviewer: _____

Instructions:

The AHRQ Scientific Resource Center (SRC) periodically conducts surveillance of published AHRQ reviews to assist with prioritization of reports for updating. One part of this process includes soliciting expert review of our synthesis of recently published literature and any identified FDA black box warnings.

The attached document includes a table highlighting the conclusions from the original report, conclusions from a surveillance review conducted in 2012, and our synthesis of the recently published literature. Abstracts from relevant literature are included at the end of the attached document. If you would like a list of our full search results, please let us know.

Please review the table in the attached document and provide responses to the questions for each key question below. The primary goal of this review is to identify any missing studies, drugs, interventions, or devices; and ensure the accuracy of our synthesis of the recently published literature.

Key Question 1:

In patients receiving intensive insulin therapy, does mode of delivery (CSII vs. MDI) have a differential effect on process measures, intermediate outcomes, and clinical outcomes in patients with diabetes mellitus? Do these effects differ by:

- a. Type 1 or type 2 diabetes status?
- b. Age: very young children, adolescents, and adults, including older adults (age >65 years)?
- c. Pregnancy status: per-existing type 1 or type 2 diabetes?

SRC Literature Analysis:

- In adults with type 1 diabetes:
 - One randomized controlled trial (Buse 2011) found that baseline HbA_{1c} ($\geq 9.1\%$), age at randomization (≥ 36 years), and age at diabetes diagnosis (≥ 17 years) were associated with a greater SAP benefit relative to MDI than other cutpoints.
 - Another study (Buse 2012) found that at 1 year, sensor glucose values at HbA_{1c} levels $\geq 6.5\%$ were similar in the SAP and MDI groups. However, sensor glucose SD and coefficient of variation values were lower at HbA_{1c} levels $< 8\%$ among SAP than among MDI subjects; the overall between-group difference was significant for both SD ($P < 0.01$) and CV ($P = 0.01$).

Reviewer Questions:

1. Are the original report conclusions still supported by the current evidence?

[Click here to enter text.](#)

2. Are there any published or unpublished studies that you know of that we may have overlooked?

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Key Question 2:

In patients using intensive insulin therapy (MDI or CSII), does the type of glucose monitoring (rt-CGM vs. SMBG) have a differential effect on process measures, intermediate outcomes, and clinical outcomes in patients with diabetes mellitus (i.e., what is the incremental benefit of rt-CGM in patients already using intensive insulin therapy)? Do these effects differ by:

- a. Type 1 or type 2 diabetes status?
- b. Age: very young children, adolescents, and adults, including older adults (age >65 years)?
- c. Pregnancy status: pre-existing type 1 or type 2 diabetes?
- d. Intensive insulin delivery: MDI or CSII?

SRC Literature Analysis:

- Studies comparing rt-CGM vs. SMBG
 - One randomized controlled, multicenter study (Battelino 2011) of 120 children and adults with type 1 diabetes and a HbA_{1c} screening level of $< 7.5\%$ found that time spent in hypoglycemia was significantly shorter in the rt-CGM group ($P = .03$), as compared with self-monitoring. HbA_{1c} at 26 weeks was lower in the rt-CGM group, with a difference of -0.27% ($P = .008$).
 - One randomized, controlled, multicenter study (Battelino 2011) found that rt-CGM was associated with reduced time spent in hypoglycemia and a concomitant decrease in HbA_{1c} in children and adults with type 1 diabetes (mean \pm SD 0.48 ± 0.57 and 0.97 ± 1.55 h/day, respectively; ratio of means 0.49 ; 95% CI $0.26-0.76$; $P = 0.03$).
 - One randomized controlled trial (Cordua 2013) observed pregnant women with type 1 diabetes using rt-CGM during labor and delivery. In infants of the women involved in the rt-CGM group, approximately 10 (37%) developed neonatal hypoglycemia vs. 27 (46%) in the self-monitoring arm ($P = .45$). Among 10 infants with and 17 infants without neonatal hypoglycaemia within the rt-CGM arm, median maternal self-monitored plasma glucose was 6.2 (range $4.2-7.8$) vs. 5.6 ($3.3-8.5$) mmol/l ($P = 0.26$) during labor and delivery, with maternal hyperglycaemia present in 17 (0-94) vs. 4 (0-46)% of the time ($P = 0.02$), and birthweight was 4040 ($3102-4322$) vs. 3500 ($1829-4320$) g ($P = 0.04$).
- Studies comparing rt-CGM + CSII (sensor-augmented pump) versus MDI/SMBG
 - One randomized controlled trial (Buse 2011) analyzed for significant relationships with -0.5% HbA_{1c} change at 1 year of therapy without incidence of severe hypoglycemia (defined as HbA_{1c}

benefit). The conclusion was that people with type 1 diabetes who had high HbA_{1c} ($\geq 9.1\%$) and who were older at diagnosis (≥ 17 years) and older at randomization (≥ 36 years) experienced the most benefit from sensor augmented pump (SAP) therapy as compared with MDI.

One study (Luo 2013) comparing MDI, CSII and sensor augmented pump SAP therapy observed improvement in mean blood glucose (MBG), standard deviation of blood glucose (SDBG), mean amplitude of glycemic excursions (MAGE), and absolute means of daily differences (MODD), and area under the curve at 10 hours (AUC10) of the SAP group over the 4 days of intervention compared with the CSII and MDI groups; however, no significant differences were observed among the three groups in terms of area under the curve at 3.9 hours AUC3.9 and low blood glucose index (LBGI). **Reviewer Questions:**

1. Are the original report conclusions still supported by the current evidence?

[Click here to enter text.](#)

2. Are there any published or unpublished studies that you know of that we may have overlooked?

[Click here to enter text.](#)

Original Review Conclusions and Literature Analysis

Title of Original Review: Methods for Insulin Delivery and Glucose Monitoring: Comparative Effectiveness

[Link to Report](#)

The conclusions from the original report, conclusions from a prior surveillance assessment and an analysis of recent literature identified by the Scientific Resource Center (SRC) are summarized below. Abstracts are provided for included literature at the end of the document.

Conclusions From Original Review	SRC Literature Analysis (July 2015)
<p>Key Question 1: In patients receiving intensive insulin therapy, does mode of delivery (CSII vs. MDI) have a differential effect on process measures, intermediate outcomes, and clinical outcomes in patients with diabetes mellitus? Do these effects differ by:</p> <ol style="list-style-type: none"> a. Type 1 or type 2 diabetes status? b. Age: very young children, adolescents, and adults, including older adults (age >65 years)? c. Pregnancy status: per-existing type 1 or type 2 diabetes? 	
<p>Summary of evidence of the comparative effectiveness of CSII versus MDI in children and adolescents with type 1 diabetes</p>	
<p>Outcome: HbA_{1c} SOE: Moderate # of studies / # of Good-Quality studies: 9 (7 RCTs; 2 non-RCTs) / 1</p> <p>Adolescents over 12 years of age vs. less than 12 years of age:</p> <ul style="list-style-type: none"> • Mean between-group difference in HbA_{1c} change from baseline: -0.14 percent • Slight decrease with CSII than with MDI (95% CI, -0.48 to 0.20%, P = 0.41). • Similar results among adolescents over 12 years old (mean between-group difference in the change from baseline HbA_{1c}, -0.10%; 95% CI, -0.47 to 0.27%) • Less different among children 12 years old or less (mean between-group difference in the change from baseline HbA_{1c}, -0.05%; 95% CI, -1.01 to 0.96%). 	<p>No studies were identified.</p>
<p>Outcome: Daytime hypoglycemia SOE: Low # of studies / # of Good-Quality studies: 3 (all RCTs) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • No significant difference in frequency of daytime hypoglycemia • Mean between-group difference in: <ul style="list-style-type: none"> ○ Perceived hypoglycemic events over 104 weeks: 0; 95% CI, -1.1 to 1.1 ○ Change from baseline to 24 weeks in the number of blood 	<p>No studies were identified.</p>

Conclusions From Original Review	SRC Literature Analysis (July 2015)
<p>glucose excursions below 70 mg/dL: -0.9; 95% CI, -2.1 to 0.3</p> <ul style="list-style-type: none"> ○ Number of hypoglycemic episodes/patient at 52 weeks: -3.7; 95% CI, -13.2 to 5.8 	
<p>Outcome: Nocturnal hypoglycemia SOE: Low # of studies / # of Good-Quality studies: 2 (all RCTs) / 1</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • No significant difference in frequency • 1 study reported 4 (MDI) events/patient/study period (95% CI, 0.3 to 7.7) vs. 3 (CSII) events/patient/study period (95% CI, 1.0 to 5.0) over 52 weeks. • 1 study reported 2 patients with 1 or more events (CSII); no events (MDI) over 16 weeks 	<p>No studies were identified.</p>
<p>Outcome: Mild hypoglycemia SOE: Insufficient # of studies / # of Good-Quality studies: 1 (RCT) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • 1 study reported no significant difference in mild hypoglycemia (events with blood glucose less than 70 mg/dL) over 14 weeks. <ul style="list-style-type: none"> ○ MDI: 22 events/patient ○ CSII: 19.8 events/patient 	<p>No studies were identified.</p>
<p>Outcome: Severe hypoglycemia SOE: Low # of studies / # of Good-Quality studies: 6 (5 RCTs; 1 non-RCT) / 1</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • Similar rates of severe hypoglycemia • Mean incidence ratio in hypoglycemic event rates in RCTs: 0.99 (95% CI, 0.57 to 1.71, P=0.97). <p>Adolescents over 12 years of age vs. less than 12 years:</p> <ul style="list-style-type: none"> • Similar results between both groups 	<p>No studies were identified.</p>

Conclusions From Original Review	SRC Literature Analysis (July 2015)
<ul style="list-style-type: none"> • Mean Incidence Ratio: <ul style="list-style-type: none"> ○ ≥12 years: 0.95; 95% CI, 0.42 to 2.13 ○ ≤12 years: 1.02; 95% CI, 0.49 to 2.16 	
<p>Outcome: Hyperglycemia SOE: Insufficient # of studies / # of Good-Quality studies: 1 (RCT) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • 1 study reported no difference in frequency over 14 weeks. <ul style="list-style-type: none"> ○ MDI: 6.7 events ○ CSII: 9 events 	No studies were identified.
<p>Outcome: Ratio basal to bolus insulin SOE: Insufficient # of studies / # of Good-Quality studies: 1 (non-RCT) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • 1 study found no difference • Mean between-group difference: 1.7; 95% CI, -2.5 to 5.9 	No studies were identified.
<p>Outcome: Weight SOE: Low # of studies / # of Good-Quality studies: 3 (all RCTs) / 1</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • Mean between-group difference in how BMI standard deviation score changed from baseline: -0.12 units • Standard deviation decreased slightly more for CSII (95% CI, -0.55 to 0.30) 	No studies were identified.
<p>Outcome: General QOL SOE: Low # of studies / # of Good-Quality studies: 2 (all RCTs) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • Meta-analysis of 2 studies showed no significant difference • Mean between-group difference, 2.3; 95% CI, -6.9 to 11.5; P = 0.95 	No studies were identified.

Conclusions From Original Review	SRC Literature Analysis (July 2015)
<p>Outcome: Diabetes-specific QOL SOE: Low # of studies / # of Good-Quality studies: 4 (all RCTs) / 1</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • 1 study showed improvement in diabetes QoL, favoring CSII⁴⁵ <ul style="list-style-type: none"> ○ Diabetes QoL Youth Score at end of study: 77.4 (95% CI, 69.5 to 85.3) at baseline <ul style="list-style-type: none"> ▪ MDI: 76.4 (95% CI, 68.3 to 84.5) ▪ CSII: 82.7 (95% CI, 75.3 to 90.1) • 1 study found no difference (numerical data not presented)⁴⁴ 	<p>No studies were identified.</p>
<p>Outcome: Diabetes treatment-related QOL SOE: Low # of studies / # of Good-Quality studies: 3 (all RCTs) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • Meta-analysis of 2 studies showed improvement, favoring CSII • Mean between-group difference in the Diabetes Treatment Satisfaction Questionnaire, 5.7; 95% CI, 5.0 to 6.4 	<p>No studies were identified.</p>
<p>Outcome: Process measures, clinical outcomes SOE: Insufficient # of studies / # of Good-Quality studies: 0</p> <p>No relevant studies addressing certain measures: frequency of adjusting insulin therapy, adherence, health visits) and clinical outcomes (microvascular and macrovascular disease and mortality).</p>	<p>No studies were identified.</p>
Summary of evidence of the comparative effectiveness of CSII versus MDI in adults with type 1 diabetes	
<p>Outcome: HbA_{1c} SOE: Low # of studies / # of Good-Quality studies: 1 (all RCTs) / 2</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • HbA_{1c} decreased more with CSII • Results were heavily by 1 study <ul style="list-style-type: none"> ○ Participants had a higher baseline HbA_{1c} than in the other 	<p>One randomized controlled trial (Buse 2011) found that baseline HbA_{1c} ($\geq 9.1\%$), age at randomization (≥ 36 years), and age at diabetes diagnosis (≥ 17 years) were associated with a greater SAP benefit relative to MDI than other cutpoints.</p> <p>Another study (Buse 2012) found that at 1 year, sensor glucose values at HbA_{1c} levels $\geq 6.5\%$ were similar in the SAP and MDI groups. However, sensor glucose SD and coefficient of variation values were lower at HbA_{1c}</p>

Conclusions From Original Review	SRC Literature Analysis (July 2015)
<p>studies (mean between-group difference from baseline, -0.30%; 95% CI, -0.58 to -0.02)</p> <ul style="list-style-type: none"> ○ After removing the study, the difference between the two groups became null (mean between-group difference from baseline, -0.01 percent, 95% CI, -0.35 to 0.34 percent) 	<p>levels <8% among SAP than among MDI subjects; the overall between-group difference was significant for both SD (P<0.01) and CV (P=0.01).</p>
<p>Outcome: Daytime hypoglycemia SOE: Low # of studies / # of Good-Quality studies: 1 (RCT) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • 1 study reported more symptomatic and asymptomatic hypoglycemia between 8 a.m. and midnight in the MDI (P=<0.05) 	<p>No studies were identified.</p>
<p>Outcome: Nocturnal hypoglycemia SOE: Low # of studies / # of Good-Quality studies: 3 (all RCTs) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • 3 studies reported hypoglycemia <ul style="list-style-type: none"> ○ 1 crossover trial: proportion of patients was similar (RR for any, 0.98; 98% CI, 0.83 to 1.17; RR for symptomatic, 0.87; 95% CI, 0.64 to 1.19) ○ Fewer episodes per person in CSII group (IRR, 0.76; 95% CI, 0.63 to 0.91). • 2 studies found no statistically significant difference 	<p>No studies were identified.</p>
<p>Outcome: Symptomatic hypoglycemia SOE: Low # of studies / # of Good-Quality studies: 4 (all RCTs) / 1</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • Increased risk for CSII (combined IRR, 1.3; 95% CI, 1.2 to 1.4) • Found evidence of substantial statistical heterogeneity for the meta-analysis. • No relative difference in incidence when excluding a study that required participants to have had recent severe hypoglycemia 	<p>No studies were identified.</p>

Conclusions From Original Review	SRC Literature Analysis (July 2015)
<p>(compared to the other 2, which excluded those with recent severe hypoglycemia)</p> <ul style="list-style-type: none"> • IRR suggested no relative difference (combined IRR, 1.0; 95% CI, 0.8 to 1.1) • Another study, which did not provide sufficient quantitative results, reported slightly more events with CSII (IRR, 1.1; 95% CI, 1.0 to 1.3) <ul style="list-style-type: none"> ○ Similar proportion of participants experienced events over 5 weeks (RR, 1.0; 95% CI, 0.9 to 1.2). 	
<p>Outcome: Other nonsensitive hypoglycemia SOE: Low # of studies / # of Good-Quality studies: 6 (all RCTs) / 1</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • 3 studies found no difference in nonsevere hypoglycemia <ul style="list-style-type: none"> ○ 1 study mean between-group difference in asymptomatic hypoglycemia event rate, -0.2; 95% CI, -1.39 to 0.99). • 2 studies found incidence of mild hypoglycemia higher in CSII,^{52,54} <ul style="list-style-type: none"> ○ 1 study found relative statistically significant difference (0.99; 95% CI, 0.11 to 1.87) ○ 1 study found a higher frequency in MDI (RR, 1.12; 95% CI, 1.08 to 1.17) 	<p>No studies were identified.</p>
<p>Outcome: Severe hypoglycemia SOE: Low # of studies / # of Good-Quality studies: 8 (all RCTs) / 1</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • Incidence did not differ between two groups (combined RR, 0.74; 95% CI, 0.30 to 1.83) • 4 crossover trials were not included in the meta-analysis because they did not provide quantitative results by period • 2 studies showed more severe hypoglycemia with MDI <ul style="list-style-type: none"> ○ 1 study reported a RR of 2.6 (95% CI, 2.08 to 3.25) • 1 study reported less severe hypoglycemia with MDI (IRR, 3.00; 95% CI, 0.24 to 157.49) • 1 study found similar rates of severe hypoglycemia (1.1 	<p>No studies were identified.</p>

Conclusions From Original Review	SRC Literature Analysis (July 2015)
<p>events/patient for CSII vs. 1.3 events/patient for MDI over 4 months, P = 0.33)</p>	
<p>Outcome: Hyperglycemia SOE: Low # of studies / # of Good-Quality studies: 3 (all RCTs) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • 1 study favored CSII, with the mean between-group difference in fasting glucose over 6 months being: -12.3 mg/dL (95% CI, -32.9 to 8.2 mg/dL) • 2 other studies reported no difference in fasting glucose 	<p>No studies were identified.</p>
<p>Outcome: Bedtime hyperglycemia SOE: Insufficient # of studies / # of Good-Quality studies: 1 (RCT) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • Insufficient SOE to determine the relative effects • 1 study reported no difference, but did not provide glucose results 	<p>No studies were identified.</p>
<p>Outcome: Pre-prandial glucose SOE: Low # of studies / # of Good-Quality studies: 3 (all RCTs) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • Mean between-group difference over 6 months: -17.1 mg/dL (95% CI, -42.1 to 8.0 mg/dL) <ul style="list-style-type: none"> ○ 1 study favored CSII ○ 1 study found pre-dinner glucose to be lower with CSII (128 mg/dL) vs. MDI (148 mg/dL) at the end of 5 weeks (P=NS) ○ 1 study did not find significantly lower glucose pre-dinner and pre-lunch glucose levels at 4 months <p>Outcome: Post-prandial glucose SOE: Low # of studies / # of Good-Quality studies: 3 (all RCTs) / 0</p> <p>MDI vs. CSII Intervention Groups:</p>	<p>No studies were identified.</p>

Conclusions From Original Review	SRC Literature Analysis (July 2015)
<ul style="list-style-type: none"> • Evidence suggested slightly lower levels with CSII • 1 study reported a mean difference of: -5.5 mg/dl (95% CI, -29.9 to 18.9 mg/dl) • 1 study reported a mean difference of: -24 and -15 mg/dl post-breakfast and post-dinner <p>1 study did not find significantly higher post-breakfast glucose levels in MDI</p>	
<p>Outcome: Nocturnal hyperglycemia SOE: Low # of studies / # of Good-Quality studies: 2 (all RCTs) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • 2 studies found no between-group difference <ul style="list-style-type: none"> ○ 1 study reported an increase in both arms (between-group difference, 54.8; 95% CI, -7.2 to 116.7 mg/dl) 	No studies were identified.
<p>Outcome: Weight SOE: Low # of studies / # of Good-Quality studies: 4 (all RCTs) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • No difference in weight gain (combined mean between-group difference, -0.25 kg; 95% CI, -3.14 to 2.64 kg). • 2 studies reported no difference in weight gain, but did not report sufficient quantitative results. 	No studies were identified.
<p>Outcome: General QOL SOE: Low # of studies / # of Good-Quality studies: 2 (all RCTs) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <p>2 studies showed an improvement between two groups, favoring CSII.</p> <ul style="list-style-type: none"> • 1 study reported change in: <ul style="list-style-type: none"> ○ SF-36 Physical Component Score (P=0.048): <ul style="list-style-type: none"> ▪ CSII: -1.2 ▪ MDI: 5.9 ○ Mental Component Score (P=0.05): <ul style="list-style-type: none"> ▪ CSII: -0.6 	No studies were identified.

Conclusions From Original Review	SRC Literature Analysis (July 2015)
<ul style="list-style-type: none"> ▪ MDI: 5.2 • 1 study did not report estimates <ul style="list-style-type: none"> ○ No difference in the Physical Component Score ○ Change in Mental Component Score, favoring CSII (P<0.05) 	
<p>Outcome: Diabetes-specific QOL SOE: Low # of studies / # of Good-Quality studies: 5 (all RCTs) / 1</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • 3 studies showed an improvement, favoring CSII • 1 meta-analysis favored CSII mean between-group difference in Diabetes Quality of Life, 2.99; 95% CI, 0.006 to 5.97) • 1 study showed improvement, favoring MDI (Diabetes Quality of Life mean between-group difference in change from baseline, -18.00; 95% CI, -50.14 to 14.14). 	No studies were identified.
<p>Outcome: Diabetes treatment-related QOL SOE: Insufficient # of studies / # of Good-Quality studies: 1 (RCT) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • Altered Hypoglycemia Awareness Questionnaire scores were similar in the CSII and MDI groups over 24 weeks (RR of Altered Hypoglycemia Awareness Questionnaire score greater than 4, 0.75; 95% CI, 0.26 to 2.18) • Hypoglycemia Fear Survey scores decreased in both: <ul style="list-style-type: none"> ○ CSII: (-3±25) ○ MDI: (-8±33) • Mean between-group difference in the change from baseline (5; 95% CI, -32.66 to 42.66) 	No studies were identified.
<p>Outcome: Process measures, clinical outcomes SOE: Insufficient # of studies / # of Good-Quality studies: 0</p> <p>None of the studies evaluated the effects of MDI vs. CSII among adults with</p>	No studies were identified.

Conclusions From Original Review	SRC Literature Analysis (July 2015)
type 1 diabetes in terms of any process measures or clinical outcomes.	
Summary of the evidence of the comparative effectiveness of CSII versus MDI in adults with type 2 diabetes	
Outcome: Mortality SOE: Insufficient # of studies / # of Good-Quality studies: 1 (RCT) / 0 1 study reported 1 death due to cancer in the CSII treatment arm	No studies were identified.
Outcome: HbA_{1c} SOE: Moderate # of studies / # of Good-Quality studies: 4 (all RCTs) / 0 MDI vs. CSII Intervention Groups: <ul style="list-style-type: none"> The effects did not differ between the intervention groups (mean between-group difference from baseline with negative value favoring CSII, -0.16; 95% CI, -0.42 to 0.09) 	No studies were identified
Outcome: Mild hypoglycemia SOE: Moderate # of studies / # of Good-Quality studies: 3 (all RCTs) / 0 MDI vs. CSII Intervention Groups: <ul style="list-style-type: none"> Risk did not differ between the intervention groups (combined RR, 0.90; 95% CI, 0.78 to 1.03). 	No studies were identified
Outcome: Nocturnal hypoglycemia SOE: Insufficient # of studies / # of Good-Quality studies: 1 (RCT) / 0 MDI vs. CSII Intervention Groups: <ul style="list-style-type: none"> 1 study reported nocturnal hypoglycemia was less common in patients in the CSII arm (RR, 0.73; 95% CI, 0.35 to 1.54) 	No studies were identified.
Outcome: Severe hypoglycemia SOE: Low # of studies / # of Good-Quality studies: 3 (all RCTs) / 0 MDI vs. CSII Intervention Groups:	No studies were identified.

Conclusions From Original Review	SRC Literature Analysis (July 2015)
<ul style="list-style-type: none"> Risk of severe hypoglycemia did not differ (RR, 0.76; 95% CI, 0.26 to 2.19). 	
<p>Outcome: Hyperglycemia SOE: Low # of studies / # of Good-Quality studies: 2 (all RCTs) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> Mean post-prandial glucose (90 minutes after breakfast) at 24 weeks: <ul style="list-style-type: none"> CSII: 167 mg/dL MDI: 192 mg/ dL Mean between-group difference, -25 mg/dL; 95% CI, -45 to -5 mg/ dL Glucose measurements from other time points were similar between treatment groups at the end of the study. Incidence of blood glucose over 350 mg/dL was higher in the MDI arm vs. CSII (26 vs. 6 events) <ul style="list-style-type: none"> Affected 18% and 5% of participants in MDI and CSII arms respectively (RR, 0.28; 95% CI, 0.08 to 0.94). 	No studies were identified.
<p>Outcome: Weight SOE: Low # of studies / # of Good-Quality studies: 2 (all RCTs) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> No difference between intervention groups (combined mean between-group difference in weight change from baseline, -0.49 kg; 95% CI, -1.25 to 0.26 kg). 	No studies were identified.
<p>Outcome: General QOL SOE: Insufficient^a # of studies / # of Good-Quality studies: 1 (RCT) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> 1 study reported no difference between intervention groups Difference from baseline to follow-up: <ul style="list-style-type: none"> SF-36v2 Component Score: <ul style="list-style-type: none"> CSII: 0.6 	No studies were identified.

Conclusions From Original Review	SRC Literature Analysis (July 2015)
<ul style="list-style-type: none"> ▪ MDI: 0.4 ○ Mental Component Score: <ul style="list-style-type: none"> ▪ CSII: 1.0 ▪ MDI: 2.5 	
<p>Outcome: Diabetes-specific QOL SOE: Insufficient # of studies / # of Good-Quality studies: 1 (RCT) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • 1 study reported no difference between the intervention groups <ul style="list-style-type: none"> ○ Diabetes Quality of Life Clinical Trials Questionnaire scores improved over 12 months from: <ul style="list-style-type: none"> ▪ CSII: 52 to 81 ▪ MDI: 50 to 78 	No studies were identified.
<p>Outcome: Diabetes treatment-related QOL SOE: Insufficient # of studies / # of Good-Quality studies: 1 (RCT) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • 1 study reported improvement in treatment satisfaction, favoring CSII mean between-group difference in Phase V Outcomes System Diabetes Treatment Satisfaction score change from baseline in 24 weeks, 13.1; 95% CI, 7.4 to 18.8) 	No studies were identified.
<p>Outcome: Process measures, microvascular disease, macrovascular disease SOE: Insufficient # of studies / # of Good-Quality studies: 0</p> <p>No studies evaluating the effects of MDI vs. CSII among patients with type 2 diabetes in terms of any of the process measures, microvascular disease, or macrovascular disease were identified.</p>	No studies were identified.
Summary of the evidence of the comparative effectiveness of CSII versus MDI in pregnant women with pre-existing type 1 diabetes	
<p>Outcome: HbA_{1c} SOE: Low # of studies / # of Good-Quality studies: 6 (all OBS) / 0</p>	No studies were identified.

Conclusions From Original Review	SRC Literature Analysis (July 2015)
<p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • 6 observational studies reported an improvement in HbA_{1c} in both intervention groups during pregnancy. <ul style="list-style-type: none"> ○ No significant difference between groups in HbA_{1c} in any of the trimesters ○ Mean between-group differences in third-trimester HbA_{1c} values in each of the studies were: 0.2 (95% CI, -0.3 to 0.7), -0.4 (95% CI, -0.8 to 0.04), 0.6 (95% CI, -0.7 to 1.9), -0.3 (95% CI, -0.6 to -0.03), 0.2 (95% CI, -0.2 to 0.6), and 0.4 (95% CI, -0.9 to 1.7). 	
<p>Outcome: Cesarean section rates SOE: Insufficient # of studies / # of Good-Quality studies: 3 (all OBS) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • 1 meta-analysis of 4 retrospective studies showed a pooled RR of 1.02 (95% CI, 0.86 to 1.20), which was inconclusive because of high-risk bias 	No studies were identified.
<p>Outcome: Maternal hypoglycemia SOE: Insufficient # of studies / # of Good-Quality studies: 2 (all OBS) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • 1 meta-analysis of 3 retrospective studies for rate of severe hypoglycemia showed a pooled RR of 0.78, which was inconclusive because of high risk of bias (95% CI, 0.23 to 2.65). 	No studies were identified.
<p>Outcome: Maternal weight gain SOE: Insufficient # of studies / # of Good-Quality studies: 3 (all OBS) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • 3 studies reported no difference between the two intervention groups, with high risk of bias. • Mean between-group difference: <ul style="list-style-type: none"> ○ 1 study: 1.9 kg (95% CI, -0.9 to 4.7 kg) ○ 1 study: 0.1 kg (95% CI, -2.4 to 2.6 kg) 	No studies were identified.

Conclusions From Original Review	SRC Literature Analysis (July 2015)
<ul style="list-style-type: none"> • 1 study reported a median weight gain of: <ul style="list-style-type: none"> ○ CSII: 13.5 kg ○ MDI: 13.9 kg 	
<p>Outcome: Other maternal outcomes SOE: Insufficient # of studies / # of Good-Quality studies: 0</p> <p>None of the studies evaluated maternal mortality, microvascular or macrovascular disease, quality of life, or any of the process measures.</p>	No studies were identified.
<p>Outcome: Gestational age at delivery SOE: Insufficient # of studies / # of Good-Quality studies: 4 (all OBS) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • Range: <ul style="list-style-type: none"> ○ MDI: 36.6 to 37.5 weeks ○ CSII: 36.3 to 36.6 weeks • No significant difference between intervention groups, but studies had high risk of bias 	No studies were identified.
<p>Outcome: Neonatal hypoglycemia SOE: Insufficient # of studies / # of Good-Quality studies: 4 (all OBS) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • 1 meta-analysis of 4 retrospective cohort studies for frequency showed a pooled RR of 1.10 (95% CI, 0.86 to 1.20), which was inconclusive because of high risk of bias. 	No studies were identified.
<p>Outcome: Birth weight SOE: Insufficient # of studies / # of Good-Quality studies: 3 (all OBS) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • 1 meta-analysis of 3 retrospective cohort studies showed a pooled mean between-group difference in birth weight of 107.2 g (95% CI, -86.6 to 295.9 g), which was inconclusive because of high risk of bias. 	No studies were identified.

Conclusions From Original Review	SRC Literature Analysis (July 2015)
<p>Outcome: Major congenital anomalies SOE: Insufficient # of studies / # of Good-Quality studies: 2 (all OBS) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • 1 meta-analysis of 2 retrospective cohort studies showed a pooled RR of 2.12 favoring MDI (95% CI, 0.38 to 11.77), which was inconclusive because of high risk of bias. 	<p>No studies were identified.</p>
<p>Outcome: Minor congenital anomalies SOE: Insufficient # of studies / # of Good-Quality studies: 3 (all OBS) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • 3 studies with high risk of bias found no difference between intervention groups • 2 group studies reported no minor congenital anomalies in either group • Rates of minor congenital anomalies and pregnancy termination rates: <ul style="list-style-type: none"> ○ MDI: 2.3% (2/86 patients) ○ CSII: 13% (P=0.05) 	<p>No studies were identified.</p>
<p>Outcome: NICU admissions SOE: Insufficient # of studies / # of Good-Quality studies: 2 (all OBS) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • 1 meta-analysis of 2 retrospective cohort studies showed a pooled RR of 0.84 (95% CI, 0.43 to 1.68), which was inconclusive because of high risk of bias 	<p>No studies were identified.</p>
<p>Outcome: Preterm delivery SOE: Insufficient # of studies / # of Good-Quality studies: 4 (all OBS) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • 1 meta-analysis of 4 retrospective cohort studies showed a pooled 	<p>No studies were identified.</p>

Conclusions From Original Review	SRC Literature Analysis (July 2015)
<p>RR of 0.98 (95% CI, 0.67 to 1.43), which was inconclusive because of high risk of bias.</p>	
<p>Outcome: Stillbirth rates SOE: Insufficient # of studies / # of Good-Quality studies: 4 (all OBS) / 0</p> <p>MDI vs. CSII Intervention Groups: 4 studies reported on stillbirth rates</p> <ul style="list-style-type: none"> • 3 studies reported no stillbirths in either group • 1 study reported having 1 stillbirth in MDI group 	<p>No studies were identified.</p>
<p>Outcome: Neonatal mortality SOE: Insufficient # of studies / # of Good-Quality studies: 3 (all OBS) / 0</p> <p>MDI vs. CSII Intervention Groups: 3 studies reported on neonatal mortality rate</p> <ul style="list-style-type: none"> • 1 study reported 1 neonatal death in each group • 1 study did not have neonatal deaths in either group • 1 study reported mortality rates of: <ul style="list-style-type: none"> ○ MDI: 0% ○ CSII: 2.7% 	<p>No studies were identified.</p>
<p>Outcome: Perinatal mortality SOE: Insufficient # of studies / # of Good-Quality studies: 2 (all OBS) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • 1 study reported a mortality rate of: <ul style="list-style-type: none"> ○ CSII: 3% ○ MDI: 4% • 1 study reported a mortality rate of: <ul style="list-style-type: none"> ○ CSII: 2.7% ○ MDI: 0% 	<p>No studies were identified.</p>
<p>Outcome: Birth trauma</p>	<p>No studies were identified.</p>

Conclusions From Original Review	SRC Literature Analysis (July 2015)
<p>SOE: Insufficient # of studies / # of Good-Quality studies: 0</p> <p>None of the studies reported on birth trauma.</p>	
<p>Key Question 2. In patients using intensive insulin therapy (MDI or CSII), does the type of glucose monitoring (rt-CGM vs. SMBG) have a differential effect on process measures, intermediate outcomes, and clinical outcomes in patients with diabetes mellitus (i.e., what is the incremental benefit of rt-CGM in patients already using intensive insulin therapy)? Do these effects differ by:</p> <ol style="list-style-type: none"> Type 1 or type 2 diabetes status? Age: very young children, adolescents, and adults, including older adults (age >65 years)? Pregnancy status: pre-existing type 1 or type 2 diabetes? Intensive insulin delivery: MDI or CSII? 	
<p>Summary of evidence of the comparative effectiveness of rt-CGM versus SMBG</p>	
<p>Outcome: HbA_{1c} SOE: High # of studies / # of Good-Quality studies: 8 (all RCTs) / 4</p> <p>Rt-CGM vs. SMBG groups:</p> <ul style="list-style-type: none"> Rt-CGM favored for the effects of HbA_{1c} Mean between-group change from baseline was 0.30% (95% CI, -0.37 to -0.22%) 1 sensitivity analysis (which included only studies with more than 60% compliance, 7 estimates) reported a greater HbA_{1c} reduction (mean between-group difference from baseline, -0.36%; 95% CI, -0.44 to -0.27%) 1 meta-analysis of 4 studies in children and adolescents ≤18 years showed a significant combined mean between-group difference in HbA_{1c} change from baseline of -0.26% favoring rt-CGM (95% CI, -0.46 to -0.06%). 	<p>One randomized controlled, multicenter study (Battelino 2011) of 120 children and adults with type 1 diabetes and a HbA_{1c} screening level of <7.5% found that time spent in hypoglycemia was significantly shorter in the rt-CGM group (P = .03), as compared with self monitoring. HbA_{1c} at 26 weeks was lower in the rt-CGM group, with a difference of -0.27% (P = .008).</p>
<p>Outcome: Non-severe hypoglycemia SOE: Moderate # of studies / # of Good-Quality studies: 6 (all RCTs) / 3</p> <p>Rt-CGM vs. SMBG groups:</p> <ul style="list-style-type: none"> 1 meta-analysis of 4 studies (6 estimates) showed no difference in time spend in the hypoglycemic range (glucose level less than 70 mg/dL) Mean between-group difference was -2.11 minutes/day (95% CI, -5.66 to 1.44 minutes/day). 	<p>One randomized, controlled, multicenter study (Battelino 2011) found that rt-CGM was associated with reduced time spent in hypoglycemia and a concomitant decrease in HbA_{1c} in children and adults with type 1 diabetes (mean +/- SD 0.48 +/- 0.57 and 0.97 +/- 1.55 h/day, respectively; ratio of means 0.49; 95% CI 0.26-0.76; P = 0.03).</p> <p>One randomized controlled trial (Cordua 2013) observed pregnant women with type 1 diabetes using rt-CGM during labor and delivery. In infants of the women involved in the rt-CGM group, approximately 10 (37%) developed neonatal hypoglycaemia vs. 27 (46%) in the self monitoring arm</p>

Conclusions From Original Review	SRC Literature Analysis (July 2015)
	(P = .45). Among 10 infants with and 17 infants without neonatal hypoglycaemia within the rt-CGM arm, median maternal self-monitored plasma glucose was 6.2 (range 4.2-7.8) vs. 5.6 (3.3-8.5) mmol/l (P = 0.26) during labor and delivery, with maternal hyperglycaemia present in 17 (0-94) vs. 4 (0-46)% of the time (P = 0.02), and birthweight was 4040 (3102-4322) vs. 3500 (1829-4320) g (P = 0.04).
<p>Outcome: Severe hypoglycemia SOE: Low # of studies / # of Good-Quality studies: 7 (all RCTs) / 4</p> <p>Rt-CGM vs. SMBG groups:</p> <ul style="list-style-type: none"> • No difference in rate (pooled RR, 0.95; 95% CI, 0.53 to 1.69) • 2 trials reported data in pediatric populations <ul style="list-style-type: none"> ○ 1 study reported severe hypoglycemia as less common among patients using rt-CGM (SMBG 4/78 vs. rt-CGM 0/76, P = 0.046). ○ 1 study's pediatric subgroups (ages 8-14 years) showed a similar incidence in both arms (SMBG 6/58 vs. rt-CGM 4/56, P = 0.74). 	No studies were identified.
<p>Outcome: Hyperglycemia SOE: Moderate # of studies / # of Good-Quality studies: 5 (all RCTs) / 3</p> <p>Rt-CGM vs. SMBG groups:</p> <ul style="list-style-type: none"> • 1 meta-analysis of 4 studies (6 estimates) indicated a significant reduction in time spent in the hyperglycemic range (glucose level greater than 180 mg/dL), favoring rt-CGM <ul style="list-style-type: none"> ○ Mean between-group difference: -68.56 minutes/day favoring rt-CGM (95% CI, -101.17 to -35.96). 	One study (Cordua 2013) found hyperglycemia present in 17 (0-94) vs. 4 (0-46)% of in women (P=0.02) within the rt-CGM arm during labor and delivery.
<p>Outcome: Ratio of basal to bolus insulin SOE: Low # of studies / # of Good-Quality studies: 2 (all RCTs) / 1</p> <p>Rt-CGM vs. SMBG groups:</p> <ul style="list-style-type: none"> • 1 study reported that the basal rate was a higher proportion of total daily insulin dose in the rt-CGM group (mean between-group difference in final basal rate, 4.3%; 95% CI, 0.8 to 7.8%). 	No studies were identified.

Conclusions From Original Review	SRC Literature Analysis (July 2015)
<ul style="list-style-type: none"> 1 study reported a higher percentage of insulin delivered as bolus in the rt-CGM group (mean between-group difference in final percentage of insulin delivered as bolus, -4.0%; 95% CI, -9.3 to 1.3%). 	
<p>Outcome: General QOL SOE: Low # of studies / # of Good-Quality studies: 2 (all RCTs) / 1</p> <p>Rt-CGM vs. SMBG groups:</p> <ul style="list-style-type: none"> 1 study found no difference in parental satisfaction between the intervention arms at 12 months: <ul style="list-style-type: none"> Mean between-group difference in change from baseline (WHO Well Being Index-5 mother's well-being score) was 2.7; 95% CI, -14.2 to 8.8 1 study assessed general QoL at 26 weeks (SF-12) <ul style="list-style-type: none"> Physical Component Score: improvement, favoring rt-CGM <ul style="list-style-type: none"> Mean between-group difference in change from baseline, 1.4; 95% CI, -1.5 to 4.3 Mental Component Score: no difference <ul style="list-style-type: none"> Mean between-group difference in change from baseline, -1.6; 95% CI, -5.9 to 2.7 	No studies were identified.
<p>Outcome: Diabetes-specific QOL SOE: Low # of studies / # of Good-Quality studies: 2 (all RCTs) / 0</p> <p>Rt-CGM vs. SMBG groups:</p> <ul style="list-style-type: none"> No difference between the two groups in either study at 26 weeks <ul style="list-style-type: none"> Problem Areas in Diabetes score mean between-group difference in the change from baseline: -0.9; 95% CI, -7.9 to 6.1 Diabetes QoL score mean between-group difference in the change from baseline: -3.0; 95% CI, -6.6 to 0.6). 	No studies were identified.
<p>Outcome: Diabetes treatment-related QOL SOE: Insufficient # of studies / # of Good-Quality studies: 1 (RCT) / 0</p>	No studies were identified

Conclusions From Original Review	SRC Literature Analysis (July 2015)
<p>Rt-CGM vs. SMBG groups:</p> <ul style="list-style-type: none"> • Fear of hypoglycemia was less with the rt-CGM group <ul style="list-style-type: none"> ○ Mean between-group difference in change from baseline score, -2.3; 95% CI, -8.2 to 3.6 	
<p>Outcome: Process measures, weight, and clinical outcomes SOE: Insufficient # of studies / # of Good-Quality studies: 0</p> <p>None of the studies evaluated the effects of rt-CGM vs. SMBG in terms of mortality, microvascular or macrovascular disease, weight, or any other process measure.</p>	<p>No studies were identified.</p>
<p>Summary of the evidence of the comparative effectiveness of rt-CGM + CSII (sensor-augmented pump) versus MDI/SMBG</p>	
<p>Outcome: HbA_{1c} SOE: Moderate # of studies / # of Good-Quality studies: 4 (all RCTs) / 2</p> <p>Sensor-augmented pumps vs. MDI/SMBG:</p> <ul style="list-style-type: none"> • Sensor-augmented pumps were favored over MDI/SMBG for their effects on HbA_{1c} • Mean between-group difference in HbA_{1c} change, -0.68%; 95% CI, -0.81 to -0.54% 	<p>No studies were identified.</p>
<p>Outcome: Non-severe hypoglycemia SOE: Moderate # of studies / # of Good-Quality studies: 2 (all RCTs) / 2</p> <p>Sensor-augmented pumps vs. MDI/SMBG:</p> <ul style="list-style-type: none"> • No difference in time spent with non-severe hypoglycemia between the intervention groups 	<p>One randomized controlled trial (Buse 2011) analyzed for significant relationships with -0.5% HbA_{1c} change at 1 year of therapy without incidence of severe hypoglycemia (defined as HbA_{1c} benefit). The conclusion was that people with type 1 diabetes who had high HbA_{1c} ($\geq 9.1\%$) and who were older at diagnosis (≥ 17 years) and older at randomization (≥ 36 years) experienced the most benefit from SAP therapy as compared with MDI.</p> <p>One study (Luo 2013) comparing MDI, CSII and SAP observed improvement in MBG, SDBG, MAGE, MODD, and total area under the curve 10 (AUC10) of the SAP group over the 4 days of intervention compared with the CSII and MDI groups; however, no significant differences were observed among the three groups in terms of total AUC3.9 and low blood glucose index (LBGI).</p>

Conclusions From Original Review	SRC Literature Analysis (July 2015)
<p>Outcome: Severe hypoglycemia SOE: Moderate # of studies / # of Good-Quality studies: 4 (all RCTs) / 2</p> <p>Sensor-augmented pumps vs. MDI/SMBG:</p> <ul style="list-style-type: none"> • No difference in incidence between the intervention groups (RR, 1.2; 95% CI, 0.7 to 2.3) <ul style="list-style-type: none"> ○ Number of events: <ul style="list-style-type: none"> ▪ 0 (SAP) vs. 3 (MDI/SMBG) ▪ 0/8 (SAP) vs. 1/8 (MDI.SMBG) ▪ RR 3.5; 95% CI, 0.4 to 304 	<p>No studies were identified.</p>
<p>Outcome: Hyperglycemia SOE: Moderate # of studies / # of Good-Quality studies: 2 (all RCTs) / 2</p> <p>Two trials suggested time spent with hyperglycemia was significantly less in the sensor-augmented pump group than the MDI/SMBG intervention group (P < 0.001).</p>	<p>No studies were identified.</p>
<p>Outcome: Weight SOE: Low # of studies / # of Good-Quality studies: 2 (all RCTs) / 1</p> <p>Sensor-augmented pumps vs. MDI/SMBG:</p> <ul style="list-style-type: none"> • 1 study reported no significant difference in weight gain between intervention groups (mean, 2.4 kg vs. 1.8 kg; P = 0.19) • 1 study reported weight increase, but difference was not significant: <ul style="list-style-type: none"> ○ SAP group: 0.7 kg ○ MDI/SMBG: 2.0 kg ○ Mean between-group difference, 1.3 kg; 95% CI, -21.2 to 23.8 kg 	<p>No studies were identified.</p>
<p>Outcome: Diabetes treatment-related QOL SOE: Low # of studies / # of Good-Quality studies: 2 (all RCTs) / 1</p> <p>Sensor-augmented pumps vs. MDI/SMBG:</p> <ul style="list-style-type: none"> • User acceptance and overall diabetes treatment satisfaction were greater in sensor-augmented pump arm • Scores for Blood Glucose Monitoring System Rating Questionnaire: 	<p>No studies were identified.</p>

Conclusions From Original Review	SRC Literature Analysis (July 2015)
<ul style="list-style-type: none"> ○ SAP: 83.3±21.7 ○ MDI/SMBG: 33.3±22.6 ○ Mean between-group difference in final scores, 50.0; 95% CI, 33.6 to 66. 	
<p>Outcome: Process measures, weight, and clinical outcomes SOE: Insufficient # of studies / # of Good-Quality studies: 0 None of the studies evaluated the effects of sensor-augmented pumps vs. MDI/SMBG in terms of mortality, microvascular or macrovascular disease, or any of the process measures.</p>	<p>No studies were identified.</p>

Legend: SOE = strength of evidence; CSII = continuous subcutaneous insulin infusion; MDI = multiple daily injections; CI = confidence interval; RCT = randomized controlled trial; BMI = body mass index; QOL = quality of life; IRR = internal rate of return; RR = rate of return; rt-CGM = real-time continuous glucose monitoring; SMBG = self-monitoring of blood glucose; SAP = sensor-augmented pump;

Abstracts from Relevant Literature

Battelino, T. Phillip, M. Bratina, N. Nimri, R. Oskarsson, P. and Bolinder, J. 2011.

Effect of continuous glucose monitoring on hypoglycemia in type 1 diabetes.

OBJECTIVE: To assess the impact of continuous glucose monitoring on hypoglycemia in people with type 1 diabetes. RESEARCH DESIGN AND METHODS: In this randomized, controlled, multicenter study, 120 children and adults on intensive therapy for type 1 diabetes and a screening level of glycated hemoglobin A(1c) (HbA(1c)) <7.5% were randomly assigned to a control group performing conventional home monitoring with a blood glucose meter and wearing a masked continuous glucose monitor every second week for five days or to a group with real-time continuous glucose monitoring. The primary outcome was the time spent in hypoglycemia (interstitial glucose concentration <63 mg/dL) over a period of 26 weeks. Analysis was by intention to treat for all randomized patients. RESULTS: The time per day spent in hypoglycemia was significantly shorter in the continuous monitoring group than in the control group (mean +/- SD 0.48 +/- 0.57 and 0.97 +/- 1.55 h/day, respectively; ratio of means 0.49; 95% CI 0.26-0.76; P = 0.03). HbA(1c) at 26 weeks was lower in the continuous monitoring group than in the control group (difference -0.27%; 95% CI -0.47 to -0.07; P = 0.008). Time spent in 70 to 180 mg/dL normoglycemia was significantly longer in the continuous glucose monitoring group compared with the control group (mean hours per day, 17.6 vs. 16.0, P = 0.009). CONCLUSIONS: Continuous glucose monitoring was associated with reduced time spent in hypoglycemia and a concomitant decrease in HbA(1c) in children and adults with type 1 diabetes.

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Buse, J.B. Dailey, G. Ahmann, A.A. Bergenstal, R.M. Green, J.B. Peoples, T. Tanenberg, R.J. and Yang, Q. 2011.

Baseline predictors of A1C reduction in adults using sensor-augmented pump therapy or multiple daily injection therapy: the STAR 3 experience.

BACKGROUND: Baseline characteristics from the adult cohort of a randomized controlled trial comparing sensor-augmented pump (SAP) and multiple daily injection (MDI) therapy were analyzed for significant relationships with -0.5% A1C change at 1 year of therapy without incidence of severe hypoglycemia (defined as A1C benefit). METHODS: Baseline characteristics were compared with A1C benefit. Statistically significant predictors were analyzed further to determine appropriate cutpoints of relative A1C benefit. RESULTS: Baseline A1C >=9.1%, age at randomization >=36 years, and age at diabetes diagnosis of >=17 years were associated with a greater SAP benefit relative to MDI than other cutpoints. CONCLUSIONS: People with type 1 diabetes who had a high A1C and who were older at diagnosis and older at randomization experienced the most benefit from SAP therapy.

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Buse, J.B. Kudva, Y.C. Battelino, T. Davis, S.N. Shin, J. and Welsh, J.B. 2012.

Effects of sensor-augmented pump therapy on glycemic variability in well-controlled type 1 diabetes in the STAR 3 study.

BACKGROUND: Compared with multiple daily injections (MDI), sensor-augmented pump (SAP) insulin therapy may reduce glycemic variability and oxidative stress in type 1 diabetes in a glycosylated hemoglobin (A1C)-independent manner. SUBJECTS AND METHODS: The STAR 3 study compared SAP with MDI therapy for 1 year. Week-long continuous glucose monitoring studies were conducted at baseline and 1 year for assessment of glycemic variability in both groups. Soluble CD40 ligand (CD40L), a biomarker of inflammation and thrombocyte function, was measured at baseline and 1 year. Subjects were classified according to treatment group and 1-year A1C levels (<6.5%, 6.5-6.9%, 7-7.9%, >=8%). Glycemic parameters were compared between SAP and MDI subjects in each A1C cohort. RESULTS: At 1 year, sensor glucose values at A1C levels >=6.5% were similar in the SAP and MDI groups. However, sensor glucose SD and coefficient of variation (CV) values were lower at A1C levels <8% among SAP than among MDI subjects; the overall between-group difference was significant for both SD (P<0.01) and CV (P=0.01). The overall mean amplitude of glycemic excursion was similar in MDI and SAP groups (P=0.23). CD40L levels fell over the course of the study in both groups, but the between-group difference was not significant (P=0.18). CD40L concentrations were unrelated to A1C, change in A1C from baseline, or glycemic variability. CONCLUSIONS: At comparable A1C levels of <8%, SAP reduced glycemic variability as measured by SD and CV compared with MDI. SAP may provide beneficial reductions in the number and severity of glycemic excursions.

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Cordua, S. Secher, A.L. Ringholm, L. Damm, P. and Mathiesen, E.R. 2013.

Real-time continuous glucose monitoring during labour and delivery in women with type 1 diabetes – observations from a randomized controlled trial.

AIMS: To explore whether real-time continuous glucose monitoring during labour and delivery supplementary to hourly self-monitored plasma glucose in women with Type 1 diabetes reduces the prevalence of neonatal hypoglycaemia. METHODS: Women with Type 1 diabetes participating in a randomized controlled trial on the effect of real-time continuous glucose monitoring in pregnancy were included in this study. Twenty-seven of 60 (45%) women in the intervention arm used real-time continuous glucose monitoring during labour and delivery, supplementary to hourly self-monitored plasma glucose. Real-time continuous glucose monitoring glucose data covering the last 8 h prior to delivery were retrospectively evaluated, and maternal hypo- and hyperglycaemia were defined as glucose values <= 3.9 mmol/l and > 7.0 mmol/l, respectively. Women in the control arm (n = 59) solely used self-monitored plasma glucose. Neonatal hypoglycaemia was defined as a 2-h plasma glucose < 2.5 mmol/l. RESULTS: In infants of women using real-time continuous glucose monitoring during labour and delivery, 10 (37%) developed neonatal hypoglycaemia vs. 27 (46%) infants in the control arm (P = 0.45). Among 10 infants with and 17 infants without neonatal hypoglycaemia within the real-time continuous glucose monitoring arm, median maternal self-monitored plasma glucose was 6.2 (range 4.2-7.8) vs. 5.6 (3.3-8.5) mmol/l (P = 0.26) during labour and delivery, with maternal hyperglycaemia present in 17 (0-94) vs. 4 (0-46)% of the time (P = 0.02), and birthweight was 4040 (3102-4322) vs. 3500 (1829-4320) g (P = 0.04). Maternal hypoglycaemia up to delivery was relatively rare. CONCLUSIONS: The prevalence of neonatal hypoglycaemia was comparable between infants of women using real-time continuous glucose monitoring supplementary to self-monitored plasma glucose during labour and delivery and infants of women solely using self-monitored plasma glucose.

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*Luo, P. Cheng, Q. Chen, B. Li, Y. Wu, J. Zhang, X. Jiao, X. Zhao, J. and Lv, X. 2013.
Hypoglycemia and blood glucose fluctuations in the application of a sensor-augmented insulin pump.*

BACKGROUND: The purpose of this study was to understand the effect of sensor-augmented insulin pump (SAP) use on hypoglycemia and blood glucose (BG) fluctuations. SUBJECTS AND METHODS: Sixty patients with type 2 diabetes mellitus were randomly assigned to three groups of treatment with SAP, continuous subcutaneous insulin infusion (CSII), or multiple daily injection (MDI) therapy for 6 days. Parameters of glycemic control that were determined included mean BG concentration (MBG), SD of BG (SDBG), mean amplitude of glycemic excursions (MAGE), absolute means of daily differences (MODD), 24-h area under the curve at 10 h (AUC10), 24-h area under the curve at 3.9 h (AUC3.9), and Low Blood Glucose Index (LBGI). RESULTS: No significant differences were observed among the three groups in terms of MBG, SDBG, MAGE, or MODD at the beginning of treatment. The MBG, SDBG, MAGE, MODD, and total AUC10 of the SAP group improved over the 4 days of the intervention compared with the CSII and MDI groups; however, no significant differences were observed among the three groups in terms of total AUC3.9 and LBGI. CONCLUSIONS: Compared with CSII and MDI therapy, SAP therapy was able to rapidly lower mean BG and reduce BG level fluctuations with no increased risks of hypoglycemia.

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Appendix G. Summary Table

Conclusions From Systematic Review Executive Summary	Current Literature Search (July 2015)	FDA Class I Device Recalls	Expert Opinion	Surveillance Assessment
<p>Key Question 1: In patients receiving intensive insulin therapy, does mode of delivery (CSII vs. MDI) have a differential effect on process measures, intermediate outcomes, and clinical outcomes in patients with diabetes mellitus? Do these effects differ by:</p> <p>a. Type 1 or type 2 diabetes status?</p> <p>b. Age: very young children, adolescents, and adults, including older adults (age >65 years)?</p> <p>Pregnancy status: per-existing type 1 or type 2 diabetes?</p>				
<p>Summary of evidence of the comparative effectiveness of CSII versus MDI in children and adolescents with type 1 diabetes</p>				
<p>Outcome: HbA_{1c} SOE: Moderate # of studies / # of Good-Quality studies: 9 (7 RCTS; 2 non-RCTs) / 1</p> <p>Adolescents over 12 years of age vs. less than 12 years of age:</p> <ul style="list-style-type: none"> • Mean between-group difference in HbA_{1c} change from baseline: -0.14 percent • Slight decrease with CSII than with MDI (95% CI, -0.48 to 0.20%, P = 0.41). • Similar results among adolescents over 12 years old (mean between-group difference in the change from baseline HbA_{1c}, -0.10%; 95% CI, -0.47 to 0.27%) • Less different among children 12 years old or less (mean between-group difference in the change from baseline HbA_{1c}, -0.05%; 95% CI, -1.01 to 0.96%). 	<p>No studies were identified.</p>	<p>The Animas 2020 Insulin Infusion Pump, a CSII, insulin pump was recalled in April of 2013. The manufacturer identified a component issue affecting a small supply of this product. This component issue may trigger pumps to sound a false alarm indicating there has been a loss of prime, an occlusion, or no cartridge has been detected.</p>	<p>Both reviewers felt that the report's conclusions were up to date, but should provide more information on the limitations of the available literature. One expert noted that these conclusions may not apply to infants, toddlers, and children with neonatal diabetes mellitus due to limited data in these populations. This reviewer also felt that conclusions on adolescents should be interpreted with caution due to different ages among those in MDI vs. CSII treatment groups.</p> <p>One reviewer suggested two studies^{1,2} on the differential effects of mode of insulin delivery on HbA_{1c} in young children (<6 years old) but these were excluded due to their cross-sectional study design.</p>	<p>Likely current.</p>

<p>Outcome: Daytime hypoglycemia SOE: Low # of studies / # of Good-Quality studies: 3 (all RCTs) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • No significant difference in frequency of daytime hypoglycemia • Mean between-group difference in: <ul style="list-style-type: none"> ○ Perceived hypoglycemic events over 104 weeks: 0; 95% CI, -1.1 to 1.1; ○ Change from baseline to 24 weeks in the number of blood glucose excursions below 70 mg/dL: -0.9; 95% CI, -2.1 to 0.3 ○ Number of hypoglycemic episodes/patient at 52 weeks: -3.7; 95% CI, -13.2 to 5.8 	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date.	Likely current.
<p>Outcome: Nocturnal hypoglycemia SOE: Low # of studies / # of Good-Quality studies: 2 (all RCTs) / 1</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • No significant difference in frequency • 1 study reported 4 (MDI) events/patient/study period (95% CI, 0.3 to 7.7) vs. 3 (CSII) events/patient/study period (95% CI, 1.0 to 5.0) over 52 weeks. • 1 study reported 2 patients with 1 or more events (CSII); no events (MDI) over 16 weeks 	No studies were identified.	See above.	<p>Both reviewers felt that the report's conclusions were up to date.</p> <p>One reviewer suggested a study on a unified safety system in providing overnight closed-loop control in insulin delivery among children and adolescents with type 1 diabetes³ This study was excluded due to comparator criteria.</p>	Likely current.
<p>Outcome: Mild hypoglycemia SOE: Insufficient # of studies / # of Good-Quality studies: 1</p>	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date.	Likely current.

<p>(RCT) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • 1 study reported no significant difference in mild hypoglycemia (events with blood glucose less than 70 mg/dL) over 14 weeks. <ul style="list-style-type: none"> ○ MDI: 22 events/patient ○ CSII: 19.8 events/patient 				
<p>Outcome: Severe hypoglycemia SOE: Low # of studies / # of Good-Quality studies: 6 (5 RCTs; 1 non-RCT) / 1</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • Similar rates of severe hypoglycemia • Mean incidence ratio in hypoglycemic event rates in RCTs: 0.99 (95% CI, 0.57 to 1.71, P=0.97). <p>Adolescents over 12 years of age vs. less than 12 years:</p> <ul style="list-style-type: none"> • Similar results between both groups • Mean Incidence Ratio: <ul style="list-style-type: none"> ○ ≥12 years: 0.95; 95% CI, 0.42 to 2.13 ○ ≤12 years: 1.02; 95% CI, 0.49 to 2.16 	<p>No studies were identified.</p>	<p>See above.</p>	<p>Both reviewers felt that the report's conclusions were up to date.</p> <p>One reviewer suggested two studies^{1,2} on the differential effects of mode of insulin delivery on severe hypoglycemia in young children (<6 years old). These studies were excluded due to their cross-sectional study design.</p>	<p>Likely current.</p>
<p>Outcome: Hyperglycemia SOE: Insufficient # of studies / # of Good-Quality studies: 1 (RCT) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • 1 study reported no difference in frequency over 14 weeks. <ul style="list-style-type: none"> ○ MDI: 6.7 events ○ CSII: 9 events 	<p>No studies were identified.</p>	<p>See above.</p>	<p>Both reviewers felt that the report's conclusions were up to date.</p>	<p>Likely current.</p>

<p>Outcome: Ratio basal to bolus insulin SOE: Insufficient # of studies / # of Good-Quality studies: 1 (non-RCT) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • 1 study found no difference • Mean between-group difference: 1.7; 95% CI, -2.5 to 5.9 	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date.	Likely current.
<p>Outcome: Weight SOE: Low # of studies / # of Good-Quality studies: 3 (all RCTs) / 1</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • Mean between-group difference in how BMI standard deviation score changed from baseline: -0.12 units • Standard deviation decreased slightly more for CSII (95% CI, -0.55 to 0.30) 	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date, but should provide more information on the limitations of the available literature. One expert noted that these conclusions may not apply to infants, toddlers, and children with neonatal diabetes mellitus due to limited data in these populations. This reviewer also felt that conclusions on adolescents should be interpreted with caution due to different ages among those in MDI vs. CSII treatment groups.	Likely current.
<p>Outcome: General QOL SOE: Low # of studies / # of Good-Quality studies: 2 (all RCTs) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • Meta-analysis of 2 studies showed no significant difference 	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date.	Likely current.

<ul style="list-style-type: none"> • Mean between-group difference, 2.3; 95% CI, -6.9 to 11.5; P = 0.95 				
<p>Outcome: Diabetes-specific QOL SOE: Low # of studies / # of Good-Quality studies: 4 (all RCTs) / 1</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • 1 study showed improvement in diabetes QoL, favoring CSII <ul style="list-style-type: none"> ○ Diabetes QoL Youth Score at end of study: 77.4 (95% CI, 69.5 to 85.3) at baseline <ul style="list-style-type: none"> ▪ MDI: 76.4 (95% CI, 68.3 to 84.5) ▪ CSII: 82.7 (95% CI, 75.3 to 90.1) • 1 study found no difference (numerical data not presented) 	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date, but should provide more information on the limitations of the available literature. One expert noted that these conclusions may not apply to infants, toddlers, and children with neonatal diabetes mellitus due to limited data in these populations. This reviewer also felt that conclusions on adolescents should be interpreted with caution due to different ages among those in MDI vs. CSII treatment groups.	Likely current.
<p>Outcome: Diabetes treatment-related QOL SOE: Low # of studies / # of Good-Quality studies: 3 (all RCTs) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • Meta-analysis of 2 studies showed improvement, favoring CSII • Mean between-group difference in the Diabetes Treatment Satisfaction Questionnaire, 5.7; 95% CI, 5.0 to 6.4 	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date, but should provide more information on the limitations of the available literature. One expert noted that these conclusions may not apply to infants, toddlers, and children with neonatal diabetes mellitus due to limited data in these populations. This reviewer also felt that conclusions on adolescents should be interpreted with caution due to different ages among those in	Likely current.

			MDI vs. CSII treatment groups.	
<p>Outcome: Process measures, clinical outcomes SOE: Insufficient # of studies / # of Good-Quality studies: 0</p> <p>No relevant studies addressing certain measures: frequency of adjusting insulin therapy, adherence, health visits) and clinical outcomes (microvascular and macrovascular disease and mortality.</p>	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date	Likely current.
Summary of evidence of the comparative effectiveness of CSII versus MDI in adults with type 1 diabetes				
<p>Outcome: HbA_{1c} SOE: Low # of studies / # of Good-Quality studies: 1 (all RCTs) / 2</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • HbA_{1c} decreased more with CSII • Results were heavily by 1 study <ul style="list-style-type: none"> ○ Participants had a higher baseline HbA_{1c} than in the other studies (mean between-group difference from baseline, -0.30%; 95% CI, -0.58 to -0.02) ○ After removing the study, the difference between the two groups became null (mean between-group difference from baseline, -0.01 percent, 95% CI, -0.35 to 0.34 percent) 	No studies were identified.	The Animas 2020 Insulin Infusion Pump, a CSII, insulin pump was recalled in April of 2013. The manufacturer identified a component issue affecting a small supply of this product. This component issue may trigger pumps to sound a false alarm indicating there has been a loss of prime, an occlusion, or no cartridge has been detected.	Both reviewers felt that the report's conclusions were up to date One reviewer suggested a study ⁴ on the effects of CSII threshold suspend features on HbA _{1c} among adults with type 1 diabetes, The study was excluded due to comparator criteria	Likely current.

<p>Outcome: Daytime hypoglycemia SOE: Low # of studies / # of Good-Quality studies: 1 (RCT) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> 1 study reported more symptomatic and asymptomatic hypoglycemia between 8 a.m. and midnight in the MDI ($P \leq 0.05$) 	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date	Likely current.
<p>Outcome: Nocturnal hypoglycemia SOE: Low # of studies / # of Good-Quality studies: 3 (all RCTs) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> 3 studies reported hypoglycemia <ul style="list-style-type: none"> 1 crossover trial: proportion of patients was similar (RR for any, 0.98; 98% CI, 0.83 to 1.17; RR for symptomatic, 0.87; 95% CI, 0.64 to 1.19) Fewer episodes per person in CSII group (IRR, 0.76; 95% CI, 0.63 to 0.91). 2 studies found no statistically significant difference 	No studies were identified.	See above.	<p>Both reviewers felt that the report's conclusions were up to date.</p> <p>One reviewer suggested two studies^{4,5} on the effects of CSII threshold suspend features on nocturnal hypoglycemia among adults with type 1 diabetes. These studies were excluded due to comparator criteria.</p>	Likely current.
<p>Outcome: Symptomatic hypoglycemia SOE: Low # of studies / # of Good-Quality studies: 4 (all RCTs) / 1</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> Increased risk for CSII (combined IRR, 1.3; 95% CI, 1.2 to 1.4) Found evidence of substantial statistical heterogeneity for the meta-analysis. 	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date	Likely current.

<ul style="list-style-type: none"> • No relative difference in incidence when excluding a study that required participants to have had recent severe hypoglycemia (compared to the other 2, which excluded those with recent severe hypoglycemia) • IRR suggested no relative difference (combined IRR, 1.0; 95% CI, 0.8 to 1.1) • Another study, which did not provide sufficient quantitative results, reported slightly more events with CSII (IRR, 1.1; 95% CI, 1.0 to 1.3) <ul style="list-style-type: none"> ○ Similar proportion of participants experienced events over 5 weeks (RR, 1.0; 95% CI, 0.9 to 1.2). 				
<p>Outcome: Other nonsensitive hypoglycemia SOE: Low # of studies / # of Good-Quality studies: 6 (all RCTs) / 1</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • 3 studies found no difference in nonsevere hypoglycemia <ul style="list-style-type: none"> ○ 1 study mean between-group difference in asymptomatic hypoglycemia event rate, -0.2; 95% CI, -1.39 to 0.99). • 2 studies found incidence of mild hypoglycemia higher in CSII, <ul style="list-style-type: none"> ○ 1 study found relative statistically significant difference (0.99; 95% CI, 0.11 to 1.87) ○ 1 study found a higher frequency in MDI (RR, 1.12; 95% CI, 1.08 to 1.17) 	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date	Likely current.

<p>Outcome: Severe hypoglycemia SOE: Low # of studies / # of Good-Quality studies: 8 (all RCTs) / 1</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • Incidence did not differ between two groups (combined RR, 0.74; 95% CI, 0.30 to 1.83) • 4 crossover trials were not included in the meta-analysis because they did not provide quantitative results by period • 2 studies showed more severe hypoglycemia with MDI <ul style="list-style-type: none"> ◦ 1 study reported a RR of 2.6 (95% CI, 2.08 to 3.25) • 1 study reported less severe hypoglycemia with MDI (IRR, 3.00; 95% CI, 0.24 to 157.49) • 1 study found similar rates of severe hypoglycemia (1.1 events/patient for CSII vs. 1.3 events/patient for MDI over 4 months, P = 0.33) 	<p>No studies were identified.</p>	<p>See above.</p>	<p>Both reviewers felt that the report's conclusions were up to date</p>	<p>Likely current.</p>
<p>Outcome: Hyperglycemia SOE: Low # of studies / # of Good-Quality studies: 3 (all RCTs) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • 1 study favored CSII, with the mean between-group difference in fasting glucose over 6 months being: -12.3 mg/dL (95% CI, -32.9 to 8.2 mg/dL) • 2 other studies reported no difference in fasting glucose 	<p>No studies were identified.</p>	<p>See above.</p>	<p>Both reviewers felt that the report's conclusions were up to date</p>	<p>Likely current.</p>

<p>Outcome: Bedtime hyperglycemia SOE: Insufficient # of studies / # of Good-Quality studies: 1 (RCT) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • Insufficient SOE to determine the relative effects • 1 study reported no difference, but did not provide glucose results 	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date	Likely current.
<p>Outcome: Pre-prandial glucose SOE: Low # of studies / # of Good-Quality studies: 3 (all RCTs) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • Mean between-group difference over 6 months: -17.1 mg/dL (95% CI, -42.1 to 8.0 mg/dL) <ul style="list-style-type: none"> ○ 1 study favored CSII ○ 1 study found pre-dinner glucose to be lower with CSII (128 mg/dL) vs. MDI (148 mg/dL) at the end of 5 weeks (P=NS) ○ 1 study did not find significantly lower glucose pre-dinner and pre-lunch glucose levels at 4 months 	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date	Likely current.
<p>Outcome: Post-prandial glucose SOE: Low # of studies / # of Good-Quality studies: 3 (all RCTs) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • Evidence suggested slightly lower levels with CSII • 1 study reported a mean difference of: 	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date	Likely current.

<p>-5.5 mg/dl (95% CI, -29.9 to 18.9 mg/dl)</p> <ul style="list-style-type: none"> 1 study reported a mean difference of: -24 and -15 mg/dl post-breakfast and post-dinner <p>1 study did not find significantly higher post-breakfast glucose levels in MDI</p>				
<p>Outcome: Nocturnal hyperglycemia SOE: Low # of studies / # of Good-Quality studies: 2 (all RCTs) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> 2 studies found no between-group difference <ul style="list-style-type: none"> 1 study reported an increase in both arms (between-group difference, 54.8; 95% CI, -7.2 to 116.7 mg/dl) 	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date	Likely current.
<p>Outcome: Weight SOE: Low # of studies / # of Good-Quality studies: 4 (all RCTs) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> No difference in weight gain (combined mean between-group difference, -0.25 kg; 95% CI, -3.14 to 2.64 kg). 2 studies reported no difference in weight gain, but did not report sufficient quantitative results. 	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date	Likely current.
<p>Outcome: General QOL SOE: Low # of studies / # of Good-Quality studies: 2 (all RCTs) / 0</p> <p>MDI vs. CSII Intervention Groups: 2 studies showed an improvement between two</p>	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date	Likely current.

<p>groups, favoring CSII.</p> <ul style="list-style-type: none"> • 1 study reported change in: <ul style="list-style-type: none"> ○ SF-36 Physical Component Score (P=0.048): <ul style="list-style-type: none"> ▪ CSII: -1.2 ▪ MDI: 5.9 ○ Mental Component Score (P=0.05): <ul style="list-style-type: none"> ▪ CSII: -0.6 ▪ MDI: 5.2 • 1 study did not report estimates <ul style="list-style-type: none"> ○ No difference in the Physical Component Score ○ Change in Mental Component Score, favoring CSII (P<0.05) 				
<p>Outcome: Diabetes-specific QOL SOE: Low # of studies / # of Good-Quality studies: 5 (all RCTs) / 1</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • 3 studies showed an improvement, favoring CSII • 1 meta-analysis favored CSII mean between-group difference in Diabetes Quality of Life, 2.99; 95% CI, 0.006 to 5.97) • 1 study showed improvement, favoring MDI (Diabetes Quality of Life mean between-group difference in change from baseline, -18.00; 95% CI, -50.14 to 14.14). 	<p>No studies were identified.</p>	<p>See above.</p>	<p>Both reviewers felt that the report's conclusions were up to date</p>	<p>Likely current.</p>

<p>Outcome: Diabetes treatment-related QOL SOE: Insufficient # of studies / # of Good-Quality studies: 1 (RCT) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • Altered Hypoglycemia Awareness Questionnaire scores were similar in the CSII and MDI groups over 24 weeks (RR of Altered Hypoglycemia Awareness Questionnaire score greater than 4, 0.75; 95% CI, 0.26 to 2.18) • Hypoglycemia Fear Survey scores decreased in both: <ul style="list-style-type: none"> ○ CSII: (-3±25) ○ MDI: (-8±33) • Mean between-group difference in the change from baseline (5; 95% CI, -32.66 to 42.66) 	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date	Likely current.
<p>Outcome: Process measures, clinical outcomes SOE: Insufficient # of studies / # of Good-Quality studies: 0</p> <p>None of the studies evaluated the effects of MDI vs. CSII among adults with type 1 diabetes in terms of any process measures or clinical outcomes.</p>	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date.	Likely current.
Summary of the evidence of the comparative effectiveness of CSII versus MDI in adults with type 2 diabetes				
<p>Outcome: Mortality SOE: Insufficient # of studies / # of Good-Quality studies: 1 (RCT) / 0</p> <p>1 study reported 1 death due to cancer in the CSII treatment arm</p>	No studies were identified.	The Animas 2020 Insulin Infusion Pump, a CSII, insulin pump was recalled in April of 2013. The manufacturer identified a component issue affecting a small supply of this product. This component issue may	Both reviewers felt that the report's conclusions were up to date.	Likely current.

		trigger pumps to sound a false alarm indicating there has been a loss of prime, an occlusion, or no cartridge has been detected.		
<p>Outcome: HbA_{1c} SOE: Moderate # of studies / # of Good-Quality studies: 4 (all RCTs) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> The effects did not differ between the intervention groups (mean between-group difference from baseline with negative value favoring CSII, -0.16; 95% CI, -0.42 to 0.09) 	No studies were identified	See above.	Both reviewers felt that the report's conclusions were up to date.	Likely current.
<p>Outcome: Mild hypoglycemia SOE: Moderate # of studies / # of Good-Quality studies: 3 (all RCTs) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> Risk did not differ between the intervention groups (combined RR, 0.90; 95% CI, 0.78 to 1.03). 	No studies were identified	See above.	Both reviewers felt that the report's conclusions were up to date.	Likely current.
<p>Outcome: Nocturnal hypoglycemia SOE: Insufficient # of studies / # of Good-Quality studies: 1 (RCT) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> 1 study reported nocturnal hypoglycemia was less common in patients in the CSII arm (RR, 0.73; 95% CI, 0.35 to 1.54) 	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date.	Likely current.

<p>Outcome: Severe hypoglycemia SOE: Low # of studies / # of Good-Quality studies: 3 (all RCTs) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • Risk of severe hypoglycemia did not differ (RR, 0.76; 95% CI, 0.26 to 2.19). 	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date.	Likely current.
<p>Outcome: Hyperglycemia SOE: Low # of studies / # of Good-Quality studies: 2 (all RCTs) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • Mean post-prandial glucose (90 minutes after breakfast) at 24 weeks: <ul style="list-style-type: none"> ○ CSII: 167 mg/dL ○ MDI: 192 mg/ dL ○ Mean between-group difference, -25 mg/dL; 95% CI, -45 to -5 mg/ dL • Glucose measurements from other time points were similar between treatment groups at the end of the study. • Incidence of blood glucose over 350 mg/dL was higher in the MDI arm vs. CSII (26 vs. 6 events) <ul style="list-style-type: none"> ○ Affected 18% and 5% of participants in MDI and CSII arms respectively (RR, 0.28; 95% CI, 0.08 to 0.94). 	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date.	Likely current.
<p>Outcome: Weight SOE: Low # of studies / # of Good-Quality studies: 2 (all RCTs) / 0</p>	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date.	Likely current.

<p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> No difference between intervention groups (combined mean between-group difference in weight change from baseline, -0.49 kg; 95% CI, -1.25 to 0.26 kg). 				
<p>Outcome: General QOL SOE: Insufficient # of studies / # of Good-Quality studies: 1 (RCT) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> 1 study reported no difference between intervention groups Difference from baseline to follow-up <ul style="list-style-type: none"> SF-36v2 Component Score: <ul style="list-style-type: none"> CSII: 0.6 MDI: 0.4 Mental Component Score: <ul style="list-style-type: none"> CSII: 1.0 MDI: 2.5 	<p>No studies were identified.</p>	<p>See above.</p>	<p>Both reviewers felt that the report's conclusions were up to date.</p>	<p>Likely current.</p>
<p>Outcome: Diabetes-specific QOL SOE: Insufficient # of studies / # of Good-Quality studies: 1 (RCT) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> 1 study reported no difference between the intervention groups <ul style="list-style-type: none"> Diabetes Quality of Life Clinical Trials Questionnaire scores improved over 12 months from: <ul style="list-style-type: none"> CSII: 52 to 81 MDI: 50 to 78 	<p>No studies were identified.</p>	<p>See above.</p>	<p>Both reviewers felt that the report's conclusions were up to date.</p>	<p>Likely current.</p>

<p>Outcome: Diabetes treatment-related QOL SOE: Insufficient # of studies / # of Good-Quality studies: 1 (RCT) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> 1 study reported improvement in treatment satisfaction, favoring CSII mean between-group difference in Phase V Outcomes System Diabetes Treatment Satisfaction score change from baseline in 24 weeks, 13.1; 95% CI, 7.4 to 18.8) 	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date.	Likely current.
<p>Outcome: Process measures, microvascular disease, macrovascular disease SOE: Insufficient # of studies / # of Good-Quality studies: 0</p> <p>No studies evaluating the effects of MDI vs. CSII among patients with type 2 diabetes in terms of any of the process measures, microvascular disease, or macrovascular disease were identified.</p>	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date.	Likely current.
Summary of the evidence of the comparative effectiveness of CSII versus MDI in pregnant women with pre-existing type 1 diabetes				
<p>Outcome: HbA_{1c} SOE: Low # of studies / # of Good-Quality studies: 6 (all OBS) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> 6 observational studies reported an improvement in HbA_{1c} in both intervention groups during pregnancy. <ul style="list-style-type: none"> No significant difference between groups in HbA_{1c} in any of the trimesters Mean between-group 	No studies were identified.	The Animas 2020 Insulin Infusion Pump, a CSII, insulin pump was recalled in April of 2013. The manufacturer identified a component issue affecting a small supply of this product. This component issue may trigger pumps to sound a false alarm indicating there has been a loss of prime, an occlusion, or no cartridge has been detected. .	Both reviewers felt that the report's conclusions were up to date.	Likely current.

<p>differences in third-trimester HbA_{1c} values in each of the studies were: 0.2 (95% CI, -0.3 to 0.7), -0.4 (95% CI, -0.8 to 0.04), 0.6 (95% CI, -0.7 to 1.9), -0.3 (95% CI, -0.6 to -0.03), 0.2 (95% CI, -0.2 to 0.6), and 0.4 (95% CI, -0.9 to 1.7).</p>				
<p>Outcome: Cesarean section rates SOE: Insufficient # of studies / # of Good-Quality studies: 3 (all OBS) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> 1 meta-analysis of 4 retrospective studies showed a pooled RR of 1.02 (95% CI, 0.86 to 1.20), which was inconclusive because of high-risk bias 	<p>No studies were identified.</p>	<p>See above.</p>	<p>Both reviewers felt that the report's conclusions were up to date.</p>	<p>Likely current.</p>
<p>Outcome: Maternal hypoglycemia SOE: Insufficient # of studies / # of Good-Quality studies: 2 (all OBS) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> 1 meta-analysis of 3 retrospective studies for rate of severe hypoglycemia showed a pooled RR of 0.78, which was inconclusive because of high risk of bias (95% CI, 0.23 to 2.65). 	<p>No studies were identified.</p>	<p>See above.</p>	<p>Both reviewers felt that the report's conclusions were up to date.</p>	<p>Likely current.</p>
<p>Outcome: Maternal weight gain SOE: Insufficient # of studies / # of Good-Quality studies: 3 (all OBS) / 0</p> <p>MDI vs. CSII Intervention Groups:</p>	<p>No studies were identified.</p>	<p>See above.</p>	<p>Both reviewers felt that the report's conclusions were up to date.</p>	<p>Likely current.</p>

<ul style="list-style-type: none"> • 3 studies reported no difference between the two intervention groups, with high risk of bias. • Mean between-group difference: <ul style="list-style-type: none"> ○ 1 study: 1.9 kg (95% CI, -0.9 to 4.7 kg) ○ 1 study: 0.1 kg (95% CI, -2.4 to 2.6 kg) • 1 study reported a median weight gain of: <ul style="list-style-type: none"> ○ CSII: 13.5 kg ○ MDI: 13.9 kg 				
<p>Outcome: Other maternal outcomes SOE: Insufficient # of studies / # of Good-Quality studies: 0</p> <p>None of the studies evaluated maternal mortality, microvascular or macrovascular disease, quality of life, or any of the process measures.</p>	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date.	Likely current.
<p>Outcome: Gestational age at delivery SOE: Insufficient # of studies / # of Good-Quality studies: 4 (all OBS) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • Range: <ul style="list-style-type: none"> ○ MDI: 36.6 to 37.5 weeks ○ CSII: 36.3 to 36.6 weeks • No significant difference between intervention groups, but studies had high risk of bias 	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date.	Likely current.
<p>Outcome: Neonatal hypoglycemia SOE: Insufficient # of studies / # of Good-Quality studies: 4 (all OBS) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • 1 meta-analysis of 4 retrospective 	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date.	Likely current.

cohort studies for frequency showed a pooled RR of 1.10 (95% CI, 0.86 to 1.20), which was inconclusive because of high risk of bias.				
<p>Outcome: Birth weight SOE: Insufficient # of studies / # of Good-Quality studies: 3 (all OBS) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> 1 meta-analysis of 3 retrospective cohort studies showed a pooled mean between-group difference in birth weight of 107.2 g (95% CI, -86.6 to 295.9 g), which was inconclusive because of high risk of bias. 	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date.	Likely current.
<p>Outcome: Major congenital anomalies SOE: Insufficient # of studies / # of Good-Quality studies: 2 (all OBS) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> 1 meta-analysis of 2 retrospective cohort studies showed a pooled RR of 2.12 favoring MDI (95% CI, 0.38 to 11.77), which was inconclusive because of high risk of bias. 	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date.	Likely current.
<p>Outcome: Minor congenital anomalies SOE: Insufficient # of studies / # of Good-Quality studies: 3 (all OBS) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> 3 studies with high risk of bias found no difference between intervention groups 2 group studies reported no minor 	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date.	Likely current.

<ul style="list-style-type: none"> congenital anomalies in either group Rates of minor congenital anomalies and pregnancy termination rates: <ul style="list-style-type: none"> MDI: 2.3% (2/86 patients) CSII: 13% (P=0.05) 				
<p>Outcome: NICU admissions SOE: Insufficient # of studies / # of Good-Quality studies: 2 (all OBS) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> 1 meta-analysis of 2 retrospective cohort studies showed a pooled RR of 0.84 (95% CI, 0.43 to 1.68), which was inconclusive because of high risk of bias 	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date.	Likely current.
<p>Outcome: Preterm delivery SOE: Insufficient # of studies / # of Good-Quality studies: 4 (all OBS) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> 1 meta-analysis of 4 retrospective cohort studies showed a pooled RR of 0.98 (95% CI, 0.67 to 1.43), which was inconclusive because of high risk of bias. 	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date.	Likely current.
<p>Outcome: Stillbirth rates SOE: Insufficient # of studies / # of Good-Quality studies: 4 (all OBS) / 0</p> <p>MDI vs. CSII Intervention Groups: 4 studies reported on stillbirth rates</p> <ul style="list-style-type: none"> 3 studies reported no stillbirths in either group 1 study reported having 1 stillbirth in MDI group 	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date.	Likely current.

<p>Outcome: Neonatal mortality SOE: Insufficient^a # of studies / # of Good-Quality studies: 3 (all OBS) / 0</p> <p>MDI vs. CSII Intervention Groups: 3 studies reported on neonatal mortality rate</p> <ul style="list-style-type: none"> • 1 study reported 1 neonatal death in each group • 1 study did not have neonatal deaths in either group⁶¹ • 1 study reported mortality rates of: <ul style="list-style-type: none"> ○ MDI: 0% ○ CSII: 2.7% 	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date.	Likely current.
<p>Outcome: Perinatal mortality SOE: Insufficient # of studies / # of Good-Quality studies: 2 (all OBS) / 0</p> <p>MDI vs. CSII Intervention Groups:</p> <ul style="list-style-type: none"> • 1 study reported a mortality rate of: <ul style="list-style-type: none"> ○ CSII: 3% ○ MDI: 4% • 1 study reported a mortality rate of: <ul style="list-style-type: none"> ○ CSII: 2.7% ○ MDI: 0% 	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date.	Likely current.
<p>Outcome: Birth trauma SOE: Insufficient # of studies / # of Good-Quality studies: 0</p> <p>None of the studies reported on birth trauma.</p>	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date.	Likely current.
<p>Key Question 2. In patients using intensive insulin therapy (MDI or CSII), does the type of glucose monitoring (rt-CGM vs. SMBG) have a differential effect on process measures, intermediate outcomes, and clinical outcomes in patients with diabetes mellitus (i.e., what is the incremental benefit of rt-CGM in patients already using intensive insulin therapy)? Do these effects differ by:</p> <ol style="list-style-type: none"> a. Type 1 or type 2 diabetes status? b. Age: very young children, adolescents, and adults, including older adults (age >65 years)? 				

c. Pregnancy status: pre-existing type 1 or type 2 diabetes? Intensive insulin delivery: MDI or CSII?				
Summary of evidence of the comparative effectiveness of rt-CGM versus SMBG				
<p>Outcome: HbA_{1c} SOE: High # of studies / # of Good-Quality studies: 8 (all RCTs) / 4</p> <p>Rt-CGM vs. SMBG groups:</p> <ul style="list-style-type: none"> • Rt-CGM favored for the effects of HbA_{1c} • Mean between-group change from baseline was 0.30% (95% CI, -0.37 to -0.22%) • 1 sensitivity analysis (which included only studies with more than 60% compliance, 7 estimates) reported a greater HbA_{1c} reduction (mean between-group difference from baseline, -0.36%; 95% CI, -0.44 to -0.27%) • 1 meta-analysis of 4 studies in children and adolescents ≤18 years showed a significant combined mean between-group difference in HbA_{1c} change from baseline of -0.26% favoring rt-CGM (95% CI, -0.46 to -0.06%). 	No studies were identified.	The Animas 2020 Insulin Infusion Pump, a CSII, insulin pump was recalled in April of 2013. The manufacturer identified a component issue affecting a small supply of this product. This component issue may trigger pumps to sound a false alarm indicating there has been a loss of prime, an occlusion, or no cartridge has been detected	Both reviewers felt that the report's conclusions were up to date.	Likely current.
<p>Outcome: Non-severe hypoglycemia SOE: Moderate # of studies / # of Good-Quality studies: 6 (all RCTs) / 3</p> <p>Rt-CGM vs. SMBG groups:</p> <ul style="list-style-type: none"> • 1 meta-analysis of 4 studies (6 estimates) showed no difference in time spend in the hypoglycemic range (glucose level less than 70 mg/dL • Mean between-group difference was - 	One randomized controlled trial ⁶ observed pregnant women with type 1 diabetes using rt-CGM during labor and delivery. In infants of the women involved in the rt-CGM group, approximately 10 (37%) developed neonatal hypoglycemia vs. 27 (46%) in the self monitoring arm (P = .45). Among 10 infants	See above.	Both reviewers felt that the report's conclusions were up to date.	Conclusions may not be current.

<p>2.11 minutes/day (95% CI, -5.66 to 1.44 minutes/day).</p>	<p>with and 17 infants without neonatal hypoglycaemia within the rt-CGM arm, median maternal self-monitored plasma glucose was 6.2 (range 4.2-7.8) vs. 5.6 (3.3-8.5) mmol/l (P = 0.26) during labor and delivery, with maternal hyperglycemia present in 17 (0-94) vs. 4 (0-46)% of the time (P = 0.02), and birthweight was 4040 (3102-4322) vs. 3500 (1829-4320) g (P = 0.04).</p>			
<p>Outcome: Severe hypoglycemia SOE: Low # of studies / # of Good-Quality studies: 7 (all RCTs) / 4</p> <p>Rt-CGM vs. SMBG groups:</p> <ul style="list-style-type: none"> • No difference in rate (pooled RR, 0.95; 95% CI, 0.53 to 1.69) • 2 trials reported data in pediatric populations <ul style="list-style-type: none"> ○ 1 study reported severe hypoglycemia as less common among patients using rt-CGM (SMBG 4/78 vs. rt-CGM 0/76, P = 0.046). ○ 1 study's pediatric subgroups (ages 8-14 years) showed a similar incidence in both arms (SMBG 6/58 vs. rt-CGM 4/56, P = 0.74). 	<p>No studies were identified.</p>	<p>See above.</p>	<p>Both reviewers felt that the report's conclusions were up to date.</p>	<p>Likely current.</p>

<p>Outcome: Hyperglycemia SOE: Moderate # of studies / # of Good-Quality studies: 5 (all RCTs) / 3</p> <p>Rt-CGM vs. SMBG groups:</p> <ul style="list-style-type: none"> • 1 meta-analysis of 4 studies (6 estimates) indicated a significant reduction in time spent in the hyperglycemic range (glucose level greater than 180 mg/dL), favoring rt-CGM <ul style="list-style-type: none"> ○ Mean between-group difference: -68.56 minutes/day favoring rt-CGM (95% CI, -101.17 to -35.96). 	<p>One study⁶ found hyperglycemia present in 17 (0-94) vs. 4 (0-46)% of women (P=0.02) within the rt-CGM arm during labor and delivery.</p>	<p>See above.</p>	<p>Both reviewers felt that the report's conclusions were up to date.</p>	<p>Likely current.</p>
<p>Outcome: Ratio of basal to bolus insulin SOE: Low # of studies / # of Good-Quality studies: 2 (all RCTs) / 1</p> <p>Rt-CGM vs. SMBG groups:</p> <ul style="list-style-type: none"> • 1 study reported that the basal rate was a higher proportion of total daily insulin dose in the rt-CGM group (mean between-group difference in final basal rate, 4.3%; 95% CI, 0.8 to 7.8%). • 1 study reported a higher percentage of insulin delivered as bolus in the rt-CGM group (mean between-group difference in final percentage of insulin delivered as bolus, -4.0%; 95% CI, -9.3 to 1.3%). 	<p>No studies were identified.</p>	<p>See above.</p>	<p>Both reviewers felt that the report's conclusions were up to date.</p>	<p>Likely current.</p>

<p>Outcome: General QOL SOE: Low # of studies / # of Good-Quality studies: 2 (all RCTs) / 1</p> <p>Rt-CGM vs. SMBG groups:</p> <ul style="list-style-type: none"> • 1 study found no difference in parental satisfaction between the intervention arms at 12 months: <ul style="list-style-type: none"> ○ Mean between-group difference in change from baseline (WHO Well Being Index-5 mother's well-being score) was 2.7; 95% CI, -14.2 to 8.8 • 1 study assessed general QoL at 26 weeks (SF-12) <ul style="list-style-type: none"> ○ Physical Component Score: improvement, favoring rt-CGM <ul style="list-style-type: none"> ▪ Mean between-group difference in change from baseline, 1.4; 95% CI, -1.5 to 4.3 ○ Mental Component Score: no difference <ul style="list-style-type: none"> ▪ Mean between-group difference in change from baseline, -1.6; 95% CI, -5.9 to 2.7 	<p>No studies were identified.</p>	<p>See above.</p>	<p>Both reviewers felt that the report's conclusions were up to date.</p>	<p>Likely current.</p>
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<p>Outcome: Diabetes-specific QOL SOE: Low # of studies / # of Good-Quality studies: 2 (all RCTs) / 0</p> <p>Rt-CGM vs. SMBG groups:</p> <ul style="list-style-type: none"> • No difference between the two groups in either study at 26 weeks <ul style="list-style-type: none"> ○ Problem Areas in Diabetes score mean between-group difference in the change from baseline: -0.9; 95% CI, -7.9 to 6.1 ○ Diabetes QoL score mean between-group difference in the change from baseline: -3.0; 95% CI, -6.6 to 0.6). 	<p>No studies were identified.</p>	<p>See above.</p>	<p>Both reviewers felt that the report's conclusions were up to date.</p>	<p>Likely current.</p>
<p>Outcome: Diabetes treatment-related QOL SOE: Insufficient # of studies / # of Good-Quality studies: 1 (RCT) / 0</p> <p>Rt-CGM vs. SMBG groups:</p> <ul style="list-style-type: none"> • Fear of hypoglycemia was less with the rt-CGM group <ul style="list-style-type: none"> ○ Mean between-group difference in change from baseline score, -2.3; 95% CI, -8.2 to 3.6 	<p>No studies were identified</p>	<p>See above.</p>	<p>Both reviewers felt that the report's conclusions were up to date.</p>	<p>Likely current.</p>

<p>Outcome: Process measures, weight, and clinical outcomes SOE: Insufficient # of studies / # of Good-Quality studies: 0</p> <p>None of the studies evaluated the effects of rt-CGM vs. SMBG in terms of mortality, microvascular or macrovascular disease, weight, or any other process measure.</p>	<p>No studies were identified.</p>	<p>See above.</p>	<p>Both reviewers felt that the report's conclusions were up to date.</p>	<p>Likely current.</p>
<p>Summary of the evidence of the comparative effectiveness of rt-CGM + CSII (sensor-augmented pump) versus MDI/SMBG</p>				
<p>Outcome: HbA_{1c} SOE: Moderate # of studies / # of Good-Quality studies: 4 (all RCTs) / 2</p> <p>Sensor-augmented pumps vs. MDI/SMBG:</p> <ul style="list-style-type: none"> • Sensor-augmented pumps were favored over MDI/SMBG for their effects on HbA_{1c} • Mean between-group difference in HbA_{1c} change, -0.68%; 95% CI, -0.81 to -0.54%) 	<p>One study⁷ examined predictors of lower HbA_{1c} at 1 year among patients receiving SAP therapy versus those receiving MDI. This study was an additional analysis of data from a RCT⁸- called STAR 3- which published findings in 2010 and was included in the original review. According to the 2010 article⁸, although both groups had lower HbA_{1c} levels at 1 year, patients receiving SAP therapy had significantly lower HbA_{1c} levels compared to patients receiving MDI/SMBG (7.5% to 8.1%, p<0.001) at 1 year. The 2010 article also reported that a greater proportion of SAP patients reached target HbA_{1c} levels at 1 year compared to MDI/SMBG patients. The new 2011 Buse et al. article⁷ built on these findings by analyzing which baseline factors were associated with -.5% HbA_{1c}</p>	<p>The Animas 2020 Insulin Infusion Pump, a CSII, insulin pump was recalled in April of 2013. The manufacturer identified a component issue affecting a small supply of this product. This component issue may trigger pumps to sound false alarm indicating there has been a loss of prime, an occlusion, or no cartridge has been detected</p>	<p>Both reviewers felt that the report's conclusions were up to date.</p>	<p>Conclusions may not be current.</p>

	change at 1 year without incidence of severe hypoglycemia. This analysis determined that baseline HbA1c ($\geq 9.1\%$), age at randomization (≥ 36 years), and age at diabetes diagnosis (≥ 17 years) were associated with a greater SAP benefit relative to MDI/SMBG than other cutpoints.			
<p>Outcome: Non-severe hypoglycemia SOE: Moderate # of studies / # of Good-Quality studies: 2 (all RCTs) / 2</p> <p>Sensor-augmented pumps vs. MDI/SMBG:</p> <ul style="list-style-type: none"> • No difference in time spent with non-severe hypoglycemia between the intervention groups 	No studies were identified.	See above.	Both reviewers felt that the report's conclusions were up to date.	Conclusions may not be current.
<p>Outcome: Severe hypoglycemia SOE: Moderate # of studies / # of Good-Quality studies: 4 (all RCTs) / 2</p> <p>Sensor-augmented pumps vs. MDI/SMBG:</p> <ul style="list-style-type: none"> • No difference in incidence between the intervention groups (RR, 1.2; 95% CI, 0.7 to 2.3) <ul style="list-style-type: none"> ○ Number of events: <ul style="list-style-type: none"> ▪ 0 (SAP) vs. 3 (MDI/SMBG) ▪ 0/8 (SAP) vs. 1/8 (MDI/SMBG) ▪ RR 3.5; 95% CI, 0.4 to 304 	No studies were identified	See above.	Both reviewers felt that the report's conclusions were up to date.	Conclusions may not be current.

<p>Outcome: Hyperglycemia SOE: Moderate # of studies / # of Good-Quality studies: 2 (all RCTs) / 2</p> <p>Two trials suggested time spent in hyperglycemia was significantly less in the sensor-augmented pump group than the MDI/SMBG intervention group ($P < 0.001$).</p>	<p>No studies were identified.</p>	<p>See above.</p>	<p>Both reviewers felt that the report's conclusions were up to date.</p>	<p>Likely current.</p>
<p>Outcome: Weight SOE: Low # of studies / # of Good-Quality studies: 2 (all RCTs) / 1</p> <p>Sensor-augmented pumps vs. MDI/SMBG:</p> <ul style="list-style-type: none"> • 1 study reported no significant difference in weight gain between intervention groups (mean, 2.4 kg vs. 1.8 kg; $P = 0.19$) • 1 study reported weight increase, but difference was not significant: <ul style="list-style-type: none"> ○ SAP group: 0.7 kg ○ MDI/SMBG: 2.0 kg ○ Mean between-group difference, 1.3 kg; 95% CI, -21.2 to 23.8 kg 	<p>No studies were identified.</p>	<p>See above.</p>	<p>Both reviewers felt that the report's conclusions were up to date.</p>	<p>Likely current.</p>
<p>Outcome: Diabetes treatment-related QOL SOE: Low # of studies / # of Good-Quality studies: 2 (all RCTs) / 1</p> <p>Sensor-augmented pumps vs. MDI/SMBG:</p> <ul style="list-style-type: none"> • User acceptance and overall diabetes treatment satisfaction were greater in sensor-augmented pump arm • Scores for Blood Glucose Monitoring System Rating Questionnaire: <ul style="list-style-type: none"> ○ SAP: 83.3 ± 21.7 ○ MDI/SMBG: 33.3 ± 22.6 ○ Mean between-group 	<p>No studies were identified.</p>	<p>See above.</p>	<p>Both reviewers felt that the report's conclusions were up to date.</p>	<p>Likely current.</p>

<p>difference in final scores, 50.0; 95% CI, 33.6 to 66.</p>				
<p>Outcome: Process measures, weight, and clinical outcomes SOE: Insufficient # of studies / # of Good-Quality studies: 0 None of the studies evaluated the effects of sensor-augmented pumps vs. MDI/SMBG in terms of mortality, microvascular or macrovascular disease, or any of the process measures.</p>	<p>No studies were identified.</p>	<p>See above.</p>	<p>Both reviewers felt that the report's conclusions were up to date.</p>	<p>Likely current.</p>

Legend: SOE = strength of evidence; CSII = continuous subcutaneous insulin infusion; MDI = multiple daily injections; CI = confidence interval; RCT = randomized controlled trial; BMI = body mass index; QOL = quality of life; IRR = internal rate of return; RR = rate of return; rt-CGM = real-time continuous glucose monitoring; SMBG = self-monitoring of blood glucose; SAP = sensor-augmented pump;

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