Washington State Health Care Authority

Continuous glucose monitoring: update

Final evidence report: appendices

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Continuous Glucose Monitoring: Update

Aggregate Analytics, Inc.

Final Evidence Report
APPENDICES

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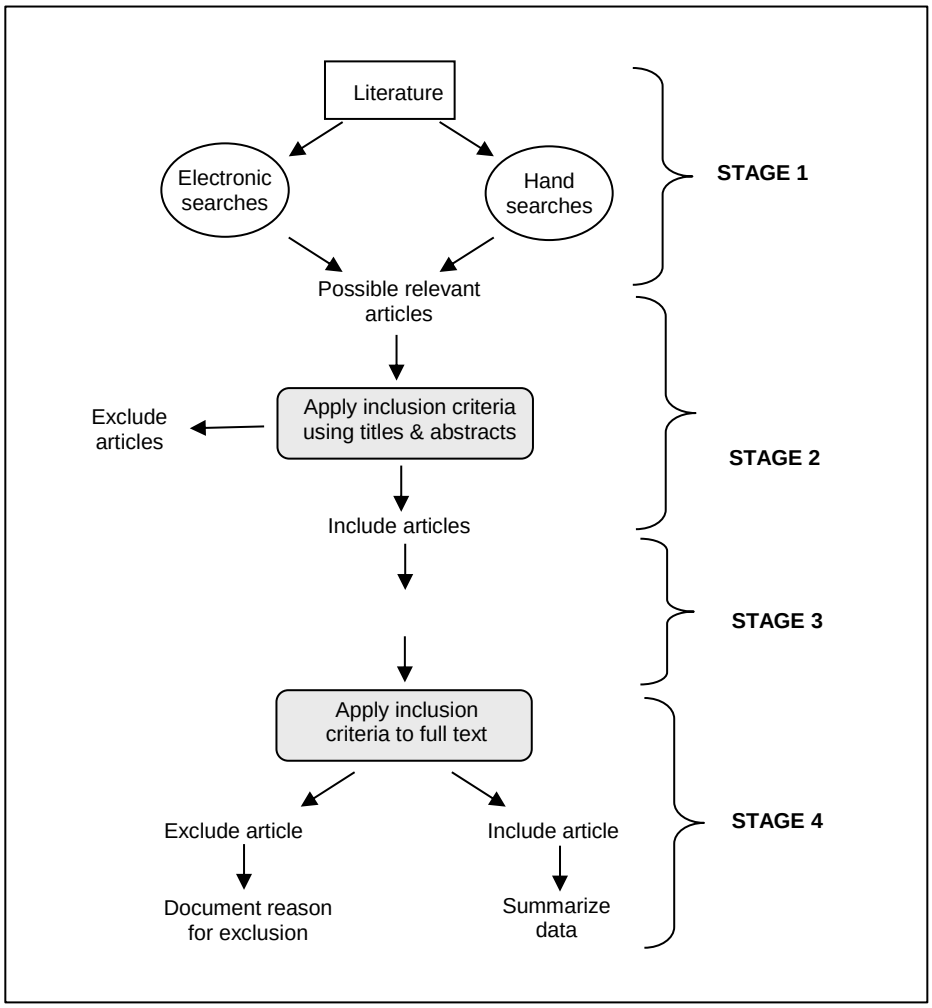

APPENDIX B. Search Strategies

Below is the search strategy for PubMed. Parallel strategies were used to search other electronic databases listed below. Keyword searches were conducted in the other listed resources.

Search strategy (PubMed)
Search date: March 2010 through 10/23/2017
Filters: Abstract available, English, Human

	Terms	Results
1	Diabetes Mellitus[MAJR:noexp] OR Diabetes, gestational[MH] OR diabetes mellitus, type 1[MH] OR diabetes mellitus, type i[MH] OR diabetes mellitus, type 2[MH] OR diabetes mellitus, type ii[MH] OR diabetes mellitus, juvenile onset[MH] OR diabetes mellitus, insulin dependent[MH]	76747
2	Blood glucose self monitoring[MH] OR continuous glucose monitor* OR continuous glucose measur* OR continuous blood glucose monitor* OR continuous blood glucose measur* OR continuous subcutaneous glucose monitor* OR ("continuous home monitoring" AND glucose[tiab]) OR continuous glucose sensor* OR cgms[tiab] OR cgm[tiab] OR chmg[tiab] OR ("Monitoring, Ambulatory"[mh] AND (glucose[tiab] OR insulin[tiab] OR glycem*[tiab] OR [tiab])) OR ("continuous glucose"[tiab] AND (monitor*[tiab] OR sensing[tiab] OR sensor*[tiab]))	3960
3	Search #1 AND #2	2414
4	Search #3 Limits: only items with abstracts, Humans, English	2005
5	Search #4 NOT (editorial[PT] OR letter[PT] OR meta-analysis[PT] OR practice guideline[PT] OR review[PT]) Limits: only items with abstracts, Humans, English	1710
6	Search #4 AND (safety[MH] OR equipment safety[MH])	13
7	Search #4 AND economics[MH]	97
8	Search #4 AND (guideline[PT] OR clinical guideline)	45
9	Search #4 AND meta-analysis [PT]	22
10	Search #4 AND (registries OR registry OR clinical trial phase IV)	28

Search strategy (EMBASE)
Search date: March 2010 through 11/10/2016
Filters: age (young adult through elderly), study type (human, controlled study, clinical trial, randomized controlled trial, controlled clinical trial, systematic review), publication type (article)

Parallel strategies were used to search the Cochrane Library, EMBASE, and others listed below. Keyword searches were conducted in the other listed resources. In addition, handsearching of included studies was performed.

Electronic Database Searches

The following databases have been searched for relevant information:

Agency for Healthcare Research and Quality (AHRQ)
Cochrane Database of Systematic Reviews
Cochrane Registry of Clinical Trials (CENTRAL)
Cochrane Review Methodology Database
Database of Reviews of Effectiveness (Cochrane Library)
EMBASE
PubMed
Informational Network of Agencies for Health Technology Assessment (INAHTA)
NHS Economic Evaluation Database

Additional Economics, Clinical Guideline and Gray Literature Databases

AHRQ - Healthcare Cost and Utilization Project
Canadian Agency for Drugs and Technologies in Health
Centers for Medicare and Medicaid Services (CMS)
Food and Drug Administration (FDA)
Google
Institute for Clinical Systems Improvement (ICSI)
National Guideline Clearinghouse

APPENDIX C. Excluded Articles

Articles excluded as primary studies after full text review, with reason for exclusion.

	Citation	Reason for exclusion after full-text review
1.	Alfadhli et al. (2016). "Use of a real time continuous glucose monitoring system as an educational tool for patients with gestational diabetes." Diabetology and Metabolic Syndrome 8(1).	Not real time CGM (retrospective use)
2.	Allen, et al. (2008). “Continuous glucose monitoring counseling improves physical activity behaviors of individuals with type 2 diabetes: a randomized clinical trial.” Diabetes research and clinical practice, 80(3), 371-379.	Not real time CGM (retrospective use)
3.	Bailey, K. J., et al. (2016). "Self-Monitoring Using Continuous Glucose Monitors with Real-Time Feedback Improves Exercise Adherence in Individuals with Impaired Blood Glucose: A Pilot Study." Diabetes Technol Ther 18(3): 185-193.	Wrong outcome: exercise adherence.
4.	Bailey, (2007). “Reduction in hemoglobin A1C with real-time continuous glucose monitoring: results from a 12-week observational study.” Diabetes technology & therapeutics, 9(3), 203-210	Case-series
5.	Battelino, T., et al. (2015). "Routine use of continuous glucose monitoring in 10 501 people with diabetes mellitus." Diabet Med 32(12): 1568-1574.	Ineligible comparison, no control group: all patients received CGM, compared based on adherence
6.	Boland, E. et al. (2001). “Limitations of conventional methods of self-monitoring of blood glucose.” Diabetes care, 24(11), 1858-1862.	Case series*
7.	Bukara-Radujkovic, G., et al. (2011). "Short-term use of continuous glucose monitoring system adds to glycemic control in young type 1 diabetes mellitus patients in the long run: a clinical trial." Vojnosanit Pregl 68(8): 650-654.	Not real time CGM (retrospective use)
8.	Cemeroglu, A. P., et al. (2010). "Use of a real-time continuous glucose monitoring system in children and young adults on insulin pump therapy: patients' and caregivers' perception of benefit." Pediatr Diabetes 11(3): 182-187.	Ineligible comparison: short- vs. long-term CGM use*
9.	Chen, R., et al. (2003). “Continuous glucose monitoring for the evaluation and improved control of gestational diabetes mellitus.” The Journal of Maternal-Fetal & Neonatal Medicine, 14(4), 256-260.	Case series
10.	Chico, A., et al. (2003). “The continuous glucose monitoring system is useful for detecting unrecognized hypoglycemias in patients with type 1 and type 2 diabetes but is not better than frequent capillary glucose measurements for improving metabolic control.” Diabetes care, 26(4), 1153-1157.	Not real time CGM (retrospective use)
11.	Choudhary, P., et al. (2013). "Do high fasting glucose levels suggest nocturnal hypoglycaemia? The Somogyi effect-more fiction than fact?" Diabet Med 30(8): 914-917	Case series
12.	Cosson, E., et al. (2009). “Multicentre, randomised, controlled study of the impact of continuous sub-cutaneous glucose monitoring (GlucoDay®) on glycaemic control in type 1 and type 2 diabetes patients.” Diabetes & metabolism, 35(4), 312-318.	Not real time CGM (retrospective use); excluded by AHRQ report

	Citation	Reason for exclusion after full-text review
13.	DRCN: Weinzimer, S., et al. (2009). Prolonged use of continuous glucose monitors in children with type 1 diabetes on continuous subcutaneous insulin infusion or intensive multiple-daily injection therapy. Pediatric diabetes, 10(2), 91-96.	Ineligible comparison: real time CGM with CSII vs. with MDI*
14.	Fonda, S. J., et al. (2013). "Heterogeneity of responses to real-time continuous glucose monitoring (RT-CGM) in patients with type 2 diabetes and its implications for application." Diabetes Care 36(4): 786-792.	Wrong outcome: characterizing groups based on responses to CGM.
15.	Gandrud, L. M., et al. (2007). "The Medtronic Minimed Gold continuous glucose monitoring system: an effective means to discover hypo-and hyperglycemia in children under 7 years of age." Diabetes technology & therapeutics, 9(4), 307-316.	Case series*
16.	Garg, S., & Jovanovic, L. (2006). "Relationship of fasting and hourly blood glucose levels to HbA1c values." Diabetes Care, 29(12), 2644-2649.	Case series
17.	Ghio, A., Lencioni, C., Romero, F., et al. (2009). A real-time continuous glucose monitoring for diabetic women during the delivery. Diabetologia 52:S462.	Wrong format: abstract only.
18.	Gimenez, M., et al. (2010). "Sustained efficacy of continuous subcutaneous insulin infusion in type 1 diabetes subjects with recurrent non-severe and severe hypoglycemia and hypoglycemia unawareness: a pilot study." Diabetes Technol Ther 12(7): 517-521.	Case series
19.	Gomez, A. M., et al. (2015). "Continuous Glucose Monitoring Versus Capillary Point-of-Care Testing for Inpatient Glycemic Control in Type 2 Diabetes Patients Hospitalized in the General Ward and Treated With a Basal Bolus Insulin Regimen." J Diabetes Sci Technol 10(2): 325-329.	Wrong intervention: used only in hospitalized patients. Wrong subjects: adults without diabetes known to have hyperglycemia.
20.	Hermanns, N., et al. (2009). "Short-term effects on patient satisfaction of continuous glucose monitoring with the GlucoDay with real-time and retrospective access to glucose values: a crossover study." Diabetes technology & therapeutics, 11(5), 275-281.	Wrong comparison: real-time access of CGM to retrospective analysis of CGM.
21.	Iafusco, D., et al. (2008). "Use of real time continuous glucose monitoring and intravenous insulin in type 1 diabetic mothers to prevent respiratory distress and hypoglycaemia in infants." BMC pregnancy and childbirth, 8(1), 23.	Case series
22.	Jamiolkowska, M., et al. (2016). "Impact of Real-Time Continuous Glucose Monitoring Use on Glucose Variability and Endothelial Function in Adolescents with Type 1 Diabetes: New Technology--New Possibility to Decrease Cardiovascular Risk?" J Diabetes Res 2016: 4385312.	Case series
23.	Jeha, G. S., et al. (2004). "Continuous glucose monitoring and the reality of metabolic control in preschool children with type 1 diabetes." Diabetes Care, 27(12), 2881-2886.	Case series*
24.	Joubert, M., et al. (2015). "Effectiveness of continuous glucose monitoring in dialysis patients with diabetes: The DIALYDIAB pilot study." Diabetes research and clinical practice, 107(3), 348-354.	Inadequate sample size, <10 patients per arm

	Citation	Reason for exclusion after full-text review
25.	Kepenekian, L., et al. (2014). "Continuous glucose monitoring in hemodialyzed patients with type 2 diabetes: a multicenter pilot study." Clin Nephrol 82(4): 240-246.	Case series
26.	Kerssen, A., de Valk, H.W., Visser, G.H. (2004). Day-to-day glucose variability during pregnancy in women with type 1 diabetes mellitus: glucose profiles measured with the continuous glucose monitoring system. BJOG 111: 919-924.	Wrong outcome: glucose variability during pregnancy.
27.	Kestilä, K. K.,(2007). "Continuous glucose monitoring versus self-monitoring of blood glucose in the treatment of gestational diabetes mellitus." Diabetes research and clinical practice, 77(2), 174-179.	Ineligible comparison:
28.	Lee, S. et al. (2007). "Combined insulin pump therapy with real-time continuous glucose monitoring significantly improves glycemic control compared to multiple daily injection therapy in pump naive patients with type 1 diabetes; single center pilot study experience." Journal of diabetes science and technology, 1(3), 400-404.	Inadequate sample size, <10 patients per arm
29.	Leinung, M., et al. (2010). "Benefits of continuous glucose monitor use in clinical practice." Endocr Pract 16(3): 371-37.	Wrong intervention: use in clinical practice only.
30.	Little, S. A., et al. (2014). "Recovery of hypoglycemia awareness in long-standing type 1 diabetes: a multicenter 2 x 2 factorial randomized controlled trial comparing insulin pump with multiple daily injections and continuous with conventional glucose self-monitoring (HypoCOMPaSS)." Diabetes Care 37(8): 2114-2122.	Device not FDA approved
31.	Ludvigsson, J., & Hanas, R. (2003). Continuous subcutaneous glucose monitoring improved metabolic control in pediatric patients with type 1 diabetes: a controlled crossover study. Pediatrics, 111(5), 933-938.	Not real time CGM (retrospective use)
32.	Ly,T. T., et al. (2013). "Effect of sensor-augmented insulin pump therapy and automated insulin suspension vs standard insulin pump therapy on hypoglycemia in patients with type 1 diabetes: A randomized clinical trial." JAMA - Journal of the American Medical Association 310(12): 1240-1247.	Ineligible comparison (standard pump vs. low glucose suspend pump, does not evaluated monitoring technology)
33.	Ly, T. T., et al. (2014). "A cost-effectiveness analysis of sensor-augmented insulin pump therapy and automated insulin suspension versus standard pump therapy for hypoglycemic unaware patients with type 1 diabetes." Value Health 17(5): 561-569.	Economic study using Ly 2013 above (excluded due to ineligible comparison)
34.	McLachlan, K., Jenkins, A., O'Neal, D., (2007). The role of continuous glucose monitoring in clinical decision-making in diabetes in pregnancy. Aust N Z J Obstet Gynaecol 47: 186-190.	Wrong intervention: use in clinical practice only.
35.	Messer, L., et al. (2009). Educating families on real time continuous glucose monitoring. The Diabetes Educator, 35(1), 124-135.	Ineligible comparison: real time CGM with CSII vs. with MDI*
36.	Murphy, H. R., et al. (2008). "Effectiveness of continuous glucose monitoring in pregnant women with diabetes: randomised clinical trial." BMJ, 337, a1680.	Not real time CGM (retrospective use); excluded by AHRQ report

	Citation	Reason for exclusion after full-text review
37.	Newman, S. P., et al. (2009). "A randomised controlled trial to compare minimally invasive glucose monitoring devices with conventional monitoring in the management of insulin-treated diabetes mellitus (MITRE)." Health Technol Assess 13(28): iii-iv, ix-xi, 1-194.	Not real time CGM (retrospective use); excluded by AHRQ report
38.	Norgaard, K., et al. (2013). "Routine sensor-augmented pump therapy in type 1 diabetes: the INTERPRET study." Diabetes Technol Ther 15(4): 273-280.	Case-series
39.	Patton, S. R., et al. (2011). "Use of continuous glucose monitoring in young children with type 1 diabetes: implications for behavioral research." Pediatr Diabetes 12(1): 18-24.	Wrong outcome: feasibility of CGM as a tool in young children.
40.	Perkins, B. A., et al. (2015). "Sensor-augmented pump and multiple daily injection therapy in the United States and Canada: post-hoc analysis of a randomized controlled trial." Can J Diabetes 39(1): 50-54.	Subanalysis of full trial; data from full trial used
41.	Petrovski, G., et al. (2011). "Is there a difference in pregnancy and glycemic outcome in patients with type 1 diabetes on insulin pump with constant or intermittent glucose monitoring? A pilot study." Diabetes Technol Ther 13(11): 1109-1113.	Ineligible comparison: continuous vs. intermittent CGM use
42.	Picard, S., et al. (2016). "Evaluation of the Adherence to Continuous Glucose Monitoring in the Management of Type 1 Diabetes Patients on Sensor -Augmented Pump Therapy: The SENLOCOR Study." Diabetes Technol Ther 18(3): 127-135.	Ineligible study design; purpose to evaluate adherence
43.	Radermecker, R. P., et al. (2010). "Continuous glucose monitoring reduces both hypoglycaemia and HbA1c in hypoglycaemia-prone type 1 diabetic patients treated with a portable pump." Diabetes Metab 36(5): 409-413.	Inadequate sample size, <10 pts per arm
44.	Rigla, M., et al. (2008). “Real-time continuous glucose monitoring together with telemedical assistance improves glycemic control and glucose stability in pump-treated patients.” Diabetes Technology & Therapeutics, 10(3), 194-199.	Small sample size (cross-over with 10 patients; excluded by AHRQ
45.	Roze, S., et al. (2016). "Cost-Effectiveness of Sensor-Augmented Pump Therapy with Low Glucose Suspend Versus Standard Insulin Pump Therapy in Two Different Patient Populations with Type 1 Diabetes in France." Diabetes Technol Ther 18(2): 75-84.	Economic study of devices with low glucose suspend feature
46.	Ryan, E. A., et al. (2009). “Use of continuous glucose monitoring system in the management of severe hypoglycemia.” Diabetes technology & therapeutics, 11(10), 635-639.	Case series
47.	Schaepelynck-Belicar, P., et al. (2003). "Improved metabolic control in diabetic adolescents using the continuous glucose monitoring system (CGMS)." Diabetes Metab 29(6): 608-612.	Case series; not real-time CGM (retrospective use)
48.	Secher, A. L., et al. (2012). "Patient satisfaction and barriers to initiating real-time continuous glucose monitoring in early pregnancy in women with diabetes." Diabet Med 29(2): 272-277.	Wrong outcome: barriers to using CGM.
49.	Schiaffini, R., et al. (2002). "The Continuous Glucose Monitoring System (CGMS) in type 1 diabetic children is the way to reduce hypoglycemic risk." Diabetes Metab Res Rev 18(4): 324-329.	Not real-time CGM (retrospective use)

	Citation	Reason for exclusion after full-text review
50.	Tanenberg, et al. (2015). "Patient behaviors associated with optimum glycemic outcomes with sensor-augmented pump therapy: insights from the STAR 3 study." Endocr Pract 21(1): 41-45	Not real-time CGM (retrospective use)
51.	Wong, L. J., et al. (2006). "Extended use of a new continuous glucose monitoring system with wireless data transmission in children with type 1 diabetes mellitus." Diabetes technology & therapeutics, 8(2), 139-145.	Not real-time CGM (retrospective use)*
52.	Weber, K. K., et al. (2007). High frequency of unrecognized hypoglycaemias in patients with type 2 diabetes is discovered by continuous glucose monitoring. Experimental and clinical endocrinology & diabetes, 115(08), 491-494.	Case series
53.	Yates, K., et al. (2006). "Continuous Glucose Monitoring–Guided Insulin Adjustment in Children and Adolescents on Near-Physiological Insulin Regimens." Diabetes Care, 29(7), 1512-1517.	Not real-time CGM (retrospective use)
54.	Yogev, Y., et al. (2003a). Continuous glucose monitoring for treatment adjustment in diabetic pregnancies—a pilot study. Diabet Med 20: 558-562.	Wrong intervention: treatment adjustment using CGM.
55.	Yogev, Y., et al. (2003b). Continuous glucose monitoring for the evaluation of gravid women with type 1 diabetes mellitus. Obstetrics & Gynecology, 101(4), 633-638.	Case series
56.	Yu, F., et al. (2014). "Continuous glucose monitoring effects on maternal glycemic control and pregnancy outcomes in patients with gestational diabetes mellitus: a prospective cohort study." J Clin Endocrinol Metab 99(12): 4674-4682.	Not real-time CGM (retrospective use)

*These studies were included in the previous report but no longer meet the inclusion criteria for this updated report.

APPENDIX D. Risk of Bias, Class of Evidence, Strength of Evidence, and QHES Determination

Each study is rated against pre-set criteria that resulted in a Risk of Bias (RoB) assessment and presented in a table. The criteria are listed in the Tables below.

Appendix Table D1. Definition of the risk of bias for studies on therapy

Risk of Bias	Studies of Therapy*	
	Study design	**Criteria***
Low risk: Study adheres to commonly held tenets of high quality design, execution and avoidance of bias	Good quality RCT	• Random sequence generation • Statement of allocation concealment • Intent-to-treat analysis • Blind or independent assessment for primary outcome(s) • Co-interventions applied equally • F/U rate of 80%+ and <10% difference in F/U between groups • Controlling for possible confounding‡
Moderately low risk: Study has potential for some bias; study does not meet all criteria for class I, but deficiencies not likely to invalidate results or introduce significant bias	Moderate quality RCT	• Violation of one or two of the criteria for good quality RCT
	Good quality cohort	• Blind or independent assessment for primary outcome(s) • Co-interventions applied equally • F/U rate of 80%+ and <10% difference in F/U between groups • Controlling for possible confounding‡
Moderately High risk: Study has significant flaws in design and/or execution that increase potential for bias that may invalidate study results	Poor quality RCT	• Violation of three or more of the criteria for good quality RCT
	Moderate quality cohort	• Violation of any of the criteria for good quality cohort
	Case-control	• Any case-control design
High risk:	Poor quality cohort	• Violation of two or more criteria for a good quality cohort
	Case series	• Any case series design

Risk of Bias	Studies of Therapy*	
	Study design	Criteria*
Study has significant potential for bias; lack of comparison group precludes direct assessment of important outcomes		

* Additional domains evaluated in studies performing a formal test of interaction for subgroup modification (i.e., HTE) based on recommendations from Oxman and Guyatt[4]:
  - Is the subgroup variable a characteristic specified at baseline or after randomization? (subgroup hypotheses should be developed a priori)
  - Did the hypothesis precede rather than follow the analysis and include a hypothesized direction that was subsequently confirmed?
  - Was the subgroup hypothesis one of a smaller number tested?

† Outcome assessment is independent of healthcare personnel judgment. Reliable data are data such as mortality or re-operation.
‡ Authors must provide a description of robust baseline characteristics, and control for those that are unequally distributed between treatment groups.

Determination of Overall Strength (Quality) of Evidence

The strength of evidence for the overall body of evidence for all critical health outcomes was assessed by one researcher following the principles for adapting GRADE (Grades of Recommendation Assessment, Development and Evaluation) as outlined by the Agency for Healthcare Research and Quality (AHRQ).[6] The strength of evidence was based on the highest quality evidence available for a given outcome. In determining the strength of body of evidence regarding a given outcome, the following domains were considered:

- Risk of bias: the extent to which the included studies have protection against bias
- Consistency: the degree to which the included studies report results that are similar in terms of range and variability.
- Directness: describes whether the evidence is directly related to patient health outcomes.
- Precision: describes the level of certainty surrounding the effect estimates.
- Publication bias: is considered when there is concern of selective publishing.

Bodies of evidence consisting of RCTs were initially considered as High strength of evidence (SoE), while those that comprised nonrandomized studies began as Low strength of evidence. The strength of evidence could be downgraded based on the limitations described above. There could also be situations where the nonrandomized studies could be upgraded, including the presence of plausible unmeasured confounding and bias that would decrease an observed effect or increase an effect if none was observed, and large magnitude of effect (strength of association). Publication and reporting bias are difficult to assess. Publication bias is particularly difficult to assess with fewer than 10 RCTs.[6] When publication bias was unknown in all studies and this domain is often eliminated from the strength of evidence tables for our reports. The final strength of evidence was assigned an overall grade of high, moderate, low, or insufficient, which are defined as follows:

- High - Very confident that effect size estimates lie close to the true effect for this outcome; there are few or no deficiencies in the body of evidence; we believe the findings are stable.
- Moderate – Moderately confident that effect size estimates lie close to the true effect for this outcome; some deficiencies in the body of evidence; we believe the findings are probably stable but some doubt remains.
- Low – Limited confidence that effect size estimates lie close to the true effect for this outcome; important or numerous deficiencies in the body of evidence; we believe that additional evidence is needed before concluding that findings are stable or that the estimate is close to the true effect.
- Insufficient – We have no evidence, are unable to estimate an effect or have no confidence in the effect estimate for this outcome; OR no available evidence or the body of evidence has unacceptable deficiencies precluding judgment.

Similar methods for determining the overall quality (strength) of evidence related to economic studies have not been reported, thus the overall strength of evidence for outcomes reported in Key Question 4 was not assessed.

All AHRQ "required" and "additional" domains (risk of bias, consistency, directness, precision, and if possible, publication bias) are assessed. Bodies of evidence consisting of RCTs were initially considered as High strength of evidence, while those comprised of nonrandomized studies began as Low strength of evidence. The strength of evidence could be downgraded based on the limitations described above. There are also situations where the *nonrandomized* studies could be upgraded, including the presence of plausible unmeasured confounding and bias that would decrease an observed effect or increase an effect if none was observed, and large magnitude of effect (strength of association).

Appendix Table D2. Example methodology outline for determining overall strength of evidence (SoE):

All AHRQ "required" and "additional" domains* are assessed. Only those that influence the baseline grade are listed in table.

Baseline strength: HIGH = RCTs. LOW = observational, cohort studies, administrative data studies.

DOWNGRADE: Risk of bias for the individual article evaluations (1 or 2); Inconsistency** of results (1 or 2); Indirectness of evidence (1 or 2); Imprecision of effect estimates (1 or 2); Sub-group analyses not stated *a priori* and no test for interaction (2)

UPGRADE (non-randomized studies): Large magnitude of effect (1 or 2); Dose response gradient (1) done for observational studies if no downgrade for domains above

Outcome	Strength of Evidence	Conclusions & Comments	Baseline	DOWNGRADE	UPGRADE
Outcome	**HIGH**	Summary of findings	**HIGH** RCTs	**NO** consistent, direct, and precise estimates	**NO**
Outcome	**MODERATE**	Summary of findings	**LOW** Cohort studies	**NO** consistent, direct, and precise estimates	**YES** Large effect
Outcome	**LOW**	Summary of findings	**HIGH** RCTs	**YES (2)** Inconsistent Indirect	**NO**

*Required domains: risk of bias, consistency, directness, precision. Plausible confounding that would decrease observed effect is accounted for in our baseline risk of bias assessment through individual article evaluation. Additional domains: dose-response, strength of association, publication bias.

**Single study = "consistency unknown", not downgraded

Cross-over Trials Evaluation

Determining risk of bias for individual cross-over trials. Each study was rated against pre-set criteria that resulted in an overall assessment of risk of bias and presented in a table. The criteria are listed in the Tables below. In addition to factors that impact the internal validity of parallel randomized controlled trials, (e.g. randomization, concealment of allocations, intention to treat), there are additional areas that may bias cross-over trials. There is currently no standardized, validated methodology for formal critical appraisal of cross-over trials. The criteria below are based on those described in the Cochrane Handbook and principles of epidemiology and biostatistical evaluation of correlated data.

Appendix Table D3. Criteria for assessing risk of bias for cross-over trials

Risk of Bias	Study design	Criteria
Low	Good quality crossover trial	**Study design:** • Random sequence generation (AB/BA) • Sequence allocation concealed • Intention to treat analysis **Other methods** • Blind or independent assessment for important outcomes • Appropriate washout period for condition • <10% between period attrition; reporting of between period attrition • F/U rate of 80%+ • Results from first phase reported separately • Accounting for missing data • Assessment of carryover effects • Use of methods to account for within-subject variation, correlated data
Moderately low	Moderate quality crossover trial	• Violation of one or two criteria
Moderately High	Poor quality crossover trial	• Violation of three or more of the criteria

Appendix Table D4. Risk of bias for cross-over trials

Methodological principle	Author (2009)	Author (2008)
Crossover trial		
Random sequence generation		
Sequence allocation concealed		
Intention to treat analysis		
Independent or blind assessment		
Appropriate washout period for condition		
Number completing period reported ;<10% between period attrition,		
F/U of 80%+		
Results from first phase reported separately		
Accounting for missing data		
Use of methods for within-subject variation, correlated data		
Analysis of carryover effect		
Risk of bias		

*Appropriate washout period***:** In crossover trials, a "washout" period is an important internal validity component. Carryover effects may happen when one treatment affects subsequent treatments. In other words, the response to a current treatment is affected by what treatment was applied in a previous period. An appropriate washout period may diminish the impact of carryover effects.

*Number completing treatment periods and between period attrition***:** Authors must report the number of subjects lost between treatment periods; attrition between periods should be less than 10%; credit may be given if appropriate methods used (and results reported) to explore the impact of missing data. Authors must describe whether participants were excluded if they only provided data for one treatment period (and should describe the impact of missing data on results). [If there are unequal numbers of subjects in each sequence and data from previous periods are missing results may be biased.]

*Accounting for missing data***:** If >10% of data are missing, authors must describe methods for accommodating missing data (e.g. imputation) and provide information on the impact of such methods on results or report on sensitivity analyses for missing data.

*Use of appropriate statistical methods to account for within-subject variability and correlated data***:** The analysis of a cross-over trial should take advantage of the within-person design (subjects act as their own controls) and use some form of paired analysis. Paired parametric (e.g. paired t-test) or non-parametric (e.g. McNemar chi-squared) tests should be used to compare Δ in all A vs. Δ in all B after assuring no carry-over effect and no calendar or temporal effect is present. [If carry-over or temporal effect present, evaluate the changes only for the first intervention period]. Use of paired statistics evaluates the value of 'measurement on experimental intervention (E)' minus 'measurement on control intervention (C)' separately for each participant. Outcomes measured in the same individual generally have smaller variance than outcomes measured between individuals. The crossover design yields a much smaller sample size because the within-patient variances are one-fourth that of the inter-patient variation. Other appropriate methods may include repeated measures or dependent data analysis e.g. repeated measures ANOVA, mixed models, models with subject-level random effect, generalized estimating equation methods and others.

*Analysis of carry-over effect***:** Comparison of results within each treatment when it is given first and second (i.e. Δ A1 vs. Δ A2 and Δ B1 vs. Δ B2); need to show that they are not statistically significantly different before combining time periods. A carry-over effect means that the observed difference between the treatments depends upon the order in which they were received; hence the estimated overall treatment effect will be affected (usually underestimated, leading to a bias towards the null). There are two strategies for dealing with carryover effects: (1) minimize the chances that they can happen by allowing enough time (washout periods) between successive treatments; and (2) include them explicitly in the statistical model. Carry-over effects may not be a large concern depending on the treatments. Not only biological impact but also impact of learning, behavioral change, conditioning and other impacts should be considered

*Independent or blind assessment***:** For outcome such as laboratory tests or validated, objective assessments, patient blinding is generally not a concern, Assessment and analysis should be blinded. No credit given if the primary outcome is a patient-reported outcome and patients are not blinded or if assessment or analyses were not blinded.

Administrative Database Study evaluation

What constitutes a high quality administrative database study? What criteria?

Although the precise guidelines that should govern high quality administrative database studies are still under development,[2] a number of criteria that should be met in a high quality administrative database study have been suggested.[2,5] The checklist below highlights many of these qualities as was used to

provide an initial assessment of administrative data studies. Individual report topics may have unique aspects of coding, requirements for developing algorithms for subject identification and potential for misclassification that need to be considered as part of an assessment of bias risk and study limitations.

Appendix Table D5. Checklist for evaluating the quality of administrative database studies.

Methodological Principle	Author 1 (2004)	Author 2 (2006)	Author (2008)
Study design Administrative database comparative study Administrative database case-control study Administrative database case series			
Why database created clearly stated			
Description of database's inclusion/exclusion criteria			
Description of methods for reducing bias in database			
Codes and search algorithms reported			
Rationale for coding algorithm reported			
Code accuracy reported			
Code validity reported			
Clinical significance assessed			
Is the period of data consistent with the outcome data?			
Statement regarding whether data stems from single or multiple hospital admissions			
Statement regarding whether data stems from single or multiple procedures			
Accounting for clustering			
Number of criteria met (maximum: 12)			

Below is a description of criteria used to evaluate administrative database studies.

Robust descriptions of the data set
High quality administrative database studies will include clear descriptions of the data set used for the study.[2,5]

- Why the database was created should be clearly stated.
- How the administrative database was created should be clearly stated, including:
  - Description of the database's inclusion and exclusion criteria.
  - Description of the methods by which the data sets are created so that the potential for biased or missing information can be assessed.[5]

Code accuracy

- The diagnostic and/or procedural codes used in the search algorithm should be clearly stated.
- The rationale for coding algorithm reported.
- Code accuracy should be clearly reported. Code accuracy allows one to estimate the percentage of misclassified data as well as the degree of resulting bias. There are several different types of studies used to measure code accuracy, and the design will affect the reliability of the results.
    - "Ecological" studies compare outcomes measured by the code to those from another more reliable method. Because these studies do not evaluate accuracy at the patient level, they are at risk for "ecological bias" and should be considered to be a relatively crude measure of code accuracy.5
    - "Reabstraction" studies reabstract a set of individual medical records and check them against the code(s) entered into the database for that patient. The reliability of statistics from reabstraction studies can be affected by missed cases (due to incorrect diagnosis or unrecorded information in the chart) as well as by misinterpreted cases (diagnosed and recorded correctly but misinterpreted by the person translating that information into code in the database).
    - "Gold standard" studies are the most reliable type of validation studies and compare the code to some gold standard, such as a set of standard clinical or laboratory criteria required for diagnosis or an accurate population-based disease registry.5
        - The validity of the codes should be clearly stated as it provides information as to whether the code or combination of used actually represent the diagnosis or outcome of interest The validity of the database study is dependent on a statistically significant association between degree to which the diagnostic or procedural code is associated with the actual diagnosis or procedure, so that the reader has confidence that the code actually represents the diagnosis or procedure under study. Note that code validity statistics are commonly reported in one of two ways:
    - PPV (positive predictive value) is most frequently used, and reflects the percentage of patients identified by the code that are "true positives", or actually have the condition (or underwent the procedure) of interest. However, this statistic bears a major drawback: its accuracy decreases with decreasing disease prevalence. While validation studies are typically done on a population of patients with the code, and thus have a high prevalence of disease, the prevalence of the disease within the database population is typically going to be much lower. Thus, the probability of a patient in the database study having the disease represented by the code is likely to be lower than the PPV reported in the validation study suggests.5
    - Sensitivity and specificity may be used, and tend to be more accurate measures of code accuracy than PPV as they don't vary as much with disease prevalence.
    - Positive likelihood ratio can be calculated from sensitivity and specificity. Positive likelihood ratio can also be combined with the baseline odds of disease to determine the likelihood that a patient identified by the code actually has the disease. Disease prevalence within the study population must be estimated in order to perform such a calculation, and is best done using data from a gold standard validation study.5

Clinical significance

- Results should not solely be based on p-values, but should be interpreted based on clinical relevance.
    - This is because in large database studies, very small differences between groups can result in statistically significant differences, but these differences may not be clinically relevant.[5]
    - Remember that additional zeroes in a p-value does not imply a more meaningful result.
    - Instead, the significance of the results should be interpreted by evaluating the absolute and relative differences between treatment groups.
    - Determining whether there is overlap in the 95% confidence intervals between groups can help the reader determine whether a result may be clinically significant, as they highlight the differences in results between the treatment groups.[5]

Time-dependent bias

- Is the period of data consistent with the outcome data? That is, if looking at hospital discharge data (like NIS), then is the reported follow-up period for outcomes of interest reflective of that?
- Does the data set specify whether it includes data from the initial hospital admission only, or were data from repeat admissions included?
- Does the data set specify whether it includes data from the first procedure only, or were data from repeat procedures included?

Clustering

- The administrative database study should properly account for clustering that may be present in the data set.
    - Patient populations in health administrative data sets are often clustered (ie., within a health care provider), and outcomes for those within the same cluster tend to be more similar than those patients in a different cluster even after adjusting for potentially confounding variables using conventional regression analysis. Multilevel (or hierarchical, random effects, or mixed effects) regression models allow the user to account for patient clustering (e.g., within health care providers and facilities) when evaluating clustered data. Inaccurate conclusions may result if the appropriate methods to account for clustering are not used.5

Assessment of Economic Studies

Full formal economic analyses evaluate both costs and clinical outcomes of two or more alternative interventions. The four primary types are cost minimization analysis (CMA), cost-utility analysis (CUA), cost-effectiveness analysis (CEA), and cost-benefit analyses (CBA). Each employs different methodologies, potentially complicating critical appraisal, but some common criteria can be assessed across studies.

No standard, universally accepted method of critical appraisal of economic analyses is currently in use. A number of checklists [Canadian, BMJ, AMA] are available to facilitate critique of such studies. The Quality of Health Economic Studies (QHES) instrument developed by Ofman, et al[3]. QHES embodies the primary components relevant for critical appraisal of economic studies[1,3]. It also incorporates a weighted scoring process and which was used as one factor to assess included economic studies. This tool has not yet undergone extensive evaluation for broader use but provides a valuable starting point for critique.

In addition to assessment of criteria in the QHES, other factors are important in critical appraisal of studies from an epidemiologic perspective to assist in evaluation of generalizability and potential sources of study bias.
Such factors include:

- Are the interventions applied to similar populations (e.g., with respect to age, gender, medical conditions, etc.)? To what extent are the populations for each intervention comparable and are differences considered or accounted for? To what extent are population characteristics consistent with "real world" applications of the comparators?
- Are the sample sizes adequate so as to provide a reasonable representation of individuals to whom the technology would be applied?
- What types of studies form the basis for the data used in the analyses? Data (e.g., complication rates) from randomized controlled trials or well-conducted, methodologically rigorous cohort studies for data collection are generally of highest quality compared with case series or studies with historical cohorts.
- Were the interventions applied in a comparable manner (e.g., similar protocols, follow-up procedures, evaluation of outcomes, etc.)?
- How were the data and/or patients selected or sampled (e.g., a random selection of claims for the intervention from a given year/source or all claims)? What specific inclusion/exclusion criteria or processes were used?
- Were the outcomes and consequences of the interventions being compared comparable for each? (e.g., were all of the relevant consequences/complications for each intervention considered or do they primarily reflect those for one intervention?)

Appendix Table D6. Definitions of the different levels of evidence for registry studies

Risk of Bias	Study design	Criteria
Moderately low risk: Study has potential for some bias; does not meet all criteria for class I but deficiencies not likely to invalidate results or introduce significant bias	Good quality registry	• Designed specifically for conditions evaluated • Includes prospective data only • Validation of completeness and quality of data • Patients followed long enough for outcomes to occur • Independent outcome assessment* • Complete follow-up of $\geq$ 85% • Controlling for possible confounding† • Accounting for time at risk‡
Moderately high risk: Study has flaws in design and/or execution that increase potential for bias that may invalidate study results	Moderate quality cohort	• Prospective data from registry designed specifically for conditions evaluated with violation of 2 of the rest of the criteria in level II
High risk: Study has significant potential for bias; does not include design features geared toward minimizing bias and/or does not have a comparison group	Poor quality cohort	• Prospective data from registry designed specifically for conditions evaluated with violation of 3 or more of the rest of the criteria in level II • Retrospective data or data from a registry not designed specifically for conditions evaluated

* Outcome assessment is independent of healthcare personnel judgment. Some examples include patient reported outcomes, death, and reoperation.
† Authors must provide a description of robust baseline characteristics, and control for those that are unequally distributed between treatment groups.
‡ Equal follow-up times or for unequal follow-up times, accounting for time at risk.

Economic Studies

Assessment of the overall strength of evidence for formal economic analyses does not appear to be documented in the literature.

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APPENDIX E. Study Quality: RoB evaluation

Appendix Table E1. Risk of Bias for RCTs Evaluating CGM versus SMBG for Type 1 DM

Methodological Principle	Battelino 2011	Bolinder 2016	Beck 2017a	Bergenstal 2010, Slover 2012, Rubin 2012	Deiss 2006	Hermanides 2011	Hirsch 2008	JDRF 2008, Lawrence 2010	JDRF 2009a	Kordonouri 2010 (ONSET)
Population(s)	**Mixed**	**Adults**	**Adults**	**Children, Adults**	**Mixed**	**Adults**	**Children, Adults, Mixed**	**Children, Adults, Mixed**	**Mixed**	**Children**
Study design										
Randomized controlled trial	▪	▪	▪	▪	▪	▪	▪	▪	▪	▪
Cohort Study										
Prospective										
Retrospective										
Random sequence generation*	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	Yes	Yes	Yes
Statement of concealed allocation*	Yes‡	Unclear	Yes	Yes	Unclear	Yes	Unclear	Yes	Yes	Yes
Intention-to-treat*	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Independent/blind assessment	No	Unclear	No	No	No	No	No	No	No	No
Co-interventions applied equally	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Complete follow-up of ≥80%	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
<10% difference in follow-up between groups	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Controlling for possible confounding†	Yes	Yes	Yes	No	Unclear	Unclear§	Yes	Yes	Yes	Yes
Risk of Bias	**Moderately Low**	**Moderately High**	**Moderately Low**	**Moderately Low**	**Moderately High**	**Moderately Low**	**Moderately High**	**Moderately Low**	**Moderately Low**	**Moderately Low**

Methodological Principle	Mauras 2012 (DirecNet)	New 2015**	O'Connell 2009	Peyrot 2009	Raccah 2009
Population(s)	**Children**	**Adults**	**Mixed**	**Adults**	**Mixed**
Study design					
Randomized controlled trial	▪	▪	▪	▪	▪
Cohort Study					
Prospective					
Retrospective					
Random sequence generation*	Yes	Yes	Yes	Unclear††	Unclear††
Statement of concealed allocation*	Yes	Yes	Yes	Unclear	Unclear
Intention-to-treat*	Yes	Yes	Yes	Unclear	Yes
Independent or blind assessment	No	No	No	Unclear	No
Co-interventions applied equally	Yes	Yes	Yes	Yes	Yes
Complete follow-up of ≥80%	Yes	Yes	Yes	Yes	Unclear
<10% difference in follow-up between groups	Yes	No	No	Yes	Unclear
Controlling for possible confounding†	Yes	Yes	Yes	Unclear	Yes
Risk of Bias	**Moderately Low**	**Moderately Low**	**Moderately Low**	**Moderately High**	**Moderately High**

*Applies to randomized controlled trials only. If authors did not describe a methodologic principle, the study did not receive credit for the criterion.
† Authors must provide a description of robust baseline characteristics, and control for those that are unequally distributed between treatment groups.
‡ Concealed but no mention of opaque or sealed.
§ Three years longer of diabetes duration avg; significant difference in contact time throughout study periods; adjusted for in multivariate linear regression model, that showed only baseline HbA1c was a significant predictor for HbA1c decrease.
**Difference in follow-up between groups was <10% at 1.3 month follow-up but not at 2.7 month follow-up
†† Method not described

Appendix Table E2. Risk of bias assessment: Cross-over trials Evaluating CGM versus SMBG in Type 1 Diabetes

Study	Random sequence	Concealed allocation	Intent to treat	Blind assessment	Appropriate washout	<10% attrition between periods	F/U > 80%	1st Phase results reported	Handling of Missing data	Statistics for within-subject variation	Analysis carryover effect	Risk of bias
Lind 2017	Yes	Yes	No*	Yes	Yes	No†	Yes	No	Yes	Yes‡	Yes	Moderately High
van Beers 2016	Yes	Yes	Yes	No	Yes	Yes†	Yes	No	No	Yes‡	Yes	Moderately High
Langeland 2012	Yes	No	Yes	No	Yes	No†	Yes	No	No	Yes‡	No	Moderately High
Battelino 2012, Hommel 2014	Yes	Yes	Yes	No	Yes	Yes†	Yes	No	Yes	Yes‡	Yes§	Moderately Low
Tumminia 2015	Yes	No	No	No	No	No	Yes	No	No	Yes‡	No	Moderately High

*Intention to treat:

- Lind: no for primary outcomes, yes for safety; full data set for primary outcomes included only individuals who had at least one measurement at each treatment period; 13 from the CGM first group and 6 from the SMBG first group were excluded from analysis of primary outcomes; safety was assessed across all randomized participants.

† Attrition between periods

- Lind: 11% total discontinued after first period: 14% (12/82) CGM first group and 7.6% (6/79) of SMBG first group;
- van Beers: 9.6% total discontinued after first period: 11.5% (3/26) of CGM first group, 7.7% (2/16) of SMBG first group
- Langeland: 10% (3/30) total discontinued during the study (no further details given)
- Battelino/Hommel: 9.8% total discontinued after first period: 9.2% (7/76) of CGM first group, 10.4% (8/77) of SMBG first group

‡Statistical methods accounting for within-patient variability

- Lind: adjusted for sequence, patient (sequence), period, and treatment as class variables in generalized linear models [accounting for within-subject variation and carryover]
- van Beers: linear mixed-model analysis with the percentage of time spent in normoglycaemia as the dependent variable, the treatment, group (CGM or SMBG) as a factor, and the participant as a random factor and Wilcoxon matched-pair signed –rank test; assessed the carryover effect by including the sequence allocation as a factor in the mixed model
- Langeland used "dependent samples t-test" which is a paired t=test
- Battelino/Hommel: the two groups were compared using ANOVA with adjustment for period effect and subject as random effect
- Tumminia: continuous variables were compared using student's t-test for paired data

§Analysis for carryover effect

- Battelino/Hommel: the two groups were compared using ANOVA with adjustment for period effect and subject as random effect

Appendix Table E3. Risk of bias for comparative observational studies evaluating CGM versus SMBG in children and adults with type 1 diabetes

	Children			Adults
Methodological Principle	**Rachmiel 2015**	**Scaramuzza 2011**	**Kordonouri 2012**	**Anderson 2011**
Study design				
Randomized controlled trial				
Prospective cohort study	■		■	
Retrospective cohort study		■		■
Case-control				
Case-series				
Random sequence generation*	NA	NA	NA	NA
Statement of concealed allocation*	NA	NA	NA	NA
Intention to treat*	NA	NA	NA	NA
Independent or blind assessment	Unclear	Unclear	Unclear	Unclear
Co-interventions applied equally	Yes	Yes	Yes	Yes
Complete follow-up of ≥80%	Unclear	Unclear	Yes	Unclear
<10% difference in follow-up between groups	Unclear	Unclear	Yes	Unclear
Controlling for possible confounding†	No	Yes	Yes	Yes
Risk of Bias	**High**	**High**	**Moderately High**	**High**

*Applies to randomized controlled trials only. If authors did not describe a methodologic principle, the study did not receive credit for the criterion.
† Authors must provide a description of robust baseline characteristics, and control for those that are unequally distributed between treatment groups.

Appendix Table E4. Methodological quality of registry studies evaluating CGM versus SMBG in type 1 diabetes

Methodological principle	Wong 2014 T1D Exchange Clinical Network registry (United States)	Ludwig-Seibold 2012 Diabetes patient documentation (DPV) registry (Germany and Austria)
Designed specifically for conditions evaluated	+	+
Includes prospective data only	–	+
Validation of completeness and quality of data	–	–
Patients followed long enough for outcomes to occur	+	–
Independent outcome assessment*	+	+
Complete follow-up of ≥ 80%	–	–
Controlling for possible confounding†	+	+
Accounting for time at risk‡	+	+
Risk of Bias	**High**	**High**

* Outcome assessment is independent of healthcare personnel judgment. Some examples include patient reported outcomes, death, and HbA1c.
† Authors must provide a description of robust baseline characteristics, and control for those that are unequally distributed between treatment groups.
‡ Equal follow-up times or for unequal follow-up times, accounting for time at risk.

Appendix Table E4. Risk of Bias for RCTs Evaluating CGM versus SMBG in Type 2 DM

Methodological Principle	Beck 2017b	Erhardt 2011, Vigersky 2012	Haak 2016	Tildesley 2013, Tang 2014	Yoo 2008
Population(s)	**Adults**	**Adults**	**Adults**	**Adults**	**Adults**
Study design					
Randomized controlled trial	▪	▪	▪	▪	▪
Cohort Study					
Prospective					
Retrospective					
Random sequence generation*	Yes	Unclear	Yes	Yes	Yes
Statement of concealed allocation*	Yes	Unclear	Unclear	Unclear	Yes‡
Intention-to-treat*	Yes	Yes	Yes	Yes	Yes
Independent or blind assessment	No	No	Unclear	Unclear	No

Methodological Principle	Beck 2017b	Erhardt 2011, Vigersky 2012	Haak 2016	Tildesley 2013, Tang 2014	Yoo 2008
Population(s)	Adults	Adults	Adults	Adults	Adults
Co-interventions applied equally	Yes	Yes	Yes	Yes	Yes
Complete follow-up of ≥80%	Yes	Yes	Yes	No	Yes
<10% difference in follow-up between groups	Yes	Yes	No	No	Yes
Controlling for possible confounding†	Yes	Yes	Yes	Yes	Unclear
Risk of Bias	**Moderately Low**	**Moderately High**	**Moderately High**	**Moderately High**	**Moderately Low**

*Applies to randomized controlled trials only. If authors did not describe a methodologic principle, the study did not receive credit for the criterion.
† Authors must provide a description of robust baseline characteristics, and control for those that are unequally distributed between treatment groups.
‡ Declared as concealed but method not described

Appendix Table E5. Risk of Bias for RCTs Evaluating CGM versus SMBG for Pregnant Women with Diabetes Mellitus

Methodological Principle	Feig 2017	Secher 2013	Wei 2016
Study design			
Randomized controlled trial	▪	▪	▪
Cohort Study			
Prospective			
Retrospective			
Random sequence generation*	Yes	Yes	Yes
Statement of concealed allocation*	Yes	Yes	Yes
Intention-to-treat*	Yes	Yes	No
Independent or blind assessment	No	No	No
Co-interventions applied equally	Yes	Yes	Yes
Complete follow-up of ≥80%	Yes	Yes	Yes
<10% difference in follow-up between groups	Yes	Yes	Yes
Controlling for possible confounding†	Yes	Yes	Yes
Risk of Bias	**Moderately Low**	**Moderately Low**	**Moderately Low**

*Applies to randomized controlled trials only. If authors did not describe a methodologic principle, the study did not receive credit for the criterion.
† Authors must provide a description of robust baseline characteristics, and control for those that are unequally distributed between treatment groups.

Appendix Table E6. Risk of Bias for Comparative Observational Studies Evaluating Diabetes Mellitus in Pregnancy

Methodological Principle	Secher 2014	Fresa 2013	Cordua 2013
Study design Randomized controlled trial Prospective cohort study Retrospective cohort study Case-control Case-series	■	■	■
Random sequence generation*	--	--	--
Statement of concealed allocation*	--	--	--
Intention to treat*	--	--	--
Independent or blind assessment	No	No	No
Co-interventions applied equally	Unclear	Yes	Yes
Complete follow-up of ≥80%	Unclear	Yes	Yes
<10% difference in follow-up between groups	Unclear	Yes	Yes
Controlling for possible confounding†	Yes	No	Yes
Risk of Bias	**High**	**Moderately high**	**Moderately low**

*Applies to randomized controlled trials only. If authors did not describe a methodologic principle, the study did not receive credit for the criterion.
† Authors must provide a description of robust baseline characteristics, and control for those that are unequally distributed between treatment groups.

Appendix Table E8. Quality of Health Economic Studies (QHES) scores: C-ADR economic studies

QHES Question (points possible)	Chaugule 2017	Huang 2010	Fonda 2016	McQueen 2011	Roze 2014
1. Was the study objective presented in a clear, specific, and measurable manner? (7 pts)	7	7	7	7	7
2. Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated? (4 pts)	0	4	4	4	0
3. Were variable estimates used in the analysis from the best available source (i.e. randomized controlled trial = best, expert opinion = worst)? (8 pts)	8	0	0	0	8
4. If estimates came from a subgroup analysis, were the groups prespecified at the beginning of the study? (1 pt)	1	1	1	1	1
5. Was uncertainty handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions? (9 pts)	9	9	0	9	9
6. Was incremental analysis performed between alternatives for resources and costs? (6 pts)	6	6	6	6	6
7. Was the methodology for data abstraction (including the value of health states and other benefits) stated? (5 pts)	5	5	5	5	5
8. Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given for the discount rate? (7 pts)	0	7	7	7	7
9. Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described? (8 pts)	8	8	0	8	8
10. Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term, long-term and negative outcomes included? (6 pts)	6	6	6	6	6
11. Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used? (7 pts)	7	0	7	7	7
12. Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner? (8 pts)	8	8	8	8	8

QHES Question (points possible)	Chaugule 2017	Huang 2010	Fonda 2016	McQueen 2011	Roze 2014
13. Were the choice of economic model, main assumptions, and limitations of the study stated and justified? (7 pts)	7	7	7	7	7
14. Did the author(s) explicitly discuss direction and magnitude of potential biases? (6 pts)	6	6	6	6	6
15. Were the conclusions/recommendations of the study justified and based on the study results? (8 pts)	8	8	8	8	8
16. Was there a statement disclosing the source of funding for the study? (3 pts)	0	3	3	3	0
Total score:	**86**	**85**	**75**	**92**	**93**

APPENDIX F. Study Characteristics and Patient Demographics

Appendix Table F1. Study Characteristics and Patient Demographics of RCTs Evaluating CGM versus SMBG in Children with Type 1 DM

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
Parallel Trials							
Bergenstal 2010** United States and Canada (multicenter) RCT Jan 2007—Dec 2008	N=329 adults	**SAP (n=78)** Sensor-augmented insulin pump therapy (MiniMed Paradigm REAL-Time System, Medtronic). Insulin pump therapy for 2 weeks, then glucose sensors introduced. Insulin aspart (NovoLog or NovoRapid, Novo Nordisk) was used. **Injection Therapy (n=78)** Multiple daily insulin injections with continuous glucose monitoring (Guardian REAL-Time Clinical, Medtronic). Both insulin glargine (lantus, Sanofi-Aventis) and insulin aspart were used All patients received training in intensive diabetes management including carbohydrate counting and the administration of correction doses of insulin	**Inclusion criteria:** Type 1 diabetes, aged 7–70 years, received multiple daily injections that included a long-acting analogue insulin during the previous 3 months, HbA1c 7.4%–9.5%, under the care of the principal investigator or a referring physician for ≥ 6 months, computer access, history of testing blood glucose an average of ≥ 4x/day for pervious 30 days **Exclusion criteria:** Use of insulin-pump therapy within previous 3 years, history of ≥ 2 severe glycemic events in the year before enrollment, use of a pharmacologic noninsulin treatment for diabetes during	**Children** Age, mean (SD): 12.2 (3.0) years Female: 44.3% BMI, mean (SD): 20.4 (4.1) kg/m^2 Interval since diabetes diagnosis, mean (SD): 5.05 (3.4) years HbA1c %, mean (SD): 8.3% (0.55)	**Total study population** F/U: 91.3%	• HbA1c % • Change from baseline in HbA1c at 1 year • % patients achieving target HbA1c < 7% • % patients achieving target • HbA1c < 8% (6—12 year olds) or 7.5% • Rates of severe hypoglycemia (< 50 mg/dl) • No. of Severe Hypoglemic Events • AUC <50, <70 mg/dl*min • Hyperglycemia (AUC >250, >180 mg/dl*min • DKA	Supported by Medtronic, Bayer Healthcare, and Becton Dickinson Conflict of interest: One or more authors have received funding, grants, honoraria, and consulting fees from various industries. Additional conflicts of interest were reported. See study for full conflict of interest

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
			the previous 3 months, pregnancy or the intention to become pregnant				
Rubin 2012 (Follow-up to the STAR 3 trial (Bergenstal 2010) Location: Europe Study period: RCT	481 total rand (<18 and >18), 147 <18 analyzed	**SAPT (n=77)** Pump Type: CSII(%): NR MDI(%): NR Device: MM Paradigm REAL-time System Glycemic Targets: NR Therapy Duration: 52 wks Training: Yes Description: Subjects received 2 weeks of pump therapy followed by glucose sensor use for 52 wks **MDI (n=70)** Pump Type: CSII(%): NR MDI(%): NR Device: SMBG Glycemic Targets: Therapy Duration: 52 wks Description: Subjects received insulin glargine, and insulin aspart under clinical guidance, supplied with insulin pens and received usual care throughout the 12 month period outside of the 3 month, 6 month, and 12 month follow-up visits. **Cointerventions:** None	**Inclusion Criteria:** Subjects with T1DM aged 7-70 on MDI therapy with a long-acting insulin analog for the previous 3 months, had HbA1C 7.4-9.5% (inclusive), history of testing blood glucose avg. ≥4 times/day in previous 30 days. **Exclusion Criteria:** Use of insulin pump within previous 3 years, had at least 2 severe hypoglycemic events in the year before enrollment, had used a diabetes drug other than insulin during prior 3 months, were pregnant or intending to become pregnant.	Mean Age, yrs(SD): 12.2±3.1 Female: 44% Non-hispanic white: 89% Mean Baseline Weight(kg): NR Mean Baseline BMI (kg/m2).: 20.4±4.1 Baseline HbA1c (%): 8.3±0.5 Mean duration of DM, yrs (SD): 5.0±3.4	F/U (% Total): 52 wks (NR%) **Crossover:** None	• Δ in HbA1C (%) • Severe Hypoglycemia Frequency • Hypoglycemia Fear Scale-II (HFS-II) – Worry and Behavior subscales <u>Participants ≥18 only:</u> • SF-36v2 – Physical Component Summary score (PCS) and Mental Component Summary score (MCS) <u>Participants <18 and their Parents only:</u> • PedQL •	Sponsor: Medtronic MiniMed provided financial support for this project and provided access to the data. COI: One or more of the authors received research funds and consulting fees from Medtronic MiniMed, Animas and/or Medingo.

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
Slover 2012 (Subset of the STAR-3 trials Bergenstal 2010) Location: USA Study period: NR *RCT*	156 randomized, 156 analyzed	**rtCGM (n=78)** Pump Type: CSII(%): MDI(%): Device: MM Paradigm REAL-time System Glycemic Targets: <8% for ages 6-12, <7.5% for ages 13-19 Therapy Duration: 12 months Description: Subjects randomized to CGM **SMBG (n=78)** Pump Type: CSII(%): NA MDI(%): 100 Device: SMBG Glycemic Targets: <8% for ages 6-12, <7.5% for ages 13-19 Therapy Duration: 12 months Description: Subjects placed on individualized regims by respective investigator-physicians, dosage regimens were neither restricted nor monitored. **Cointerventions:** None	**Inclusion Criteria:** Children and adolescents with T1DM aged 7-12 and 13-18 on MDI therapy with a long-acting insulin analog for the previous 3 months, had HbA1C 7.4-9.5% (inclusive), and had <2 severe hypoglycemic events in the previous year. **Exclusion Criteria:** NR	Age Group, y: 7-12, n: 82 13-18, n: 74 Mean Age, yrs (SD): Children- 9.7±1.7 Adolescents- 14.9±1.6 Total-12.2±1.7 Female: Children- 40.2% Adolescents- 49.0% Total- 44.3% Race: NR Mean Baseline Weight(kg): NR Mean Baseline BMI (kg/m2): Children- 18.3±2.7 Adolescents-22.7±4.2 Total- 20.4±3.4 Baseline HbA1c (%): Children- 8.20±0.54 Adolescent- 8.37±0.53 Total- 8.28±0.55 Mean duration of DM, yrs (SD): Children- 4.0±2.5 Adolescent- 6.27±3.86 Total- 2.35±1.45 ≥3 Insulin Shots/d (%): Children- 96% Adolescents- 98.5% Total- 97.0%	F/U (%Total): 12 months(100%) **Crossover:** None	• HbA1C (%) • % meeting HbA1C Goal • AUC >250 mg/dl, >180 mg/dl, >70 mg/dl, >60 mg/dl •	Sponsor: Funded by Medtronic COI: One or more authors received research support, travel reimbursement, speaking fees, manuscript preparation compensation, consulting fees, and are on speaker's bureau, and/or advisory board for Medtronic, Becton Dickinson, Roche, and/or Genentech
Hirsch 2008** United States (multicenter)	N=40	**Sensor group (n=23)** Sensor-augmented insulin pump therapy using the	**Inclusion criteria:** Age 12–72 years, HbA1c ≥ 7.5%, type-1 diabetes diagnosed > 1 year	**Total study population**§ Mean age (SD): 33.1 (15.5) Female: 57%	**Total Population**§ F/U (% sensor, % control): 13	• Change in A1c from baseline to 6 months • Percentage of subjects achieving 7% A1c	Supported by a grant from Medtronic, Inc.

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
Study period NR *RCT*		Paradigm 722 System (Medtronic). **Control (n=17)** Patients underwent self-monitored blood glucose measurements and a Paradigm 715 insulin pump and blinded CGM. **Cointerventions:** All patients received intensive diabetes management training.	prior to study, previously treated with CSII ≥ 6 months **Exclusion criteria:** NR	Mean duration of diabetes (SD): 18.7 (11.6) years Mean BMI (SD): 26.6 (5.3) kg/m^2	wks (100%, 100%), 26 wks (100%, 100%)	• Incidence and frequency of severe hypoglycemic and hyperglycemic events • Number of patients experiencing ketoacidosis event • Safety • Compliance	Conflict of interest: One or more authors have received funding, grants, honoraria, and consulting fees from various industries. Additional conflicts of interest were reported. See study for full conflict of interest
JDRF Trial 2008 United States (multicenter) Study Period: Feb 2007—Dec 2007 *RCT*	N=114 (age 8-14)	**CGM (n=56)** Instructed to use device on a daily basis and to verify accuracy with a home blood glucose meter. The device used was the Dex Com SEVEN (DexCom, San Diego, CA), the MiniMed Paradigm REAL-Time Insulin Pump and Continuous Glucose Monitoring System (Medtronic MiniMed, Northridge, CA), or the FreeStyle Navigator (Abbott Diabetes Care, Alameda, CA). **Control (n=58)** Home monitoring with a blood glucose meter only.	**Inclusion criteria:** 3x/daily glucose monitoring, aged > 8 years, HbA1c < 10.0%, not pregnant or planning pregnancy, naïve to sensor use **Exclusion criteria:** NR	**Children (age 8-14)** Female: 49% BMI z score: <-0.5: 2.6% -0.5 to 0.5: 23.7% >0.5: 73.7% Mean duration of diabetes (SD): 5.8 (3.0) years Insulin administration: Pump: 84.2% MDI: 15.8% HbA1c %: 7.0—8.0: 57.9% 8.1—8.9: 36% ≥9.0: 6.1% ≥1 episodes of severe hypoglycemia in previous 8 months: 4.4%	**Total study population** FU (% CGM, % control): 1 week, 4 wks, 8 wks, 13 wks, 19 wks (98%, 98%), 26 wks (100%, 100%)	• Change in HbA1c levels • Hypoglycemia (time per day, < 70 mg/dl, < 50 mg/dl) • Hyperglycemia resulting in DKA (time per day, > 180 mg/dl, > 250 mg/dl) • Unexpected study-related or device-related events • Serious adverse events regardless of causality	Funding provided by the JDRF (grants 22-20006-1107, 22-2006-1117, 22-2006-1112, 22-2006-1123, 01-2006-8031) Conflict of interest: One or more authors have received funding, grants, honoraria, and consulting fees from various industries. Additional conflicts of interest were

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
		Patients were instructed to perform SMBG ≥ 4x daily. **Cointerventions:** All patients received information on the insulin regimen including the determination of pre-meal bolus dose and guidelines for correcting high glucose levels		Mean daily home glucose-meter readings (SD): 6.9 (2.5) per day			reported. See study for full conflict of interest
Kordonouri 2010 (ONSET) Location: Europe, multicenter Study period: NR *RCT*	160 randomized, 154 analyzed	**rtCGM (n=80)** Delivery Type: CSII: 100% MDI: NA Device: MM Paradigm REAL-Time CGM Glycemic Targets: Preprandial‡ (5.0-8.0 mmol, 2 hr PPG <10.0 mmol) bedtime values (6.7-10.0 mmol) and overnight values (4.5-9.0 mmol/l) Therapy Duration: 52 weeks Description: Patients were instructed to use the CGM device daily. Alarms: NR **SMBG (n=80)** Delivery Type: CSII: 100% MDI: NA Device: Minimed Paradigm 515/715	**Inclusion Criteria:** Children and adolescents between 1-16 yrs old diagnosed with T1DM within 4 weeks of study entry **Exclusion Criteria:** Diagnosis of type 1 diabetes > 4 wks before study entry	**N=160** Mean Age (SD): 8.7(4.4) years Female: 46% Race: NR Mean Baseline Weight(kg): NR Mean Baseline BMI (kg/m2): NR Baseline HbA1c (%): 11.2(2.1) Mean duration of DM (SD): NR Diabetic Ketoacidosis, n (%): 71 (46.1)	F/U (% rtCGM, SMBG): 52 weeks (95%, 97.5%) **Crossover:** None	• HbA1c (%) • Hypoglycemia frequency • Ratio of basal to bolus insulin (Number of daily boluses) • Ratio of basal to bolus insulin (Proportion of basal insulin) • Severe hypoglycemia (not further spec) • KIDSCREEN-27	Sponsor: This study is an investigator-initiated trial supported by Medtronic International Trading Sàrl COI: One or more of the authors received honoraria, consulting fees, and/or travel reimbursements from Medtronic, Abbott Diabetes Care, DexCom, Roche, Bayer HealthCare, Eli Lilly, Sanofi-Aventis, Novo Nordisk, Lilly Deutschland, Serono, Berlin

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
		Glycemic Targets: Preprandial: 5.0-8.0 mmol, 2 hr PPG(<10.0 mmol) bedtime values (6.7-10.0 mmol) and overnight values (4.5-9.0 mmol/l) Therapy Duration: 26weeks Description: Patients were asked to perform SMBG 4+ times per day Alarms: NR **Cointerventions:** None					Chemie, and/or Terumo.
Lawrence 2010 Follow-up** Location: USA Study period: RCT	451 randomized, 446 treated, 435 analyzed	**RT-CGM (n=223)** Delivery Type: CSII: NA MDI: NA Device: Model unspecified Glycemic Targets: NR Therapy Duration: 26 wks Description: Participants were instructed to use CGM daily if possible. **SMBG (n=212)** Delivery Type: CSII(%): NA MDI(%): NA Device: SMBG Fingerstick use: Glycemic Targets: NR Therapy Duration: 26 weeks Description: Participants were instructed to perform SBGM 4+ times/day	**Inclusion Criteria:** T1DM, very young, adults, elderly **Exclusion Criteria:** NR	A+B Mean Age, yrs (SD): ≥18 years(%): 50.6 <18 years(%): 49.4 Female: NR Race: NR Mean Baseline Weight(kg): NR A vs B Mean Baseline BMI (kg/m2): 22.4 vs. 22.0 Baseline HbA1c (%): NR Mean duration of DM, yrs (SD): NR	F/U (% CGM, SMBG): 26 wks. (97.3%, 97.7%)	<u>Participants ≥18 years:</u> • Total, Worry and Behavior subscales of the Hypoglycemia Fear Survey (HFS) • Problem Areas in Diabetes scale (PAID) • Physical Component Summary Scale (SF-12 PCS) and Mental Component Summary Scale (SF-12 MCS) of the SF-12 Quality of Life scale. <u>Participants ≤18 years</u> • HFS worry subscale, by patient and parents	Sponsor: JDRF grants (22-2006-1107, 22-2006-1117, 22-2006-1112, 22-2006-1123, and 01-2006-8031). CGM and sensors purchased at discounted prices from DexCom, Medtronic Minimed and Abbott Diabetes Care. Home glucose meters and test strips provided by LifeScan and

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
		Cointerventions: None				• Pediatrics Quality of Life scale (PedsQL) Generic and Diabetes-specific subcales • PAID-Parent survey (parents only) <u>Parents of participants <18 years:</u> • PAID-Parent (PAID-P) survey • • PedsQL Parent-Proxy version	Abbott Diabetes Care COI: One or more authors have received consulting fees, speaker honorarium, and/or research funding from DexCom, Medtronic Minimed, LifeScan and/or Abbott Diabetes Care. The companies had no involvement in the design, conduct, or analysis of the trial or the manuscript preparation.
Mauras 2012 Location: USA Study period: NR *RCT*	146 randomized, treated, 137 analyzed	**RT-CGM (n=69)** Delivery Type: CSII: 59% MDI: 41% Device: Abbott Freestyle Navigator or MM MiniLink REAL-Time Glycemic Targets: Therapy Duration: 26 wks	**Inclusion Criteria:** Children aged 4 to <10 with T1DM, HbA1c ≥7.0% and basal-bolus therapy using insulin pump or at least three MDIs for the prior 3 months with no plans to switch the modality	Mean Age, yrs (SD): 7.5(1.7) Female: 46% Race: 77% nonhispanic white Mean Baseline Weight(kg): Mean Baseline BMI (kg/m2): Baseline HbA1c (%): 7.9(0.8)	F/U (% CGM, SMBG): 26 wks (93.2%, 94.4%	• ≥0.5% reduction in HbA1c • Severe Hypoglycemia	Sponsor: Research supported by grants from the NIH National Institute for Child Health and Human Development (HD-4189010, HD-41906-10,

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
		Description: After a run-in period, patients were randomly assigned to CGM **SMBG (n=68)** Delivery Type: CSII(%): 69% MDI(%): 31% Device: SMBG Fingerstick use: Glycemic Targets: Therapy Duration: Description: After a run-in period, patients were randomly assigned to usual care. Patients were asked to perform SMBG 4+ times daily. **Cointerventions:** None	within the next 6 months **Exclusion Criteria:** diagnosis of DM before 6 months of age, use of medication that could affect glycemic control, the performance of the CGM sensor, or completion of protocol, use of CGM during the prior 6 months	Median duration of DM (SD): 3.5 years Total Daily Insulin unit/kg(SD): 0.8(0.2)			HD-41908-10, HD-41915, HD-41918 and HD-56526 COI: One or more authors are on advisory boards, provides research support, received honoraria, and/or served as a paid consultant/advisor for Abbott, Medtronic MiniMed, and/or Animas/LifeScan

BG, blood glucose; BMI, body mass index-standard deviation score; CSII, continuous subcutaneous insulin infusion; dL, deciliter; DM, diabetes mellitus; HbA1c, hemoglobin A1c; IV, intravenous; kg, kilograms; kg/m2, kilograms per meter squared; MDI, multiple daily injections; mg, milligram; mg/dL, milligrams per deciliter; MM, Medtronic Minimed; mmol, micromoles; mmol/L, millimole per liter; NA, not applicable; NR, not reported; NS, not significant; PPG, post prandial glucose; RCT, randomized controlled trial; rtCGM, real-time continuous glucose monitor; SD, standard deviation; SMBG, self-monitoring of blood glucose; T1DM, Type 1 Diabetes Mellitus; T2DM, Type 2 Diabetes Mellitus; U, units; wk, week; wks, weeks; x/day, times per day; yrs, years

* Only a 'brief report' was available for data abstraction for Deiss 2006

† Group N's for Deiss 2006 inferred from description of randomization scheme, but are otherwise not specifically stated.

‡ Prandial is rapid-acting, or short-acting insulins, including lispro, regular insulin, aspart, and glulisine. Basal is long-acting or intermediate-acting insulins, such as glargine, detemi and NP.

§ Only data for the total study population was reported at baseline.

**Includes data for an adult population—abstraction can be found in corresponding adult sections

Appendix Table F2. Study Characteristics, Patient Demographics and Results from Observational Studies of Children with Type 1 DM

Study	N	Demographics	Inclusion/exclusion criteria	Study purpose	Results	Conclusions	Funding
Chase 2010 (Follow-up extension of JDRF 2008) *Prospective cohort*	80	**Group A (n=17)** CGM use ≥ 6 days/week in month 12 Age: 11.3 (2.9) years Female: 53% Duration of diabetes: 5.8 (3.1) years **Group B (n=17)** CGM use ≥ 6 days/week in month 6 and < 6 at month 12 Age: 12.7 (2.8) years Female: 59% Duration of diabetes: 6.0 (3.30 years **Group C (n=46)** CGM use < 6 days/week in both month 6 and 12 Age: 13.7 (2.8) Female: 46% Duration of diabetes: 7.2 (3.2) years	**Inclusion criteria:** T1DM for ≥1 year, use of either an insulin pump or ≥3 daily insulin injections, HbA1c level 7.0% to < 10.0%	To assess ongoing use of CGM over the course of 12 months and its association with glycemic outcomes in pediatric patients 8–17 years of age upon study entry	**A1c (mean)** *Baseline* Group A: 8.2 Group B: 7.8 Group C: 8.0 *6 months* Group A: 7.3 Group B: 7.3 Group C: 8.0 *12 months* Group A: 7.4 Group B: 7.7 Group C: 8.1 *P* < .001 for the 3-group comparisons* **Percent of subjects meeting target A1c** † *Baseline* Group A: 29% Group B: 47% Group C: 39% *6 months* Group A: 65% Group B: 76% Group C: 35% *12 months* Group A: 71% Group B: 41% Group C: 33% *P* < .03 for the 3-group comparisons*	Continued use of CGM ≥6 days/week through months 6 and month 12 was associated with lower A1c values	Juvenile Diabetes Research Foundation, Inc (grant # 22-2006-1107, 22-2006-1117, 22-2006-1123, and 01-2006-8031) COI: One or more authors have received funding, grants, honoraria, and consulting fees from various industries. Additional conflicts of interest were reported. See study for full conflict of interest.

Study	N	Demographics	Inclusion/exclusion criteria	Study purpose	Results	Conclusions	Funding
JDRF 2010 (follow-up extension of JDRF 2008) *Prospective cohort*	47	HbA1c %: 7.8% Using CGM in month 6: 0 days/week, n=11 >0 to < 4 days/week, n=15 4 to < 6 days/week, n=10 ≥ 6 days/week, n=11	**Inclusion criteria:** Randomized to SMBG in JDRF RCT, cross-over to CGM in extension study	To determine whether CGM is effective when used in a typical clinical care environment	**Mean change from baseline to 6 months, by use of CGM:** • 0 days/ week: -0.1 • > 0 to < 4 days/week: +0.2 • 4 to <6 days/week: -0.2 • ≥ 6 days/week: 0 **Rate of severe hypoglycemia:** • 6 months using SMBG during trial: 26.4/100 person years 6 months using CGM after trial: 13.0 person-years	Greater CGM use was associated with a great A1c decrease (*P* = .01 adjusted for age-group) The incidence of severe hypoglycemia trended lower in all age groups. There were no significant differences in adjusted glycemic indices between baseline and month 6.	Juvenile Diabetes Research Foundation, Inc COI: One or more authors have received funding, grants, honoraria, and consulting fees from various industries. Additional conflicts of interest were reported. See study for full conflict of interest.
JDRF 2009b (Sub-analysis of JDRF 2008) *Prospective cohort*	74 ‡	Age: 8—14 years Female: 50% Duration of diabetes < 5 years: 41%	**Inclusion criteria:** Age ≥ 8 years, T1DM for ≥ 1 year, use of either an insulin pump or ≥ 3 daily insulin injections, HbA1c level < 10.0%	To investigate factors associated with successful use of CGM among subjects with intensively treated DM	**Change in A1c (%) based on average CGM use in month 6** • < 4 days/week (n = 7): + 0.02 § • 4–6 days/week (n = 21): -0.03 § • ≥ 6 days/week (n = 28): -0.72 § *P* < .001 * *	Near daily CGM use is associated with a similar reduction in A1c regardless of age. Frequency of blood glucose meter monitoring and initial CGM use may help predict the likelihood of long-term CGM benefit in all ages	Juvenile Diabetes Research Foundation, Inc COI: One or more authors have received funding, grants, honoraria, and consulting fees from various industries. Additional conflicts of interest were reported. See study for full conflict of interest.

Study	N	Demographics	Inclusion/exclusion criteria	Study purpose	Results	Conclusions	Funding
Kordonouri 2012 (Observational Follow-up to Kordonouri 2010)†† *Prospective cohort*	131	Female: 50% Age of diabetes onset, mean (SD): 8.9 (4.3) years HbA1c %, mean (SD): 7.7 (1.2)%	**Inclusion criteria:** Children and adolescents aged 1-16, T1DM diagnosis within 4 weeks of study entry	To evaluate the metabolic control and beta cell function 1 year after the end of the European multicenter randomized Pediatric Onset Study	**Mean HbA1c %** **Baseline** Group A 11.2±2.1 vs. Group B 11.5±2.2, p=0.472 **24 month follow-up** Group A: 7.6±1.3 (n=62) Group B: 7.7±1.2 (n=69); p= 0.493 **A vs B** **% with HbA1c <7.5%** 52.5% (33/62) vs. 45.6% (31/69) p=0.436 **Severe Hypoglycemia** 24 mos. Events: 0 (n=62 vs. 1 (n=69) **Diabetic Ketoacidosis** 24 mos. Events: 0 vs 2 **Sensor use ≥1 day/week** HbA1c %, mean (SD): 7.4 (1.0) % **Irregular or no sensor use** HbA1c %, mean (SD): 7.7 (1.3) %	SAP from onset of type 1 diabetes may lead to better long-term glycemic control.	Medtronic International Trading Sarl

Study	N	Demographics	Inclusion/exclusion criteria	Study purpose	Results	Conclusions	Funding
Ludwig-Seibold 2012 *Prospective database study*	2874	< 18 years old: 49% CSII: 35% MDI: 56%	**Inclusion criteria:** Regular visits to participating centers at least every 3 months	To determine frequency, duration, and relationship of CGM to glycemic control and rate of hypoglycemia in children and adults.	**Mean HbA1c%‡‡** *Adults* No CGM use: 8.0% CGM use <30 days: 8.0% CGM use >30 days: 7.3% *Pediatrics* No CGM use: 8.4% CGM use <30 days: 8.3% CGM use >30 days: 8.3% **Hypoglycemia** Patients using CGM <30 days had significantly more hypoglycemia compared to patients without CGM. No statistically significant difference in rate of hypoglycemia between CGM use >30 days and no CGM use.	CGM use is associated with a significant reduction of HbA1c in adults but not in children. Hypoglycemia events were not reduced, irrespective of age.	German Federal Ministry of Health, Novo Nordisk Germany, the Dr Burger-Busing Foundation, the German Diabetes Foundation, and the German Diabetes competence Network
Rachmiel 2015 *Prospective cohort*	149	**RT-CGM group (n=83)** Age, mean (SD): 11.9 (3.9) years Female: 55% Duration of diabetes, mean (SD): 3.8 (2.6) HbA1c%, mean (SD): 8.1 (1.1)% Percent using CSII therapy: 90% **Control group (n=66)**	**Inclusion criteria:** T1DM diagnosis ≥ 6 months prior to enrollment, aged 1 to 17, basal-bolus insulin regimen using either CSII or MDI, periodic clinic visits. **Exclusion criteria:** Prior use of RT-CGM	To compare annual glycemic control in pediatric patients with T1DM who used healthcare-funded RT-CGM to patients using SMBG in a real-life setting. To define parameters associated with	**Mean HbA1c%** *Baseline* Intermittent RT-CGM use§§: 8.0% Consistent RT-CGM use***: 7.9% Control: 8.1% *3 months* Intermittent RT-CGM use: 8.2% Consistent RT-CGM use: 7.6%	RT-CGM in clinical practice improves glycemic control, but only among those who comply with its continuous usage. The adoptions of RT-CGM was low, even in a healthcare system that funds its use. Caregivers should consider patient	None

Study	N	Demographics	Inclusion/exclusion criteria	Study purpose	Results	Conclusions	Funding
		Age, mean (SD): 11.8 (3.1) Female: 48% Duration of diabetes, mean (SD): 3.9 (2.7) HbA1c%, mean (SD): 8.1 (1.2)% Percent using CSII therapy: 59%		compliance and glycemic control.	Control: 8.1% *6 months* Intermittent RT-CGM use: 8.1% Consistent RT-CGM use: 7.7% Control: 8.1% *9 months* Intermittent RT-CGM use: 8.2 Consistent RT-CGM use: 7.6% Control: 8.1% *12 months* Intermittent RT-CGM use: 8.2% Consistent RT-CGM use: 7.7% Control: 8.1% **Severe hypoglycemia episodes** CGM group: 18.1 episodes per 100 patient years Control: 10.6 episodes per 100 patient years **Diabetic ketoacidosis episodes** CGM group: 8.4 episodes per 100 patient years Control: 3.0 episodes per 100 patient years	characteristics when recommending RT-CGM use.	
Scaramuzza 2011 †††	622	**SAP users (n=129)** Age, mean (SD): 13.5 (3.8) years	**Inclusion criteria:** T1DM, ≤ 18 years old, using SAP for ≥ 6	Examining the usefulness and safety of SAP in a	**HbA1c %** SAP users, mean (SD): 7.4 (0.8) %	Patients using SAP compared with patients using	NR

Study	N	Demographics	Inclusion/exclusion criteria	Study purpose	Results	Conclusions	Funding
Retrospecti ve cohort		Duration of diabetes, mean (SD): 6.3 (3.4) years HbA1c %, mean (SD): 8.0 (1.5)% **Conventional insulin pump users (n=493)** Age, mean (SD):12.9 (3.4) years Duration of diabetes, mean (SD): 6.2 (3.3) years HbA1c %, mean (SD): 8.0 (1.6)%		large population of pediatric patients with type 1 diabetes mellitus, evaluated at baseline and after a 3 year follow-up.	Conventional insulin pump users, mean (SD): 7.7 (1.1) %	conventional insulin pump therapy demonstrated significant improvement in glycemic control.	
Wong 2014 *Retrospecti ve registry*	9882	**< 13 years old, CGM (n=278) vs non-CGM (n=4749)** Female: 51% vs 48% Duration of diabetes, median (IQR): 4 (2 to 6) years vs 3 (1 to 5 years) Percent using CSII: 88% vs 58% Percent using MDI: 12% vs 42% **13 to <18 years old, CGM (n=179) vs non-CGM (n=4676)** Female: 51% vs 49% Duration of diabetes, median (IQR): 7 (4 to 11) vs 6 (3 to 9) Percent using CSII: 89% vs 55%	**Inclusion criteria:** Patients with T1DM **Exclusion criteria:** NR	To assess the frequency of CGM device use, factors associated with its use, and the relationship of CGM with the diabetic outcomes of HbA1c, severe hypoglycemia, and diabetic ketoacidosis	**Mean % HbA1c** • <13 years, CGM vs non-CGM: 8.3% vs 8.6% • 13 to <18 years old, CGM vs non-CGM: 9.0% vs 9.0% *CGM use <4 days/wk‡‡‡:* • <13 years: 8.0% • 13 to <18 years: 10.2% *CGM use 4 to <6 days/wk ‡‡‡:* • <13 years: 8.0% • 13 to <18 years: 9.0% *CGM use ≥6 days/wk*:‡‡‡ <13 years: 7.9% • 13 to <18 years: 9.1%	CGM use is uncommon but associated with lower HbA1c in children and adults, though not in 13 to < 26 year olds, especially when used more frequently. Future efforts should be made at improving CGM technology and features to address common obstacles. Special attention should be paid to patients with lower socioeconomic status and lack of private insurance.	Leona M and Harry B. Helmsley Charitable Trust and National Institutes of Health Grant funding (K12-DK094726; K12 in Diabetes [KIDS]) Conflict of interest: 1 or more author has received research grants or payments from industry. 1 or more author has consulted or served on scientific advisory board for industry.

Study	N	Demographics	Inclusion/exclusion criteria	Study purpose	Results	Conclusions	Funding
		Percent using MDI: 11% vs 45%			**≥1 SH event in previous 3 months** *CGM use <4 days/wk:* • <13 years: 4.2% • 13 to <18 years: 10.0% *CGM use 4 to <6 days/wk*: • <13 years: 2.1% • 13 to <18 years: 4.0% *CGM use ≥6 days/wk:* • <13 years: 5.6% • 13 to <18 years: 5.8% **≥1 DKA event in previous 3 months** *CGM use <4 days/wk:* • <13 years: 2.8% • 13 to <18 years: 10.0% *CGM use 4 to <6 days/wk*: • <13 years: 2.1% • 13 to <18 years: 8.0% *CGM use ≥6 days/wk:* • <13 years: 2.1% • 13 to <18 years: 5.8%		See article for full conflict of interest

CGM, continuous glucose monitoring; COI, conflict of interest; CSII, continuous subcutaneous insulin infusion; DKA, diabetic ketoacidosis; Hba1c, hemoglobin A1C; MDI, multiple daily injections; SAP, sensor-assisted pump; SMBG, self-monitoring of blood glucose; T1DM, type 1 diabetes mellitus; RCT, randomized controlled trial; wk, week;

*Adjusted for baseline A1c value and age

†A1c target < 8.0% for 8–12 year olds and < 7.5% for 13–17 year olds.

‡ Demographics and results are reported for the 8–14 year age group only. In total there were 232 subjects, 53% female, age range 8–72 years.

§ Mean values were estimated from figure 1 in article.
**Adjusted for baseline A1c
†† In the study, patients were able to choose their treatment method, breaking randomization and making the study observational
‡‡ Values for intermittent and consistent RT-CGM use were estimated from a graph.
§§ Intermittent use defined as those who used RT-CGM for less than 75% of the time.
*** Consistent use defined as those who used RT-CGM for more than 75% of the time.
††† Unclear if device was FDA approved; study was conducted in Italy and the device used not specified.
‡‡‡ <13 years, 13 to <18 years, and 18 to <26 year values were estimated from graph

Appendix Table F3. Study Characteristics and Patient Demographics of RCTs Evaluating CGM versus SMBG in Adults with Type 1 DM

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
Parallel Trials							
Beck 2017 (DIAMOND) **Polonsky 2017** United States (multicenter) RCT Oct 2014—May 2016	N=158	**CGM (n=105)** CGM Device: Dexcom G4 platinum CGM system SMBG device: Bayer Contour Next Protocol: CGM used daily for study duration, calibrated ≥2 times/day, CGM values verified using SMBG, values used to modify diabetes management **Usual care (n=53)** SMBG device: Bayer Contour Next Protocol: Home blood glucose monitoring ≥4 times/day **Cointervention(s)** General diabetes management education	**Inclusion criteria:** ≥ 25 years old, diagnosis of type 1 diabetes, followed regularly by a physician or diabetes education for diabetes management, MDI for ≥ 12 months prior to study, persistent hyperglycemia (≥ 7.7%, ≤ 10%), desire to lower A1c, stable control of diabetes, stable weight for 3 months prior to study, no plans for structured weight reduction interventions, willing to wear CGM device, willing to avoid acetaminophen	Age, mean (SD): 49 (12) years Female: 44% Duration of diabetes CGM group, median (IQR): 19 (9-29) Duration of diabetes control group, median (IQR): 19 (11-35) BMI, mean (SD): 28 (6) Weight, mean (SD): 83 (19) kg HbA1c%, mean (SD): 8.6 (0.7)% ≥1 episode of severe hypoglycemia (in past 12 mos): 13% WHO-5, mean (SD): 70.2 (14.8) EQ-5D-5L, mean (SD): 0.90 (0.11)	F/U (% CGM, % control): 1 month, 3 mos, 6 mos (97%, 100%)	• Change in HbA1c levels • % patients with HbA1c levels <7.0% • % patients with HbA1c levels <7.5% • Relative reduction HbA1c ≥10% • Reduction in % HbA1c ≥1% • Reduction in % HbA1c ≥1% or HbA1c < 7.0% • Duration of hypoglycemia (<70 mg/dl, <60 mg/dl, <50 mg/dl) • Area above curve 70 mg/dl • Duration of hyperglycemia (>180 mg/dl, >250 mg/dl, >300 mg/dl)	Dexcom, Inc.

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
			throughout study, performing SMBG ≥3 times/day **Exclusion criteria:** Use of personal RT-CGM 3 months prior to study, use of CSII 2 months prior to study, plan to use personal CGM and/or pump during study, addition of any new oral or injectable hypoglycemic agents within 3 months prior to study, use of pre-mixed insulin 6 months prior to study, current or anticipated acute uses of glucocorticoids, pregnancy or plans to become pregnant, medical conditions that make it inappropriate or unsafe for A1C <7%			• Area under curve 180 mg/dl • WHO-5 • EQ-5D-5L • DDS • HFS-II • HCS	
Bergenstal 2010* United States and Canada (multicenter) RCT	N=329 adults	**Pump Therapy (n=166)** Sensor-augmented insulin pump therapy (MiniMed Paradigm REAL-Time System, Medtronic). Insulin pump therapy for 2 weeks, then glucose sensors introduced. Insulin	**Inclusion criteria:** Type 1 diabetes, aged 7–70 years, received multiple daily injections that included a long-acting analogue insulin during the	**Adults** Age, mean (SD): 41.3 (12.2) years Female: 57% BMI, mean (SD): 27.9 (5.1) kg/m^2	**Total study population** F/U: 91.3%	• Change from baseline in HbA1c at 1 year • Rates of severe hypoglycemia (< 50 mg/dl) and DKA • HFS • SF-36	Supported by Medtronic, Bayer Healthcare, and Becton Dickinson

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
Jan 2007—Dec 2008		aspart (NovoLog or NovoRapid, Novo Nordisk) was used. **Injection Therapy (n=163)** Multiple daily insulin injections with continuous glucose monitoring (Guardian REAL-Time Clinical, Medtronic). Both insulin glargine (lantus, Sanofi-Aventis) and insulin aspart were used All patients received training in intensive diabetes management including carbohydrate counting and the administration of correction doses of insulin	previous 3 months, HbA1c 7.4%–9.5%, under the care of the principal investigator or a referring physician for ≥ 6 months, computer access, history of testing blood glucose an average of ≥ 4x/day for pervious 30 days **Exclusion criteria:** Use of insulin-pump therapy within previous 3 years, history of ≥ 2 severe glycemic events in the year before enrollment, use of a pharmacologic noninsulin treatment for diabetes during the previous 3 months, pregnancy or the intention to become pregnant	Interval since diabetes diagnosis, mean (SD): 20.2 (11.9) years HbA1c %, mean (SD): 8.3% (0.5)			Conflict of interest: One or more authors have received funding, grants, honoraria, and consulting fees from various industries. Additional conflicts of interest were reported. See study for full conflict of interest
Bolinder 2016	N=241	**Flash CGM (n=120)** Flash sensor based glucose monitoring used continuously throughout study. Device used was Freestyle Libre. **Control group (n=121)**	**Inclusion criteria:** Age ≥18 years, T1DM diagnosis for ≥5 years, on current insulin regimen for ≥3 months before study entry, HbA1c concentration ≤7.5%, SMBG ≥3 times per	Age flash CGM group, median (IQR): 42 (33-51) years Age control group, median (IQR): 45 (33-57) years Female: 43%	**F/U (% flash CGM, % control group):** 6 months (92%, 83%)	• HbA1c % • Time spent in hypoglycemic range (<70 mg/dL, <55 mg/dL, <45 mg/dL, <40 mg/dL) • Time spent in nocturnal hypoglycemic range	Abbott Diabetes Care Abbott Diabetes Care helped design study protocol, helped collect data and report

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
		Subjects performed SMBG using either MDI or CSII. After 3 and 6 month follow-up, subjects underwent blinded flash sensor based glucose monitoring for 14 days. **Cointervention(s)** None	day for ≥2 months before study entry, considered by investigator to be technically capable of using the flash sensor-based glucose monitoring system. **Exclusion criteria:** Current diagnosis of hypoglycemia unawareness, diabetic ketoacidosis or myocardial infarction in previous 6 months, known allergy to medical-grade adhesives, use of CGM within previous 4 months, current use of SAP, pregnant or planning pregnancy, oral steroid therapy for any disorders	Race white non-Hispanic n/N (%): 238/239 (99%) BMI, mean (SD): 25.0 (2.6) kg/m^2 HbA1c %: 6.7 (0.6) % Insulin administration method: MDI: 67% CSII: 33%		(<70 mg/dL, <55 mg/dL, <45 mg/dL) • Proportion of participants who achieved time spent in hypoglycemia ≤1 hour/day • Time spent in hyperglycemic range (>240 mg/dL) • Time spent in target glycemic range (70.2-180 mg/dL) • DQoL • DDS • DTSQ • HFS	results, funded medical writing services, and gave approval to submit for publication. See study for full conflict of interest COI: One author has received consulting or lecture fees from various study funder, one or more author has received lecture honoraria from study funder, one or more author serves on advisory board of study funder. Additional conflicts of interest were reported. See study for full conflict of interest.
Hermanides 2011 Location: Europe, multicenter	83 randomized,	**CSII+rtCGM (n=44)** Delivery Type: CSII: 100%	**Inclusion Criteria:** Adults age 18-65 diagnosed with	Mean Age (SD): 38.4(11.3) years	F/U (% CSII+rtCGM, SMBG): 26	• Severe hypoglycemia	Sponsor: The trial was financially

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
Study period: Apr 2007-Jan 2009 RCT, open-label	78 treated	MDI: NA Device: MM Paradigm Provider Titration Guidelines, Glycemic Targets: Between Visit guidelines Therapy Duration: 26 weeks Description: Patients were randomized to receive CGM 24 hrs/day Alarms: Yes **SMBG (n=39)** Delivery Type: CSII: NA MDI: 100% Device: MDI Glycemic Targets: NR Therapy Duration: 26 weeks Description: Patients were instructed to continue standard care including MDI 3x/day. Alarms: NR **Cointerventions:** None	T1DM at least 1 year prior to study, currently treated with optimized MDI but having HbA1c ≥8.2% aT screening despite repeated re-education attempts. **Exclusion Criteria:** HbA1c < 8.2%, hearing problems that can impair hearing alarms, substance abuse other than nicotine, abdominal skin abnormalities that might hinder subcutaneous insertion, current treatment for psychiatric disorder other than depression, heart failure, cancer, kidney disease, pregnancy, CSII within 6 month, participation in other therapeutic trial	Female: 48.2% Race: NR Mean Baseline Weight(kg): NR Mean Baseline BMI (kg/m2): NR Baseline HbA1c (%): 8.55(0.90) Baseline HbA1c mmol/mol): 69.9(9.5) Mean duration of DM (SD): 18.8(10.7) years	weeks (98% vs. 90%) **Crossover:** None	• Hyperglycemia (Mild hypoglycemia: events defined as >11.1 mmol/l) • Hyperglycemia (%) • HbA1c (%) • Hypoglycemia frequency • (%)Moderate hypoglycemia frequency (defined as <4.0 mmol/l)	supported by Medtronic International. The funding source had an advising role in trial design details and drafting of the report and was only involved in the collection of the sensor data. The funding source had no role in the conduct of the analyses, interpretation of the data or in the decision to approve publication. COI: One or more authors received speaking fees, served on advisory boards, received research support, and/r fees for education

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
							activities for Medtronic, Roche, Novo Nordisk, Eli Lilly, Sanofi-Aventis, Novartis, Merck Sharp and Dohme, Astra Zeneca, and/or Becton Dickinson
Hirsch 2008* United States (multicenter) RCT Study period NR	N=98	**Sensor group (n=49)** Sensor-augmented insulin pump therapy using the Paradigm 722 System (Medtronic). **Control (n=49)** Patients underwent self-monitored blood glucose measurements and a Paradign 715 insulin pump and blinded CGM. **Cointerventions:** All patients received intensive diabetes management training.	**Inclusion criteria:** Age 12–72 years, HbA1c ≥ 7.5%, type-1 diabetes diagnosed > 1 year prior to study, previously treated with CSII ≥ 6 months **Exclusion criteria:** NR	**Total study population** Mean age (SD): 33.1 (15.5) years Female: 57% Mean duration of diabetes (SD): 18.7 (11.6) years Mean BMI (SD): 26.6 (5.3) kg/m^2	**Adults (≥ 18)** F/U (% sensor, % control): 13 wks (100%, 100%), 26 wks (100%, 100%)	• Change in A1c from baseline to 6 months • Percentage of subjects achieving 7% A1c • Hypoglycemia (< 70 mg/dl) and hyperglycemia (> 180 mg/dl) areas under the curve • Incidence and frequency of severe hypoglycemic and hyperglycemic events • Safety • Compliance •	Supported by a grant from Medtronic, Inc. Conflict of interest: One or more authors have received funding, grants, honoraria, and consulting fees from various industries. Additional conflicts of interest were reported. See study for full conflict of interest
JDRF Trial 2008*	N=98 (age ≥25)	**CGM (n=52)** Instructed to use device on a daily basis and to verify	**Inclusion criteria:** 3x/daily glucose monitoring, aged > 8	**Adults (age ≥25)** Female: 59% BMI z score:	**Total study population**	• Change in HbA1c levels	Funding provided by the JDRF (grants 22-

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
United States (multicenter) RCT Feb 2007—Dec 2007		accuracy with a home blood glucose meter. The device used was the Dex Com SEVEN (DexCom, San Diego, CA), the MiniMed Paradigm REAL-Time Insulin Pump and Continuous Glucose Monitoring System (Medtronic MiniMed, Northridge, CA), or the FreeStyle Navigator (Abbott Diabetes Care, Alameda, CA). **Control (n=46)** Home monitoring with a blood glucose meter only. Patients were instructed to perform SMBG ≥ 4x daily**.** **Cointerventions:** All patients received information on the insulin regimen including the determination of pre-meal bolus dose and guidelines for correcting high glucose levels	years, HbA1c < 10.0%, not pregnant or planning pregnancy, naïve to sensor use **Exclusion criteria:** NR	<-0.5: 18% -0.5 to 0.5: 63% >0.5: 20% Mean duration of diabetes (SD): 22.7 (10.5) years Insulin administration: Pump: 84% MDI: 16% HbA1c %: 7.0—8.0: 85% 8.1—8.9: 13% ≥9.0: 2% ≥1 episodes of severe hypoglycemia in previous 8 months: 10% Mean daily home glucose-meter readings (SD): 6.6 (2.2) per day	FU (% CGM, % control): 1 week, 4 wks, 8 wks, 13 wks, 19 wks (98%, 98%), 26 wks (100%, 100%)	• Hypoglycemia (time per day, < 70 mg/dl, < 50 mg/dl) • Hyperglycemia resulting in DKA (time per day, > 180 mg/dl, > 250 mg/dl) • Unexpected study-related or device-related events • Serious adverse events regardless of causality • SF-12 • HFS • PAID	20006-1107, 22-2006-1117, 22-2006-1112, 22-2006-1123, 01-2006-8031) Conflict of interest: One or more authors have received funding, grants, honoraria, and consulting fees from various industries. Additional conflicts of interest were reported. See study for full conflict of interest.
Lawrence 2010* Follow-up Location: USA Study period: RCT	451 randomized, 446 treated, 435 analyzed	**RT-CGM (n=223)** Delivery Type: CSII: NA MDI: NA Device: Model unspecified Glycemic Targets: NR Therapy Duration: 26 wks	**Inclusion Criteria:** T1DM, very young, adults, elderly **Exclusion Criteria:** NR	A+B Mean Age, yrs (SD): ≥18 years(%): 50.6 <18 years(%): 49.4 Female: NR Race: NR Mean Baseline Weight(kg): NR	F/U (% CGM, SMBG): 26 wks. (97.3%, 97.7%)	<u>Participants ≥18 years:</u> • Total, Worry and Behavior subscales of the Hypoglycemia Fear Survey (HFS)	Sponsor: JDRF grants (22-2006-1107, 22-2006-1117, 22-2006-1112, 22-2006-1123, and 01-2006-8031).

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
		Description: Participants were instructed to use CGM daily if possible. **SMBG (n=212)** Delivery Type: CSII(%): NA MDI(%): NA Device: SMBG Fingerstick use: Glycemic Targets: NR Therapy Duration: 26 weeks Description: Participants were instructed to perform SBGM 4+ times/day **Cointerventions:** None		A vs B Mean Baseline BMI (kg/m2): 22.4 vs. 22.0 Baseline HbA1c (%): NR Mean duration of DM, yrs (SD): NR		• Problem Areas in Diabetes scale (PAID) • Physical Component Summary Scale (SF-12 PCS) and Mental Component Summary Scale (SF-12 MCS) of the SF-12 Quality of Life scale. <u>Participants ≤18 years</u> • HFS worry subscale, by patient and parents • Pediatrics Quality of Life scale (PedsQL) Generic and Diabetes-specific subcales • PAID-Parent survey (parents only) <u>Parents of participants <18 years:</u> • PAID-Parent (PAID-P) survey • • PedsQL Parent-Proxy version	CGM and sensors purchased at discounted prices from DexCom, Medtronic Minimed and Abbott Diabetes Care. Home glucose meters and test strips provided by LifeScan and Abbott Diabetes Care COI: One or more authors have received consulting fees, speaker honorarium, and/or research funding from DexCom, Medtronic Minimed, LifeScan and/or Abbott Diabetes Care. The companies had no involvement in the design, conduct,

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
							or analysis of the trial or the manuscript preparation.
New 2015 (GLADIS) UK and Germany (multicenter) RCT Feb 2011—May 2012	N=128	**CGM without alarms (n=45)** CGM device: FreeStyle Navigator Protocol: CGM device worn for duration of study with low, high, and projected alarms inactivated **CGM with alarms (n=44)** CGM device: FreeStyle Navigator Protocol: CGM device worn for duration of study with low, high, and projected alarms activated **SMBG (n=39)** CGM device: FreeStyle Navigator Protocol: Masked use of CGM device for two 20 day periods (0.7-1.3 mos, 2-2.7 mos) **Cointervention(s)** None	**Inclusion criteria:** T1DM or T2DM, using MDI or CSII for > 6 months, 18-65 years old, HbA1c % of 7%—11%, SMBG performed 2—7 times/day **Exclusion criteria:** Concomitant disease or a condition influencing metabolic control, participating in another glucose monitoring device study, using drugs that could affect glucose management, CGM use in last 6 months, pregnancy or planned pregnancy during duration of study	**Total study population** Age, median (range): 47 (18-65) Female: 46% Type 1 diabetes: 87% Type 2 diabetes: 13% BMI, mean (SD): 27.2 (5.5) HbA1c %, mean (SD): 8.2 (1.1) % CSII: 31% MDI: 69%	F/U (% CGM w/alarms, % CGM w/o alarms, % SMBG): 1.3 mos (94%, 98%, 88%), 2.7 mos (92%, 94%, 81%)	• HbA1c % • Reduction of HbA1c % ≥0.5% • Hours/day spent in hypoglycemia • DDS • SF-8 mental component score • SF-8 physical component score	Abbott Diabetes Care Conflict of interest: 3 authors have received research funding and consulting fees from Abbott Diabetes Care, 1 author works in the industry of devices for diabetes therapy
Peyrot 2009 Location: United States Study period: NR RCT	28 randomized, 28 analyzed	**CSII+rtCGM (n=14)** Delivery Type: CSII: 100% MDI: NA Device: MM Paradigm 722 System	**Inclusion Criteria:** CSII-naïve adults with T1DM with suboptimal glucose control	**N=28** Mean Age (SD): 47.2(13.2) yrs Female: 54% Race: 79% white	F/U (% Total):16 weeks (100%) **Crossover:** None	• HbA1c (%) • Severe hypoglycemia (not further specified)	Sponsor: This study was funded by an unrestricted grant from

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
		Glycemic Targets: NR Training: Yes Therapy Duration: 16 weeks Description: Patients were exposed to an integrated CSII pump system with rtCGM and glucose data management software. Alarms: NR **MDI+SMBG (n=14)** Delivery Type: CSII: NA MDI: 100% Device: SMBG Glycemic Targets: NR Therapy Duration: 16 weeks Description: Patients received MDI+SMBG therapy alongside a glucose data management software Alarms: NA **Cointerventions:** None	**Exclusion Criteria:** Use of insulin pump ever, optimal glucose control (not specified)	Mean Baseline Weight(kg): 80.15(17.34) Mean Baseline BMI (kg/m2): 27.0(4.2) Mean Baseline HbA1c (%): NR Mean duration of DM (SD): 25.0(12.6) yrs			Medtronic MiniMed Corp. to the authors. Study sponsor supplied meters and supplies. COI: One or more authors served on advisory committees for, and/or received consulting fees, and/or research grant support from Novo Nordisk, Animas Corporation, Amylin, MannKind, Medtronic MiniMed, Rapid Trials, LifeScan, Eli Lilly, Medingo, and/or Sanofi-Aventis.
Rubin 2012 (Follow-up to the STAR 3 trial (Bergenstal 2010) Location: Europe Study period:	481 total rand (<18 and >18), 334 >18 analyzed	**SAPT (n=166)** Pump Type: CSII(%): NR MDI(%): NR Device: MM Paradigm REAL-time System Glycemic Targets: NR	**Inclusion Criteria:** Subjects with T1DM aged 7-70 on MDI therapy with a long-acting insulin analog for the previous 3 months, had HbA1C	Mean Age, yrs(SD): 41.3±12.3 Female: 43% Non-hispanic white: 92% Mean Baseline Weight(kg): NR Mean Baseline BMI	F/U (% Total): 52 wks (NR%) **Crossover:** None	• Δ in HbA1C (%) • Severe Hypoglycemia Frequency • Hypoglycemia Fear Scale-II (HFS-II) –	Sponsor: Medtronic MiniMed provided financial support for this

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
RCT		Therapy Duration: 52 wks Training: Yes Description: Subjects received 2 weeks of pump therapy followed by glucose sensor use for 52 wks **MDI (n=168)** Pump Type: CSII(%): NR MDI(%): NR Device: SMBG Glycemic Targets: Therapy Duration: 52 wks Description: Subjects received insulin glargine, and insulin aspart under clinical guidance, supplied with insulin pens and received usual care throughout the 12 month period outside of the 3 month, 6 month, and 12 month follow-up visits. **Cointerventions:** None	7.4-9.5% (inclusive), history of testing blood glucose avg. ≥4 times/day in previous 30 days. **Exclusion Criteria:** Use of insulin pump within previous 3 years, had at least 2 severe hypoglycemic events in the year before enrollment, had used a diabetes drug other than insulin during prior 3 months, were pregnant or intending to become pregnant.	(kg/m2): 27.9±5.0 Baseline HbA1c (%): 8.3±0.5 Mean duration of DM, yrs (SD): 20.2±12.0		Worry and Behavior subscales <u>Participants ≥18 only:</u> • SF-36v2 – Physical Component Summary score (PCS) and Mental Component Summary score (MCS) <u>Participants <18 and their Parents only:</u> • PedQL	project and provided access to the data. COI: One or more of the authors received research funds and consulting fees from Medtronic MiniMed, Animas and/or Medingo.
Cross-Over Trials							
GOLD trial **Lind 2017** Sweden (multicenter) Crossover trial	N = 161 adults	**CGM arm:** CGM for 26 weeks **SMBG arm:** SMBG at least 4x per day for 26 weeks During 17-week	**Inclusion criteria:** Type 1 diabetes; age 18 yrs or older; HbA1c of at least 7.5%; treated with multiple daily injections; fasting C-peptide level less than 0.91 ng/mL;	**CGM first:** Age, mean (SD): 46.7 (13.0) years Female: 46.5% White race: 100% Hispanic ethnicity: 0% BMI, mean (SD): 27.0 (4.1) kg/m^2	88.0% (142/161) Attrition • Before 1st period: 18/161 dropped out (8	• Difference in HbA1c between CGM and conventional therapy at 26 weeks and 69 weeks • Rate of severe hypoglycemia • Time spent in hypoglycemic range	Sponsored by the NU Hospital Group, Trollhättan and Uddevalla, Sweden The NU Hospital Group

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
Feb 2014 – Jun 2016		washout period, patients used conventional therapy and masked CGM was performed for 2weeks	diabetes duration greater than 1 yr **Exclusion criteria:** Use of insulin-pumps	Interval since diabetes diagnosis, mean (SD): 23.4 (11.9) years HbA1c %, mean (SD): 8.49 (0.9) Smoking: 10.1% current, 24.6% previous, 65.2% never **SMBG (Conventional therapy) first:** Age, mean (SD): 42.6 (12.2) years Female: 41.1% White race: 98.6% Hispanic ethnicity: 0% BMI, mean (SD): 27.2 (4.8) kg/m^2 Interval since diabetes diagnosis, mean (SD): 21.0 (11.7) years HbA1c %, mean (SD): 8.45 (0.9) Smoking: 13.7% current, 20.5% previous, 65.8% never	withdrew consent, 1 safety concern, 1 death due to prostate cancer, 8 for other reasons) • During 1st period:,2/ 143 dropped out (1 study noncompliance, 1 lost to follow-up) Analysis only included patients with 1 follow-up measurement in each period	• QOL as measured by DTSQ, WHO-5, Hypoglycemic Fear Behavior Scale, Hypoglycemic Fear Worry Scale, and PAID Adherence • CGM usage % mean, (range): 87.8%, (86.5% to 91.9%) Other • Mean amplitude glycemic excursions • Standard deviation of glucose levels • Amount of time in hyperglycemia and euglycemia • Number of self-measurements of blood glucose	received financial support for the current trial and CGM systems and sensors from Dexcom Inc. COI: One or more authors have received funding, grants, honoraria, and consulting fees from various industries. Additional conflicts of interest were reported.*
IN CONTROL van Beers 2016 Netherlands (two-center) Crossover trial Mar 2013 – Feb 2015	N = 52 adults	**CGM arm:** CGM for 16 weeks **SMBG arm:** SMBG + blind CGM for 16 weeks During 12-week washout period, patients only received telephone consultations every 2 weeks for taking recent	**Inclusion criteria:** Type 1 diabetes; age 18-75 yrs; Gold score of at least 4; treated with CSII or MDI; doing at least 3 SMBG measurements per day	Age, mean (SD): 48.6 (11.6) years Female: 46% BMI, mean (SD): 25.0 (3.8) HbA1c %, mean (SD): 7.5 (0.8) Diabetes duration, mean (range): 30.5 (18-5-40.8) years	88% (46/52) Attrition • During 1st period: 5/52 dropped out (5 discontinued treatment	• Difference in HbA1c from baseline 16 weeks • Episodes of severe hypoglycemia • % of type in hypoglycemia state • QOL as measured by PAID-5, HFS, CIDS, EQ5D, and WHO-5	Supported by funding from Eli Lilly and Sanofi Devices provided by Medtronic COI: One or more authors

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
		medical history and monitoring adverse events	**Exclusion criteria:** History of renal, liver, or heart disease; untreated proliferative diabetic retinopathy; malignancy; use of nonselective β blockers; psychiatric disorder; substance abuse or alcohol abuse; pregnancy; current use of CGM; hearing or vision impairments that could hinder perception of glucose display and alarms; poor command of Dutch language; any disorder that precluded full understanding of purpose and instructions of the study; participation in another clinical study; known or suspected allergy to trial-related products		and withdrew consent) • During 2nd period: 1/47 stopped (1 discontinued treatment and withdrew consent) Intent-to-treat analysis	Adherence • CGM usage % (mean, range): 89.4%, (8% to 95%) Other • Mean difference in % of time spent in normoglycemia between CGM and SMBG • Time spend in hyperglycemic state • Duration of hypoglycemic episodes • Within-day and between-day glucose variability • Satisfaction with use of CGM	have received funding, grants, honoraria, and consulting fees from various industries.
Langeland 2012 Norway Crossover trial	N = 30 adults	**CGM arm:** CGM + intermittent SMBG for 4 weeks **SMBG arm:** at least 4x per day for 4 weeks	**Inclusion criteria:** Type 1 diabetes; age 18-50 years; duration of diabetes more than 3 years; treated with insulin	**CGM first:** Age, mean ± SD: 34. ± 9 years Female: 73% Duration of diabetes, mean ± SD: 18 ± 7 years	90% Attrition • 3/30 dropped out	• Change in HbA1c during each treatment period and over observation period	Supported by The Norwegian University of Science and Technology,

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
Jan 2009 – March 2009		During 8-week washout period, patients monitored as individually preferred (additional detail not provided)	pumps or MDI; HbA1c levels ≥7% and ≤10%; at least one of following: hypoglycemic episodes at least once a week or history of at least one episode with serious hypoglycemia **Exclusion criteria:** untreated hypothyroidism; adrenal gland failure; celiac disease; serious psychiatric disorder; mental retardation	BMI, mean ± SD: 27.3 ± 4.6 kg/m^2 HbA1c %, mean ± SD: 8.1 ± 1.0 **SMBG first:** Age, mean ± SD: 34. ± 9 years Female: 47% Duration of diabetes, mean ± SD: 19 ± 9 years BMI, mean ± SD: 27.3 ± 5.0 kg/m^2 HbA1c %, mean ± SD: 7.6 ± 0.9	• Timing and reasons not specified	• Episodes of severe hypoglycemia Adherence • CGM usage (mean): 19 sensor days (defined as ≥12 hours per day) Other • Treatment satisfaction • Sensor use •	The Norwegian Diabetes Foundation and St. Olav's Hospital, Trondheim University Hospital COI: None
Tumminia 2015 Italy Crossover trial Jan 2012 – Mar 2012	N = 20 adults (10 treated w/ MDI, 10 treated w/ CSII)	**CGM arm:** CGM 2-3 weeks per month for 6 months **SMBG arm:** SMBG at least 4x per day for 6 months No washout period	**Inclusion criteria:** Type 1 diabetes; age 18-60 yrs; diabetes duration greater than 1 yr; HbA1c levels greater than 8.0% **Exclusion criteria:** pregnant women; women planning pregnancy; concomitant chronic illness; poor compliance to diet, insulin therapy, or glucose monitoring	**MDI†:** Age, mean ± SD: 36.6 ± 14.4 years Years of diabetes, mean ± SD: 19.4 ± 11.0 BMI, mean ± SD: 22.9 ± 3.1 kg/m^2 HbA1c %, mean ± SD: 8.7 ± 0.6 **CSII†:** Age, mean ± SD: 31.3 ± 7.9 years Years of diabetes, mean ± SD: 15.1 ± 7.8 BMI, mean ± SD: 25.0 ± 3.6 kg/m^2	NR Attrition None	• Difference in HbA1c from baseline to end of treatment period • Episodes of severe hypoglycemia • Episodes of DKA Adherence • CGM usage % (mean, range): 84%, 13% to 80% Other • Risk of hyperglycemia and hypoglycemia (measured by AUC)	Insulin pumps, CGM systems, and diabetes management software provided by Medtronic (Tolochenaz, Switzerland). COI: None

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
				HbA1c %, mean ± SD: 8.6 ± 1.0		• Effectiveness of CGM • Glucose fluctuations • BMI	

CGM: Continuous Glucose Monitoring; DDS, Diabetes Distress Scale; DKA: Diabetes Ketoacidosis; DTSQ: Diabetes Treatment Satisfaction Questionnaire; F/U: follow-up; HbA1C: hemoglobin A1C; mmol/l, millimole per liter; SD: standard deviation; SMBG: self-monitoring of blood glucose; ICFM: intensified conventional finger-prick method; SAP: sensor augmented pump; SF-8, Short Form-8; WHO-5: World Health Organization-5 Well Being Index; PAID: Problem Areas in Diabetes Questionnaire; PedsQL: Pediatric Quality of Life Inventory; DTSQs: Diabetes Treatment Satisfaction Questionnaire status version.

*Includes data for a pediatric population—abstraction can be found in corresponding pediatric sections
†Authors only reported baseline demographics based on method of insulin administration

Appendix Table F4. Study Characteristics, Patient Demographics and Results from Observational Studies of Adults with Type 1 DM

Study	N	Demographics	Inclusion/exclusion criteria	Study purpose	Results	Conclusions	Funding
JDRF 2010 *(Follow-up extension of JDRF 2008)* Prospective cohort	51	Age: ≥25 years HbA1c %: 7.8% Using CGM in month 6: 0 days/week, n=4 >0 to < 4 days/week, n=4 4 to < 6 days/week, n=6 ≥ 6 days/week, n=3w7	**Inclusion criteria:** Randomized to SMBG in JDRF RCT, cross-over to CGM in extension study	To determine whether CGM is effective when used in a typical clinical care environment	**Mean change from baseline to 6 months, by use of CGM:** • 0 days/ week: +0.1 • > 0 to < 4 days/week: -0.4 • 4 to <6 days/week: -0.5 • ≥ 6 days/week: -0.4 **Rate of severe hypoglycemia:** • 6 months using SMBG during trial: 33.7/100 person years • 6 months using CGM after trial: 23.0/100 person-years **N events of severe hypoglycemia** 6 months using SMBG during trial: 13	Greater CGM use was associated with a great A1c decrease (*P* = .01 adjusted for age-group) The incidence of severe hypoglycemia trended lower in all age groups. There were no significant differences in adjusted glycemic indices between baseline and month 6.	Juvenile Diabetes Research Foundation, Inc COI: One or more authors have received funding, grants, honoraria, and consulting fees from various industries. Additional conflicts of interest were reported. See study for full conflict of interest

Study	N	Demographics	Inclusion/exclusion criteria	Study purpose	Results	Conclusions	Funding
					6 months using CGM after trial: 9		
JDRF 2009b *(Sub-analysis of JDRF 2008)* *Prospective cohort*	86	Age: ≥25 years Female: 56% Duration of diabetes: < 5 years: 3% 5 to <10 years: 9% 10 to <20 years: 26% ≥20 years: 62%	**Inclusion criteria:** Age ≥ 8 years, T1DM for ≥ 1 year, use of either an insulin pump or ≥ 3 daily insulin injections, HbA1c level < 10.0%	To investigate factors associated with successful use of CGM among subjects with intensively treated DM	**Change in A1c* (%) based on average CGM use in month 6** • < 4 days/week (n = 1): +0.10 • 4–6 days/week (n = 6): -0.38 • ≥ 6 days/week (n = 43): -0.54 †	Near daily CGM use is associated with a similar reduction in A1c regardless of age. Frequency of blood glucose meter monitoring and initial CGM use may help predict the likelihood of long-term CGM benefit in all ages	Juvenile Diabetes Research Foundation, Inc COI: One or more authors have received funding, grants, honoraria, and consulting fees from various industries. Additional conflicts of interest were reported. See study for full conflict of interest
JDRF 2009c	83	Age: ≥25 years Female: NR Body weight, mean (SD): 77 (15) kg HbA1c %: 7.1 (0.8) **Baseline A1c >7.0% (n=49)** Body weight, mean (SD): 79 (16) kg HbA1c %, mean (SD): 7.6 (0.5) % **Baseline A1c <7.0% (n=34)** Body weight, mean (SD): 75 (13) kg HbA1c %, mean (SD): 6.4 (0.5) %	**Inclusion criteria:** Age ≥ 25 years, T1DM for ≥ 1 year, use of either an insulin pump or ≥ 3 daily insulin injections, HbA1c level < 10.0%	To evaluate long-term effects of continuous glucose monitoring (CGM) in intensively treated adults with type 1 diabetes	**HbA1c %, mean (SD):** *6 months* • Total population: 6.8 (0.6) • Baseline A1c ≥7.0%: 7.1 (0.5) • Baseline A1c <7.0%: 6.3 (0.5) *12 months* • Total population: 6.9 (0.7) • Baseline A1c ≥7.0%: 7.2 (0.5) • Baseline A1c <7.0%: 6.4 (0.6) **Hypoglycemia ≤70 mg/dL, minutes/day** *6 months* • Total population: 55	The benefits of CGM can be sustained for at least 12 months in motivated adults with type 1 diabetes practicing intensive diabetes management. In such individuals, CGM provides the ability to achieve target A1C levels much more safely than previously reported.	Juvenile Diabetes Research Foundation, Inc COI: One or more authors have received funding, grants, honoraria, and consulting fees from various industries. Additional conflicts of interest were reported. See study for full conflict of interest.

Study	N	Demographics	Inclusion/exclusion criteria	Study purpose	Results	Conclusions	Funding
					• Baseline A1c ≥7.0%: 53 • Baseline A1c <7.0%: 65 *12 months* • Total population: 58 • Baseline A1c ≥7.0%: 49 • Baseline A1c <7.0%: 72 **Hypoglycemia ≤60 mg/dL, minutes/day** *6 months* • Total population: 16 • Baseline A1c ≥7.0%: 16 • Baseline A1c <7.0%: 13 *12 months* • Total population: 19 • Baseline A1c ≥7.0%: 14 • Baseline A1c <7.0%: 25 **Hypoglycemia ≤50 mg/dL, minutes/day** *6 months* • Total population: 4 • Baseline A1c ≥7.0%: 3 • Baseline A1c <7.0%: 6 *12 months* • Total population: 5 • Baseline A1c ≥7.0%: 4 • Baseline A1c <7.0%: 5 **AUC <70 mg/dL** *6 months* • Total population: 0.3 • Baseline A1c ≥7.0%: 0.3 • Baseline A1c <7.0%: 0.3 *12 months*		

Study	N	Demographics	Inclusion/exclusion criteria	Study purpose	Results	Conclusions	Funding
					• Total population: 0.3 • Baseline A1c ≥7.0%: 0.3 • Baseline A1c <7.0%: 0.4 **Hypoglycemic events, n/N (%) (n events):** *Baseline to 6 months* • Total population: 8/83 (8%) (9 events) *6 to 12 months* • Total population: 3/83 (4%) (3 events) **Rate of severe hypoglycemic events** *6 months* • Total population: 21.8 events per 100 person-years • Baseline A1c ≥7.0%: 20.5 events per 100 person-years • Baseline A1c <7.0%: 23.6 events per 100 person-years *12 months* • Total population: 7.1 events per 100 person-years • Baseline A1c ≥7.0%: 12.1 events per 100 person-years • Baseline A1c <7.0%: 0 events per 100 person-years		

Study	N	Demographics	Inclusion/exclusion criteria	Study purpose	Results	Conclusions	Funding
					Hyperglycemia >180 mg/dL, minutes/day *6 months* • Total population: 321 • Baseline A1c ≥7.0%: 378 • Baseline A1c <7.0%: 231 *12 months* • Total population: 293 • Baseline A1c ≥7.0%: 422 • Baseline A1c <7.0%: 211 **Hypoglycemia >200 mg/dL, minutes/day** *6 months* • Total population: 202 • Baseline A1c ≥7.0%: 252 • Baseline A1c <7.0%: 137 *12 months* • Total population: 188 • Baseline A1c ≥7.0%: 289 • Baseline A1c <7.0%: 116 **Hypoglycemia >250 mg/dL, minutes/day** *6 months* • Total population: 48 • Baseline A1c ≥7.0%: 61 • Baseline A1c <7.0%: 33 *12 months* • Total population: 49 • Baseline A1c ≥7.0%: 78 • Baseline A1c <7.0%: 19 **AUC >180 mg/dL**		

Study	N	Demographics	Inclusion/exclusion criteria	Study purpose	Results	Conclusions	Funding
					6 months • Total population: 8.6 • Baseline A1c ≥7.0%: 11.0 • Baseline A1c <7.0%: 5.5 *12 months* • Total population: 8.1 • Baseline A1c ≥7.0%: 12.5 • Baseline A1c <7.0%: 4.8 **Glucose level 71-180 mg/dL, minutes/day** *6 months* • Total population: 1,026 • Baseline A1c ≥7.0%: 962 • Baseline A1c <7.0%: 1,139 *12 months* • Total population: 1,066 • Baseline A1c ≥7.0%: 966 • Baseline A1c <7.0%: 1,135 **CGM use, median (IQR)** *6 months* • Total population: 7.0 days/week (6.3-7.0) *12 months* Total population: 6.8 days/week (5.8-7.0)		
Wong 2014 Retrospective registry	7435	**18 to <26 years old, CGM (n=157) vs non-CGM (n=2612)** Female: 59% vs 50% Duration of diabetes, median (IQR): 11 (7 to 14) vs 9.5 (6 to 14) Percent using CSII: 16% vs 54%	**Inclusion criteria:** Patients with T1DM **Exclusion criteria:** NR	To assess the frequency of CGM device use, factors associated with its use, and the relationship of CGM with the diabetic outcomes of HbA1c, severe	**Mean % HbA1c** • 18 to <26 years old, CGM vs non-CGM: 8.4% vs 8.5% • ≥26 years, CGM vs non-CGM: 7.7% vs 7.9% *CGM use <4 days/wk‡:* • 18 to <26 years: 8.6% • ≥26 years: 7.3% *CGM use 4 to <6 days/wk‡:*	CGM use is uncommon but associated with lower HbA1c in children and adults, though not in 13 to < 26 year olds, especially when used more frequently. Future efforts should be made	Leona M and Harry B. Helmsley Charitable Trust and National Institutes of Health Grant funding (K12-DK094726; K12 in Diabetes [KIDS])

Study	N	Demographics	Inclusion/exclusion criteria	Study purpose	Results	Conclusions	Funding
		Percent using MDI: 84% vs 46% **≥26 years old, CGM (n=999) vs non-CGM (n=3667)** Female: 57% vs 55% Duration of diabetes, median (IQR): 25 (16 to 35) vs 24 (15 to 34) Percent using CSII: 84% vs 57% Percent using MDI: 16% vs 43%		hypoglycemia, and diabetic ketoacidosis	• 18 to <26 years: 8.5% • ≥26 years: 7.3% *CGM use ≥6 days/wk*‡: • 18 to <26 years: 8.6% • ≥26 years: 7.0% **≥1 SH event in previous 3 months** *CGM use <4 days/wk:* • 18 to <26 years: 1.9% • ≥26 years: 9.1% *CGM use 4 to <6 days/wk*: • 18 to <26 years: 5.9% • ≥26 years: 10.1% *CGM use ≥6 days/wk:* • 18 to <26 years: 9.8% • ≥26 years: 12.2% **≥1 DKA event in previous 3 months** *CGM use <4 days/wk:* • 18 to <26 years: 3.9% • ≥26 years: 1.8% *CGM use 4 to <6 days/wk*: • 18 to <26 years: 0% • ≥26 years: 1.9% *CGM use ≥6 days/wk:* • 18 to <26 years: 3.9% • ≥26 years: 1.9%	at improving CGM technology and features to address common obstacles. Special attention should be paid to patients with lower socioeconomic status and lack of private insurance.	Conflict of interest: 1 or more author has received research grants or payments from industry. 1 or more author has consulted or served on scientific advisory board for industry. See article for full conflict of interest

CGM, continuous glucose monitoring; COI, conflict of interest; CSII, continuous subcutaneous insulin infusion; DKA, diabetic ketoacidosis; Hba1c, hemoglobin A1C; MDI, multiple daily injections; SAP, sensor-assisted pump; SMBG, self-monitoring of blood glucose; T1DM, type 1 diabetes mellitus; RCT, randomized controlled trial; wk, week;

* Mean values were estimated from figure 1 in article.

† Adjusted for baseline A1c

‡ <13 years, 13 to <18 years, and 18 to <26 year values were estimated from graph

Appendix Table F5. Study Characteristics and Patient Demographics of RCTs Evaluating CGM versus SMBG in Mixed Adults and Children with Type 1 DM

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
Battelino 2011 Location: NR Study period: Oct. 2008-Feb 2010 RCT	120 randomized, 116 analyzed	**RT-CGM (n=62)** Delivery type: CSII: 76% MDI: 24% Device: Abbott FreeStyle Navigator Glycemic Targets: preprandial(70-130 mg/dL), 2 hrs postprandial (180 mg/dL) Therapy Duration: 6 months Description: Patients used RT-CGM 5 days continuously for 26 weeks Alarms: set by patients **SMBG+sham CGM (n=54)** Delivery type: CSII: 59% MDI: 41% Device: NR Glycemic Targets: preprandial(70-130 mg/dL), 2-hr postprandial (180 mg/dL) Therapy Duration: 6 months Description: Patients did home monitoring and performed masked CGM for 5 continuous days every second weeks Alarms: NA	**Inclusion Criteria:** Aged 10—65 T1DM for more than 1 year with reasonable metabolic control assessing carbohydrate intake and self-adjusting insulin, HbA1c < 7.5%, using an intensive insulin treatment using an insulin pump or MDIs, not using RT-CGM device for at last 4 weeks **Exclusion Criteria:** HbA1c >7.5%, not current pump or MDI user, CGM use within 4 wks, age <10 years or >65 years, T1DM diagnosis <1 year, lack of reasonable metabolic control	Mean age (SD): 25.9 (14.2) years Female: 38% Mean BMI (SD): 22.2 (3.8) kg/m^2 Mean % HbA1c: 6.92% Mean duration of diabetes (SD): 11.4 years Patients with severe hypoglycemia in the past year: 10% Mean daily insulin dose (SD): 0.67 (0.28) units/kg	F/U (% CGM, % control): 6 mos. (85%, 83%)	• Mild hypoglycemia (number of hypoglycemia excursions per day <63 mg/dL) • Moderate hypoglycemia (number of hypoglycemic excursions per day <55 mg/dL) HbA1c (%)	Abbott Diabetes Care and grants from the Slovenian National Research Agency Grants (J3-9663, J3-2412, P3-0343) COI: One or more authors have received grants and/or funds for travel and accommodations from various industries. One or more authors serve on advisory boards, serve as consultants, or a part of the speaker's bureau on various industries.

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
		Cointerventions: None					
Deiss 2006* Location: Europe Study period: NR *RCT*	162 randomized 156 treated	**rtCGM1 (n=50)**† Delivery Type: CSII: 48.1% MDI: 51.9% Device: MM guardian Glycemic Targets: NR Therapy Duration: 3 months Description: Participants were instructed to use CGM continuously Alarms: Hyperglycemia: 170-250 mg/dL Hypoglycemia: 50-80 mg/dL **rtCGM2 (n=52)**† Delivery Type: CSII: 48.1% MDI: 51.9% Device: MM guardian Glycemic Targets: NR Therapy Duration: 3 months Description: Participants were instructed to use CGM biweekly for 3 day periods every 2 wks Alarms: Hyperglycemia: 170-250 mg/dL Hypoglycemia: 50-80 mg/dL **SMBG (n=54)** Delivery Type: CSII: 48.1%	**Inclusion Criteria:** T1DM, very young, adults **Exclusion Criteria:** HbA1c > 8.1%	Mean age (SD): NR % ≥18 years: 50.0% % ≤18 years: 50.0% Female: NR Race: NR Mean weight: NR Mean Baseline BMI (kg/m2): NR Baseline HbA1c (%): 9.6(0.75) Mean duration of DM (SD): NR	F/U (% total): 3 mos. (96.3%)	• HbA1c (%) • Hypoglycemia Frequency • Severe hypoglycemia (not further specified)	Sponsor: This study was sponsored by Medtronic Europe COI: One or more others have received travel expenses, honoraria, travel grants, consulting fees and/or have served on advisory boards for Medtronic, Roche, LifeScan, Abbott, and D-Medical

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
		MDI: 51.9% Device: SMBG Glycemic Targets: NR Therapy Duration: 3 months Description: Participants were instructed to continue SMBG 5+ times/day Alarms: NA **Cointerventions:**					
JDRF Trial 2008 United States (multicenter) Study Period: Feb 2007—Dec 2007 *RCT*	N=110 (age 15-24)	**CGM (n=57)** Instructed to use device on a daily basis and to verify accuracy with a home blood glucose meter. The device used was the Dex Com SEVEN (DexCom, San Diego, CA), the MiniMed Paradigm REAL-Time Insulin Pump and Continuous Glucose Monitoring System (Medtronic MiniMed, Northridge, CA), or the FreeStyle Navigator (Abbott Diabetes Care, Alameda, CA). **Control (n=53)** Home monitoring with a blood glucose meter only. Patients were instructed to perform SMBG ≥ 4x daily**.**	**Inclusion criteria:** 3x/daily glucose monitoring, aged > 8 years, HbA1c < 10.0%, not pregnant or planning pregnancy, naïve to sensor use **Exclusion criteria:** NR	**Mixed Population (age 15-24)** Mean Age (SD): 18.5 Female: 61% BMI z score: <-0.5: 0.1% -0.5 to 0.5: 32.7% >0.5: 57.2% Mean duration of diabetes (SD): 9.15 years Insulin administration: Pump: 68.9% MDI: 31.1% HbA1c %: 7.0—8.0: 63.6% 8.1—8.9: 26.3% ≥9.0: 10% ≥1 episodes of severe hypoglycemia in previous 8 months: 8.1% Mean daily home glucose-meter readings (SD): 5.9 (2.4)	**Total study population** FU (% CGM, % control): 1 week, 4 wks, 8 wks, 13 wks, 19 wks (98%, 98%), 26 wks (100%, 100%)	• Change in HbA1c levels • Hypoglycemia (time per day, < 70 mg/dl, < 50 mg/dl) • Hyperglycemia resulting in DKA (time per day, > 180 mg/dl, > 250 mg/dl) • Unexpected study-related or device-related events • Serious adverse events regardless of causality	Funding provided by the JDRF (grants 22-20006-1107, 22-2006-1117, 22-2006-1112, 22-2006-1123, 01-2006-8031) Conflict of interest: One or more authors have received funding, grants, honoraria, and consulting fees from various industries. Additional conflicts of interest were reported. See study for full

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
		Cointerventions: All patients received information on the insulin regimen including the determination of pre-meal bolus dose and guidelines for correcting high glucose levels					conflict of interest
JDRF 2009a Location: United States, multicenter Study period: Feb 2007 to Dec 2007 *RCT*	129 randomized, 126 analyzed	**CGM (n=67)** Instructed to use device on a daily basis and to verify accuracy with a home blood glucose meter. The device used was the Dex Com SEVEN (DexCom, San Diego, CA), the MiniMed Paradigm REAL-Time Insulin Pump and Continuous Glucose Monitoring System (Medtronic MiniMed, Northridge, CA), or the FreeStyle Navigator (Abbott Diabetes Care, Alameda, CA). **Control (n=62)** Home monitoring with a blood glucose meter only. Patients were instructed to perform SMBG ≥ 4x daily**.**	**Inclusion criteria:** Age ≥ 8 years, Type-1 diabetes for at least 1 Year, Use of either an insulin pump or at least three daily insulin injections, baseline A1C level < 7.0%, successful completion of a run-in phase of "blinded" CGM use **Exclusion criteria:** NR	**All Ages** Mean Age (SD): 30.6 years Female: 52.7% Race: NR Mean Baseline Weight(kg): NR Mean Baseline BMI (kg/m2): NR Baseline HbA1c (%): 11.2(2.1) Mean duration of DM (SD): NR Diabetic Ketoacidosis, n (%): 71 (46.1	F/U % (%CGM, %Control) 26 weeks (99%, 98%) Crossover occurred in 2 patients in the control group before end of study period	• Change in HbA1c levels • Severe hypoglycemia, • Hyperglycemia resulting in DKA • Unexpected study-related or device-related events • Serious adverse events regardless of causality	Sponsor: Funding provided by the JDRF (grants 22-20006-1107, 22-2006-1117, 22-2006-1112, 22-2006-1123, 01-2006-8031) Home glucose meters and test strips were provided by LifeScan and Abbott Diabetes Care COI: One or more authors have received consulting fees, speaker honorarium, and/or research funding from DexCom, Medtronic

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
							Minimed, LifeScan and/or Abbott Diabetes Care. The companies had no involvement in the design, conduct, or analysis of the trial or the manuscript. Additional conflicts of interest were reported. See study for full conflict of interest
O'Connell 2009 Location: Australia Study period: RCT	62 randomized, 55 analyzed	**rtCGM (n=26)** Delivery Type: CSII: 100% MDI: NA Device: MM Paradigm, Glycemic Targets: NR Training: NA Therapy Duration: 3 months Description: Patients were instructed monitor use > 70% of 3-month study period Alarms: Hyperglycemia: 12 mmol/dL Hypoglycemia: 4.5 mmol/L **SMBG (n=29)**	**Inclusion Criteria:** Participants with well-controlled T1DM, aged 13-40, with bolus-dose calculator proficiency, HbA1c ≤8.5% . **Exclusion Criteria:** HbA1c > 8.5%, use of insulin pump within < 3 mo, diabetes for < 1 yr, patients without internet access, excluded patients that cannot reliably perform SMBG at	**N=62** Mean Age (SD): 23.2(8.35) years Female: 71% Race: NR Mean Baseline Weight(kg): NR Mean Baseline BMI (kg/m2): NR Baseline HbA1c (%): 7.4(0.65) Mean duration of DM (SD): 10.15(7.4) years	F/U (% Total): 3 months (83.8% 93.5%) **Crossover:** None	• HbA1c (%) • Severe hypoglycemia (episode of hypoglycemia resulting in seizure or coma or requiring assistance or the use of glucagon or IV glucose for recovery)	Sponsor: Funding support and equipment were provided by Medtronic Australasia. COI: One or more authors have received travel, educational and/or research support, and/or honoraria from Medtronic

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
		Delivery Type: CSII: 100% MDI: NA Device: SMBG, monitor use NA, Fingerstick 4+/day Glycemic Targets: NR Training: NA Therapy Duration: 3 months Description: Patients were instructed to continue their original insulin pump regimen Alarms: NA **Cointerventions:** None	least 4x/day, unwilling to use subcutaneous sensor component of system for < 70% of study period, Patients with coexistent medical issues that would interfere with their ability to use the system, history of severe hypoglycemia or coexisting illness predisposing to hypoglycemia				Australasia, Novo Nordisk, Lilly, Sanofi-Aventis and/or Animas.
Raccah 2009 Location: France Study period: May 2006-May 2008 RCT	132 rand, 115 analyzed	**rtCGM+CSII (n=55)** Delivery Type: CSII: 100% MDI: NA Device: MM Paradigm REAL-Time system Glycemic Targets: 90-120 mg/dL (7am-10pm), 100-120 mg/dL (10pm-7am) Therapy Duration: 6 months Description: Monitor use 70% of the time. All patients continued their usual BGM ≥3times/day. Alarms: NR **CSII+SMBG (n=60)**	**Inclusion Criteria:** T1DM (diagnosed for ≥12 months) patients aged 2-65 years, HbA1c ≥8%, and treatment with basal/bolus MDI with rapid insulin analogs at mealtimes. **Exclusion Criteria:** HbA1c < 8.0%, diagnosis of diabetes < 12 mo prior to randomization, follow-up by the respective investigator for < 3	Mean age (SD): 28.5(15.9) years % ≥18 years: 61.4% % ≤18 years: 38.6% Female: 44.3% Race: NR Mean Baseline Weight(kg): 64.1(18.0) Mean Baseline BMI (kg/m2): 22.98(4.26) Mean Baseline HbA1c (%): 9.2(1.2) Mean duration of DM (SD): 11.77(8.90) uears	F/U (% Total): 6 months (87.1%) **Crossover:** None	• HbA1c (%) • Hyperglycemia • Hypoglycemia frequency (moderate hypoglycemia: <70 mg/dl) • Ratio of basal to bolus insulin (number of daily boluses) • Ratio of basal to bolus insulin (proportion of basal insulin) • Severe hypoglycemia (not further specified)	Sponsor: This study was funded by Medtronic France. The study was designed by investigators and approved by the sponsor. COI: No potential conflicts of interest relevant to this article were reported.

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
		Delivery Type: CSII: 100% MDI: NA Device: Medtronic MiniMed Paradigm 512/712 SMBG, monitor Glycemic Targets: 90-120 mg/dL (7am-10pm), 100-120 mg/dL (10pm-7am) Training: NA Therapy Duration: 6 months Description: All patients continued their usual BGM ≥3times/day. Alarms: NA **Cointerventions:** None	mos., not being treated with basal/bolus MDI with rapid insulin analogs at mealtimes)				
Cross-over Trials							
SWITCH **Battelino 2012** (index publication) Hommel 2014 Switzerland (multi-center) Crossover trial Jan 2008 – Jul 2010 Provides data for both children and adults	N = 153 adults and children	**SAP arm:** SAP for 6 months **SMBG arm:** CGM for 2 weeks prior to each study visit (every 6 weeks) for 6 months During 4-month washout period, there were no study visits (additional detail not provided)	**Inclusion criteria:** age 6 to 70 yrs; Type 1 diabetes duration of more than 1 year; HbA1c level between 7.5% and 9.5%; using CSII for more than 6 months; naïve to CGM; successful completion of 5 question multiple choice test about pump therapy and general understanding of diabetes	**CGM First** Age, mean ± SD: 28 ± 16 years Female: 46% Time since diagnosis, mean ± SD: 16 ± 12 years BMI, mean ± SD: 23 ± 5.0 kg/m^2 HbA1c %, mean ± SD: 8.3 ± 0.7 **SMBG First** Age, mean ± SD: 28 ± 17 years Female: 51% Time since diagnosis, mean ± SD: 14 ± 10 years	90% (138/153) Attrition • 15/153 dropped out (4 had significant protocol violations, 9 had device issues, 2 had personal issues) • Timing not specified	• Change in HbA1c over each treatment period and difference between arms • Episodes of severe hypoglycemia • Episodes of DKA Adherence • CGM usage % (mean): all participants 80%, children 73%, adults 86%	Funded by Medtronic International Trading Sarl, Tolochenaz, Switzerland COI: One or more authors have received funding, grants, honoraria, and consulting fees from various industries. Additional conflicts of

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
			Exclusion criteria: ≥3 incidents of severe hypoglycemia in last 12 months; history of hypoglycemia unawareness; concomitant chronic disease known to affect diabetes control; any pharmacological treatment that might modify glycemic values	BMI, mean ± SD: 24 ± 4.5 kg/m^2 HbA1c %, mean ± SD: 8.5 ± 0.6	• All subjects included in primary analysis, only those who completed entire study included in secondary analyses	• 72% of participants used the sensor ≥70% of the time • 24% of participants used the sensor >90% of the time Other • Insulin treatment patterns • Sensor use • Time spent in euglycemia • Average daily glucose level and AUC for euglycaemic, hypoglycemic, and hyperglycemic ranges • Glycemic variability • Number of finger-stick blood glucose tests performed • QOL as measured by PedsQL and DTSQs (reported by Hommel 2014)	interest were reported.*

BG : blood glucose; BMI: body mass index-standard deviation score; CGM: Continuous Glucose Monitoring; CSII : continuous subcutaneous insulin infusion; dL : deciliter; DM : diabetes mellitus; DKA: Diabetes Ketoacidosis; DTSQ: Diabetes Treatment Satisfaction Questionnaire; F/U: follow-up; HbA1C: hemoglobin A1C; ICFM: intensified conventional finger-prick method; IV : intravenous; kg : kilograms; kg/m2 : kilograms per meter squared; MDI : multiple daily injections; mg : milligram; mg/dL : milligrams per deciliter; MM : Medtronic Minimed; mmol : millimoles; mmol/L : millimole per liter; NA : not applicable; NR : not reported; NS : not significant; PAID: Problem Areas in Diabetes Questionnaire; PedsQL: Pediatric Quality of Life Inventory; PPG : post prandial glucose; RCT : randomized controlled trial; SAP: sensor augmented pump; SD: standard deviation; SMBG: self-monitoring of blood glucose; T1DM : Type 1 Diabetes Mellitus; T2DM : Type 2 Diabetes Mellitus; WHO-5: World Health Organization-5 Well Being Index; wk : week; wks : weeks; x/day : times per day; yrs : years

Appendix Table F6. Study Characteristics, Patient Demographics and Results from Observational Studies Evaluating CGM versus SMBG in Mixed Adults and Children with Type 1 DM

Study	N	Demographics	Inclusion/exclusion criteria	Study purpose	Results	Conclusions	Funding
JDRF 2010 *(Follow-up extension of JDRF 2008)* *Prospective cohort*	56	Age: 15-24 years HbA1c %: 7.6% Using CGM in month 6: 0 days/week, n=11 >0 to < 4 days/week, n=26 4 to < 6 days/week, n=7 ≥ 6 days/week, n=12	**Inclusion criteria:** Randomized to SMBG in JDRF RCT, cross-over to CGM in extension study	To determine whether CGM is effective when used in a typical clinical care environment	**Mean change from baseline to 6 months, by use of CGM:** • 0 days/ week: +0.4 • > 0 to < 4 days/week: 0.0 • 4 to <6 days/week: -0.6 • ≥ 6 days/week: 0.0 **Rate of severe hypoglycemia:** • 6 months using SMBG during trial: 22.3/100 person years • 6 months using CGM after trial: 8.2/100 person-years **N events of severe hypoglycemia** 6 months using SMBG during trial: 8 • 6 months using CGM after trial: 3	Greater CGM use was associated with a great A1c decrease (*P* = .01 adjusted for age-group) The incidence of severe hypoglycemia trended lower in all age groups. There were no significant differences in adjusted glycemic indices between baseline and month 6.	Juvenile Diabetes Research Foundation, Inc COI: One or more authors have received funding, grants, honoraria, and consulting fees from various industries. Additional conflicts of interest were reported. See study for full conflict of interest
JDRF 2009b *(Sub-analysis of JDRF 2008)* *Prospective cohort*	72	Age: 15-24 years Female: 53% Duration of diabetes: < 5 years: 21% 5 to <10 years: 38% 10 to <20 years: 42% ≥20 years: 0%	**Inclusion criteria:** Age ≥ 8 years, T1DM for ≥ 1 year, use of either an insulin pump or ≥ 3 daily insulin injections, HbA1c level < 10.0%	To investigate factors associated with successful use of CGM among subjects with intensively treated DM	**Change in A1c* (%) based on average CGM use in month 6** • < 4 days/week (n = 7): + 0.02	Near daily CGM use is associated with a similar reduction in A1c regardless of age. Frequency of blood glucose meter monitoring and	Juvenile Diabetes Research Foundation, Inc

Study	N	Demographics	Inclusion/exclusion criteria	Study purpose	Results	Conclusions	Funding
					• 4–6 days/week (n = 21): -0.08 • ≥ 6 days/week (n = 28): -0.48	initial CGM use may help predict the likelihood of long-term CGM benefit in all ages	COI: One or more authors have received funding, grants, honoraria, and consulting fees from various industries. Additional conflicts of interest were reported. See study for full conflict of interest

BG : blood glucose; BMI: body mass index-standard deviation score; CSII : continuous subcutaneous insulin infusion; dL : deciliter; DM : diabetes mellitus; HbA1c : hemoglobin A1c; IV : intravenous; kg : kilograms; kg/m2 : kilograms per meter squared; MDI : multiple daily injections; mg : milligram; mg/dL : milligrams per deciliter; MM : Medtronic Minimed; NA : not applicable; NR : not reported; NS : not significant; PPG : post prandial glucose; RCT : randomized controlled trial; rtCGM : real-time continuous glucose monitor; SD : standard deviation; SMBG : self-monitoring of blood glucose; T1DM : Type 1 Diabetes Mellitus; T2DM : Type 2 Diabetes Mellitus; U : units; wk : week; wks : weeks; x/day : times per day; yrs : years
*Mean values were estimated from figure 1 in article.

Appendix Table F7. Study Characteristics and Patient Demographics of RCTs Evaluating CGM versus SMBG in Adults with Type 2 DM

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
Beck 2017b (DIAMOND) United States & Canada (multicenter) RCT Oct 2014 —May 2016	N=158 rand	**CGM (n=79)** CGM Device: Dexcom G4 platinum CGM system SMBG device: Contour Next USB meter (Ascensia Diabetes Care) Protocol: After a 2week blinded CGM phase, participants randomized to use CGM daily for study duration, calibrated ≥2 times/day, CGM values verified using SMBG, values used to modify diabetes management. Follow-up visits were made at 1 month, 3 months, and 6 months **Usual care (n=79)** SMBG device: Bayer Contour Next Protocol: Home blood glucose monitoring ≥4 times/day. Follow-up visits were made at 1 month, 3 months, and 6 months **Cointervention(s):** None	**Inclusion criteria:** age 25 years or older, diagnosis of T2DM, use of MDI of insulin for 12 months or more before study, **Exclusion criteria:** use of personal rtCGM <3 months before study entry, use of premixed insulin <6 months before study entry, current or anticipated short-term use of glucocorticoids, pregnancy or planning to become pregnant, adverse medical conditions, history of psychiatric, psychological or psychosocial illness that could limit adherence to study	Age, mean (SD): 60(10) years Female: 56% Race: 63.3% non-Hispanic White Duration of diabetes CGM group, median (IQR): 17 (11-23) Duration of diabetes control group, median (IQR): 18 (12-23) BMI, mean (SD): 36 (7.5) Weight, mean (SD): 101.5 (24) kg HbA1c%, mean (SD): 8.5% Mean total daily insulin dose(SD), units/kg/d: 1.1 (0.55) ≥1 episode of severe hypoglycemia (in past 12 mos) (SD): 2(3) WHO-5, mean (SD): EQ-5D-5L, mean (SD):	F/U (% CGM, % control): 1 month, (100%, 100%) 3 month, (97%, 95%) 6 month, (100%, 100%)	• Change in HbA1c levels • % patients with HbA1c levels <7.0% • % patients with HbA1c levels <7.5% • Relative reduction HbA1c ≥10% • Reduction in % HbA1c ≥1% • Reduction in % HbA1c ≥1% or HbA1c < 7.0% • Duration of hypoglycemia (<70 mg/dl, <60 mg/dl, <50 mg/dl) • Area above curve 70 mg/dl • Duration of hyperglycemia (>180 mg/dl, >250 mg/dl, >300 mg/dl) • Area under curve 180 mg/dl • WHO-5 • EQ-5D-5L • DDS • HFS-II • HCS	Sponsor: Dexcom, Inc. COI: One or more authors reported grants, personal fees, research support from, and/or employee/share holder status with a wide range of industry corporations. The disclosures are too numerous to report, please see the study for a full accounting.
Ehrhardt 2011 Vigersky 2012 United States	100 rand	**CGM (n=50)** CGM device: Dexcom SEVEN SMBG device: NR Protocol: Subjects completed 4 cycles (1 cycle	**Inclusion criteria:** Military health care beneficiaries ≥ 18 years old, T2DM for ≥ 3 months, initial A1C ≥7% and ≤12%, not	Age, mean (SD): 57.8 (11.0) years Female: 45% BMI, mean (SD): 32.3 (6.8) Weight, mean (SD): 201.9 (41.5) pounds	F/U (% CGM, % SMBG): 3 mos (94%, 94%), 6	• Change in HbA1c % • Percent of glucose readings < 50 mg/dl and < 70 mg/dl	Dexcom, Inc.

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
RCT Study period NR		= 2 weeks CGM + 1 week off), CGM values verified using SMBG, SMBG used during 1 week off segements **SMBG (n=50)** SMBG device: AccuChek Aviva glucometer Protocol: SMBG done at each meal and at bedtime **Cointervention(s)** Usual care from patients' primary care provider	treated with prandial insulin, able to independently measure/read finger stick blood glucose levels, willing to perform SMBG four times daily. **Exclusion criteria:** Pregnancy, lactating, attempting pregnancy, or patients on glucocorticoids, amphetamines, anabolic, or weight-reducing medications	HbA1c, mean (SD): 8.3 (1.2)%	mos*, 9.5 mos*, 12 mos*	• Percent of glucose readings > 180 mg/dl and > 240 mg/dl • PAID	
Haak 2016 Europe (multicenter) RCT Study Period NR	N=224	**CGM (n=149)** CGM Device: FreeStyle Libre, Abbott Diabetes Care SMBG device: Protocol: After a 2 week blinded CGM phase, participants randomized to use CGM continuously for study duration for self-management, including insulin dose decisions in accordance with product labeling. No training was provided. **Usual care (n=75)** SMBG device: 'standard blood glucose device' from Abbott Diabetes Care	**Inclusion criteria:** participants aged 18 years or older with type 2 diabetes treated with insulin for at least 6 months and on their current regimen (prandial only or prandial and basal intensive insulin therapy or CSII therapy) for 3 months or more, an HbA1c level 58–108 mmol/mol (7.5–12.0%), self-reported regular blood glucose testing (more than 10/week for at least 2 months prior to study	Age, mean (SD): 59.25 (10.25) Female: 67% Race: 94% white Duration of diabetes, mean(SD) years: 17.5 (8.0) BMI, mean (SD): 33.2 (6.0) Weight, mean (SD): 98.5 (20.3) HbA1c%, mean (SD): 8.81 (0.98) Mean total daily insulin dose(SD), units/d: basal- 41.35 (23.40) bolus- 52.65 (32.48)	F/U (% CGM, % control): 6 months (93.3%, 82.6%)	• Difference in HbA1c levels • proportion of participants with reduction in HbA1c of ≥5.5 mmol/mol (0.5%) or achieving HbA1c ≤ 58 mmol/mol (7.5%), • Severe hypoglycemia • Diabetic Ketoacidosis • Duration of hypoglycemic events(<3.9 mmol/L [70 mg/dL], and <3.1 mmol/L [55 mg/dL]); • time in range (3.9–10.0 mmol/L [70–180 mg/dL]	Sponsor: Abbott Diabetes Care; sponsor designed the study protocol in collaboration with the principal investigator in each country and provided all study materials. The sponsor was involved in collecting data and reporting results, but was not involved in

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
		Protocol: After a 2 week blinded CGM phase, control participants self-managed blood glucose levels. **Cointervention(s):** None	entry), considered by the investigator to be technically capable of using the flash sensor-based glucose monitoring system **Exclusion criteria:** Exclusion for any other insulin regimen to that described above; a total daily dose of insulin C1.75 units/ kg on study entry; had severe hypoglycemia (requiring third-party assistance), diabetic ketoacidosis, or hyperosmolar-hyperglycemic state in the preceding 6 months; known allergy to medical-grade adhesives; used continuous glucose monitoring within the previous 4 months; were pregnant or planning pregnancy; were receiving steroid therapy for any condition; or were considered by the			• number and duration of hyperglycemic events ([10.0 mmol/L [180 mg/dL], and [13.3 mmol/L [240 mg/dL]) • severe hypoglycemia • hypoglycemic events • Diabetes Distress Scale (DDS) • Diabetes Quality of Life (DQoL) • DTSQs	the authors' interpretation or text writing. The sponsor also gave approval to submit for publication. COI: One or more authors reported receiving personal fees, grants, and other support from Abbott Diabetes Care, Medtronic, Johnson & Johnson, Dexcom, Novo Nordisk, and/ or Lilly International. See study for full detail.

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
			investigator to be unsuitable to participate.				
Tildesley 2013, Tang 2014 Country NR RCT Study period NR	57 rand	**CGM (n=32)** CGM device: Guardian REAL-Time CGM system Protocol: CGM done for 6 months, endocrinologists made adjustments to therapy, testing frequency, and/or lifestyle modifications **IBGMS (n=25)** Patients uploaded all SMBG data electronically for 6 months, endocrinologists made adjustments to therapy, testing frequency, and/or lifestyle modifications **Cointervention(s)** Standard office based care	**Inclusion criteria:** T2DM treated with insulin alone or in combination with oral antihyperglycemic agents, A1C > 7.0%, internet access, and prior training in SMBG **Exclusion criteria:** NR	Age, mean (SD): 58.8 (9.7) years Female: 36% Duration of diabetes, mean (SD): 17.2 (7.4) years BMI, mean (SD): 34.8 (6.3) HbA1c %, mean (SD): 8.80 (1.30) %	F/U (% CGM, % IBGMS): 3 mos (78%, NR), 6 mos (63%, 80%)	• Change in HbA1c % • Diabetes Treatment Satisfaction Questionnaire	Endocrine Research Society
Yoo 2008 Location: Korea Study period: RCT	65 randomized, 57 analyzed	**rtCGM (n=29)** Delivery Type: CSII: 100% MDI: NA Device: MM Guardian RT fingerstick 3+ times/day Glycemic Targets: NR Training: NA Therapy Duration: 3 months Description: Patients underwent rtCGM once a month for 3 days for 3 months Alarms: Hyperglycemia	**Inclusion Criteria:** Adults 2-80 years of age with T2DM with use of oral hypoglycemic agents or insulin for at least 1 years, HbA1c between 8.0% and 10%, stable insulin or OHA regimen for prior 2 months, and stable dose of anti-hypertensive or lipid-	Mean Age (SD): 56(7.9) years Female: 57.9% Race: NR Mean Baseline Weight(kg): 64.48(12.35) Mean Baseline BMI (kg/m2): 25.3(3.2) Mean Baseline HbA1c (%): 8.90(0.85) Mean duration of DM (SD): 12.49(5.36) years	F/U (% rtCGM, % SMBG): 3 months (90.6%, 84.8%) **Crossover:** None	• HbA1c (%) • Hyperglycemia (Fasting glucose mmol/L)) • Hyperglycemia(PPG (mg/dL)) • Severe hypoglycemia (not further specified) • Weight gain (kg)	Sponsor: This study was supported by a grant from the Korean Health 21 R&D Project, Ministry of Health & Welfare, Republic of Korea (A050463). Assisted by

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
		(300 mg/dL) Hypoglycemia(60 mg/dL) **SMBG (n=28)** Delivery Type: CSII: NA MDI: 100% Device: monitor use NA Glycemic Targets: NR Training: NA Therapy Duration: 3 months Description: Patients conducted SMBG 4 times/week Alarms: NA **Cointerventions:** None	lowring drugs for at least 4 weeks. **Exclusion Criteria:** Severe diabetic complications (e.g. diabetic foot, retinopathy), corticosteroid use in previous 3 mo, liver/kidney disease, renal insufficiency with a serum creatinine level >2.0mg/dL other medical problems that affected study results or trial participation				Medtronic Korea Co., Ltd COI: None declared

BG = blood glucose; BMI= body mass index-standard deviation score; CSII = continuous subcutaneous insulin infusion; dL = deciliter; DM = diabetes mellitus; HbA1c = hemoglobin A1c; IV = intravenous; kg = kilograms; kg/m2 = kilograms per meter squared; MDI = multiple daily injections; mg = milligram; mg/dL = milligrams per deciliter; MM = Medtronic Minimed; mmol = micromoles; mmol/L = millimole per liter; NA = not applicable; NR = not reported; NS = not significant; PPG = post prandial glucose; RCT = randomized controlled trial; rtCGM = real-time continuous glucose monitor; SD = standard deviation; SMBG = self-monitoring of blood glucose; T1DM = Type 1 Diabetes Mellitus; T2DM = Type 2 Diabetes Mellitus; U = units; wk = week; wks = weeks; x/day = times per day; yrs = years

*Follow-up not reported

Appendix Table F8. Study Characteristics and Patient Demographics of RCTs Evaluating CGM versus SMBG for Diabetes Mellitus in Pregnancy

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
Feig 2017 Location: Canada, England, Scotland, Spain, Italy, Ireland, and the USA (multicenter) Study period: Mar 2013 to Mar 2016	n=215 pregnancy trial, n=110 pregnancy planning trial, n=34 conceived during pregnancy planning trial	**rtCGM (n=161)** Delivery Type: CSII: 46% MDI: 54% Device: Medtronic Guardian REAL-Time or MiniMed Minilink Glycemic Targets: 3.5-7.8 mmol/L Therapy Duration: Length of pregnancy Description: After a 6-day masked CGM run-in phase, participants were randomized to CGM in addition to SMBG 7+ times/day, study visits were planned for weeks 8, 12, 16, 20, 24, 28, 32, 34, and 36 weeks' in the pregnancy patients and 4, 8, 12, 16, 20, and 24 weeks post-randomization for planning pregnancy patients. Alarms: NR **SMBG (n=164)** Delivery Type: CSII: 45% MDI: 55% Device: NA Glycemic Targets: 3.5-7.8 mmol/L Therapy Duration: length of pregnancy	**Inclusion Criteria:** Women aged 18-40 with T1DM (minimum of 12 months duration) receiving intensive insulin therapy via MDI or insulin pump, who were pregnany or planning pregnancy. Pregnant women were eligible if they had a live singleton fetus, were at 13 weeks and 6 days' gestation or less, and had HbA1c between 6.5-10.0%. Women planning for pregnancy had to have HbA1c lkevels between 7.0-10.0%. **Exclusion Criteria:** Regular CGM users and women with severe nephropathy or medical conditions such as psychiatric illness requiring hospitalization that could prevent them from completing the trial were excluded.	**Pregnancy Trial** Mean Age (SD): 31.4±4.5 Female: 100% Race: 85.6% European origin Primiparous, %: 39% Mean Baseline Weight(kg): NR Mean Baseline BMI (kg/m2): 25.7±4.5 Mean Baseline HbA1c (%): 7.4±0.74 Mean Baseline Gestational Age (weeks): 10.75 (2.1) Mean duration of DM, years: 16.5 Severe Hypoglycemia in the past year: 9.3% **Pregnancy Planning Trial** Mean Age (SD): 33 (3.6) Female: 100% Race: 85.6% European origin Mean Baseline Weight(kg): NR Mean Baseline BMI (kg/m2): 26.5 (4.6) Mean Baseline HbA1c (%): 7.88±0.69 Mean duration of DM, years: 18.5 Severe Hypoglycemia in the past year: 9%	Pregnancy Trial F/U (%CGM, SMBG): HbA1c Analysis (82%,79%) CGM analysis (71%, 72%) Maternal Outcome (98%, 99%) Neonatal Outcomes (97%, 99%) Pregnancy Planning Trial F/U (%CGM, SMBG): HbA1c Analysis (85%,89%) CGM analysis (74 %, 91%) **Crossover:** None	**Pregnancy Trial:** • Change in HbA1c (baseline to 34 weeks gestation) • Percentage of time spent in, above and below the glucose control target range • AUC for glucose levels • Episodes of hypoglycemia • Gestational weight gain • Gestational hypertension • Preeclampsia • Mode of delivery • Length of hospital stay • Insulin dose • Hypoglycemia Fear • Diabetes Coping • Quality of life • Monitor Satisfaction	Sponsors: The trial is funded by Juvenile Diabetes Research Foundation (JDRF) grants #17-2011-533, and grants under the JDRF Canadian Clinical Trial Network, a public-private partnership including JDRF and FedDev Ontario and supported by JDRF #80-2010-585. Medtronic supplied the CGM sensors and CGM systems at reduced cost. The funders or Medtronic had no role in the trial design, data collection, data analysis, or data interpretation.

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
		Description: After a 6-day masked CGM run-in phase, participants were randomized to continue their SMBG 7+ times/day, study visits were planned for weeks 8, 12, 16, 20, 24, 28, 32, 34, and 36 weeks' in the pregnancy patients and 4, 8, 12, 16, 20, and 24 weeks post-randomization for planning pregnancy patients. Alarms: NR				**Planning Group**: • Change in HbA1c (baseline to 24 weeks or conception) • Percentage of time spent in, above and below the glucose control target range • AUC for glucose levels • Episodes of hypoglycemia	COI: One or more authors reported grants from JDRF, received fees or sit on advisory board for Medtronic, Novo Nordisk, Roche or Abbott Diabetes Care. See study for full details.
Secher 2013 Location: Denmark Study period: Feb 2009 to Feb 2011	154 randomized, 151 analyzed	**rtCGM (n=79)** Delivery Type: CSII: both (NR) MDI: both (NR) Device: MM Guardian Real-time Glycemic Targets: 4.0-6.0 mmol/L preprandial, 4.0-8.0 mmol/L 1.5h postprandial, 6.0-8.0 mmol/L prebedtime Therapy Duration: duration of pregnancy Description: Use of intermittent CGM during pregnancy (for 6 days at a time, at weeks 12, 21, 27,	**Inclusion Criteria:** Danish speaking pregnant women with T1DM and T2DM, prior to 14 completed gestational weeks, with one fetus. **Exclusion Criteria:** Use of rtCGM, severe mental or psychiatric barriers, diabetic nephropathy or severe concurrent comorbidity	Mean Age (SD): 31.5 years Female: 100% Race: NR Mean Baseline Weight(kg): NR Mean Baseline BMI (kg/m2): 25.1 vs. 24.7 Mean Baseline HbA1c (%): 6.6 vs. 6.8 Mean duration of DM (SD): 11 years	F/U (% Total): (98%) **Crossover:** None	• HbA1c (%) • Macrosomia • Miscarriage • Birth weight • Neonatal hypoglycemia • Congenital malformation •	Sponsor: Medtronic supplied CGM monitors, glucose sensors, but had no influence on study design, handling of data, writing of the manuscript. COI: One or more authors received financial support from

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
		and 33) in addition to routine care. Alarms: <4.0 mmol/L **SMBG (n=75)** Delivery Type: CSII: NA MDI: 100% Device: End of pregnancy Glycemic Targets: 4.0-6.0 mmol/L preprandial, 4.0-8.0 mmol/L 1.5h postprandial, 6.0-8.0 mmol/L prebedtime Therapy Duration: duration of pregnancy Description: SMBG seven times daily (before and 1.5 h after each main meal, and bedtime) **Cointerventions:** none.					and/or holds stocks with the European Foundation for the Study of Diabetes and LifeScan, Rigshospitalet's Research Foundation, the Capital Region of Denmark, the Medical Faculty Foundation of Copenhagen University, Aase and Ejnar Danielsen Foundation, and Master Joiner Sophus Jacobsen and his wife Astrid Jacobsen's Foundation, and/or Novo Nordisk Foundation
Wei 2016 Location: China Study period: NR Open-label RCT	120 randomized, 106 analyzed	**CGM (n=55)** Delivery Type: CSII: 100% MDI: NA Device: MM Gold Glycemic Targets: Fasting > 105 mg/dL, 1h postprandial >155 mg/dL, 2 h postprandial >130	**Inclusion Criteria:** Pregnant women at 24-28 wks gestation with singleton pregnancy, with GDM as defined by at least one abnormally high plasma glucose value out of three on OGTT.	Mean Age (SD): 30.13 (3.48) Female: 100% Race: NR Pre-pregnancy Baseline Weight(kg): NR Mean Baseline BMI (kg/m2): NR Mean Baseline HbA1c (%): 5.75(0.35)	F/U (% CGM,%SMBG): (92.7% 88.7%) **Crossover:** None	• HbA1c (%) • Apgar Score • Caesarian Section • Birth Weight • Neonatal hypoglycemia ≤45mg/dL	Sponsor: NR COI: NR

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
		Therapy Duration: duration of pregnancy Description: All patients took 75 g OGTT. Patients given lifestyle/dietary advice, clinical follow-ups and glucose monitoring with CGM. Insulin treatment was administered if two abnormal glucose values were reached. Patients instructed to check 4+ times/day Alarms **SMBG (n=51)** Delivery Type: CSII: NR MDI: 100% Device: SMBG Glycemic Targets: NR Therapy Duration: duration of pregnancy Description: All patients took 75 g OGTT. Patients given lifestyle/dietary advice, clinical follow-ups and glucose monitoring with SMBG. Insulin treatment was administered if two abnormal glucose values were reached. Patients instructed to check 4+ times/day Alarms: Fasting > 105 mg/dL, 1h postprandial	**Exclusion Criteria:** Diagnosis of DM, previous treatment for GDM, presence of infection or other severe metabolic, endocrine, medical or psychological comorbidities.	Mean duration of DM (SD): NR		• Macrosomia	

Study	N	Interventions	Inclusion, Exclusion Criteria	Demographic	F/U %	Outcomes	Funding
		>155 mg/dL, 2 h postprandial >130 **Cointerventions:** None					

BG: blood glucose; BMI: body mass index-standard deviation score; CSII: continuous subcutaneous insulin infusion; dL: deciliter; DM: diabetes mellitus; GDM: gestational diabetes miltetus; HbA1c: hemoglobin A1c; IV: intravenous; kg: kilograms; kg/m2: kilograms per meter squared; MDI: multiple daily injections; mg: milligram; mg/dL: milligrams per deciliter; MM: Medtronic Minimed; mmol: millimoles; mmol/L: millimole per liter; NA: not applicable; NR: not reported; NS: not significant; PPG: post prandial glucose; OGTT: oral glucose tolerance test; RCT: randomized controlled trial; rtCGM: real-time continuous glucose monitor; SD: standard deviation; SMBG: self-monitoring of blood glucose; T1DM: Type 1 Diabetes Mellitus; T2DM: Type 2 Diabetes Mellitus; U: units; wk: week; wks: weeks; x/day: times per day; yrs: years

* Primipara indicates that it is a mother's first time giving birth.

Appendix Table F9. Study Characteristics, Patient Demographics and Results from Observational Studies Evaluating CGM versus SMBG in Adults with Mixed Type 1 and Type 2 DM

Study	N	Demographics	Inclusion/ exclusion criteria	Study purpose	Results	Conclusions	Funding
Anderson 2011 *Retrospective database*	77	**Group 1 (n=34)** *Long term CGM use (≥3 months)* Age, mean (SD): 44.0 (10.2) years Female: 44% Weight, mean (SD): 76.4 (16.0) kg BMI, mean (SD): 24.7 (4.3) Duration of diabetes, mean (SD): 26.4 (13.2) years HbA1c %: 8.8%* Hypoglycemia events at in previous month†: • 0 to <5: 31% • 5 to <10: 23% • 10 to <15: 19% • ≥15: 27%	**Inclusion criteria:** Adult men and non-pregnant women with T1DM, HbA1c ≥1 at both start and during use (after at least 3 months) of CGM therapy **Exclusion criteria:** Patients without HbA1c value ≥1 at initial CGM use	To understand the effect of CGM on HbA1c in clinical practice.	**HbA1c%*** *1.1 years* Group 1: 8.2% Group 2: 8.4% Group 3: 8.4% Group 4: 8.0% *2.6 years* Group 1: NR Group 2: NR Group 3: 8.3% Group 3: 8.0% **Number of hypoglycemic events in previous month** Group 1: • 0 to <5: 42.3% • 5 to <10: 46.2% • 10 to <15: 3.8% • ≥15: 7.7% Group 3:	Long-term CGM use was associated with improved glycemic control in clinical practice and a reduction in non-severe hypoglycemic events, whereas short-term use had no effect on HbA1c. The effect on glycemic control varied by indication.	Grants from Abbott Scandinavia, the John and Asta Falkman Foundation, and the Therese Sandwall Foundation. Conflict of interest: 1 or more authors served as a consultant for related industry

Study	N	Demographics	Inclusion/ exclusion criteria	Study purpose	Results	Conclusions	Funding
		Group 2 (n=408) *Long-term controls* Age, mean (SD): 44.6 (16.1) years Female: 53% Weight, mean (SD): 74.2 (14.5) kg BMI, mean (SD): 24.6 (3.9) Duration of diabetes, mean (SD): 25.8 (16.2) years HbA1c %: 8.3%* **Group 3 (n=43)** *Short term CGM use (<3 months)* Age, mean (SD): 42.7 (10.4) years Female: 65% Weight, mean (SD): 74.5 (12.2) kg BMI, mean (SD): 25.4 (4.0) Duration of diabetes, mean (SD): 26.8 (10.6) years HbA1c %: 8.5%* Hypoglycemia events in previous month†: • 0 to <5: 29% • 5 to <10: 20% • 10 to <15: 37% • ≥15: 15% **Group 4 (n=1204)** *Short term control* Age, mean (SD): 44.2 (15.5) years			• 0 to <5: 29.3% • 5 to <10: 24.4% • 10 to <15: 26.8% • ≥15: 19.5% **Reduction in hypoglycemia (2 steps in 5 step scale‡)** Group 1: 26.9% Group 3: 12.2% **Reduction in hypoglycemia (1 step in 5 step scale)** Group 1: 23.1% Group 3: 9.8% **Hypoglycemia cases in the same 5 step scale** Group 1: 38.5% Group 3: 51.2% **Increase in hypoglycemia (1 step in 5 step scale)** Group 1: 11.5% Group 3: 19.5% **Increase in hypoglycemia (2 steps in 5 step scale)** Group 1: 0% Group 3: 7.3%		companies. 1 or more authors received honoraria.

Study	N	Demographics	Inclusion/ exclusion criteria	Study purpose	Results	Conclusions	Funding
		Female: 48% Weight, mean (SD): 74.0 (14.0) kg BMI, mean (SD): 24.5 (3.7) Duration of diabetes, mean (SD): 23.9 (15.3) years HbA1c %: 8.0%*					
Battelino 2015 *Retrospectived atabase study*	10501	**Group 1 (n=2585)** *Non-sensor users* Age: NR Blood glucose concentration, mean (SD): 9.3 (4.5) mmol/l (167.4 mg/dl) **Group 2 (n=2782)** *Sensor users <25% of the time* Age: NR Blood glucose concentration, mean (SD): 9.3 (4.4) mmol/l (167.4 mg/dl) **Group 3 (n=1789)** *Sensor users 25-49% of the time* Age: NR Blood glucose concentration, mean (SD): 9.3 (4.3) mmol/l (167.4 mg/dl) **Group 4 (n=1585)** *Sensor users 50-74% of the time* Age: NR	**Inclusion criteria:** Patients receiving insulin pump therapy (insulin pumps or sensor-augmented pumps from Medtronic), ≥6 months downloadable data, ≥1 sensor reading in CareLink **Exclusion criteria:** NR	To analyze blood glucose control according to CGM use in data from the CareLink database, and to identify factors associated with continuation of sensor use during sensor-augmented pump therapy	**Number of events of hypoglycemia per patient per year (<2.8 mmol/l)** Group 1: 45.0 Group 2: 41.0 Group 3: 36.0 Group 4: 32.1 Group 5: 27.5 **Number of events of hypoglycemia per patient per year (<3.3 mmol/l)** Group 1: 115.3 Group 2: 105.7 Group 3: 92.6 Group 4: 84.3 Group 5: 76.9 **Number of events of hypoglycemia per patient per year (<3.9 mmol/l)** Group 1: 203.6 Group 2: 188.8 Group 3: 167.4 Group 4: 154.9 Group 5: 148.9 **Mean percent blood glucose values <2.8 mmol/l (50.4 mg/dl)** Group 1: 2.0 (0.04) Group 2: 1.9 (0.04) Group 3: 1.6 (0.04) Group 4: 1.4 (0.04)	The use of CGM was significantly associated with reductions in hypoglycemia and slightly improved metabolic control during insulin pump therapy. Sensor use during the first month was strongly associated with long-term adherence; patient education and training may be helpful in achieving this.	None Conflict of interest: 1 or more authors is a board member for related industry companies, 1 or more author received research grant support and honoraria from a related industry company. See article for full conflict of interest

Study	N	Demographics	Inclusion/ exclusion criteria	Study purpose	Results	Conclusions	Funding
		Blood glucose concentration, mean (SD): 9.3 (4.1) mmol/l (167.4 mg/dl) **Group 5 (n=1760)** *Sensor users ≥75% of the time* Age: NR Blood glucose concentration, mean (SD): 9.1 (3.8) mmol/l (163.8 mg/dl)			Group 5: 1.2 (0.03) **Mean percent blood glucose values <3.3 mmol/l (59.4 mg/dl)** Group 1: 5.1 (0.07) Group 2: 4.8 (0.07) Group 3: 4.2 (0.08) Group 4: 3.8 (0.08) Group 5: 3.3 (0.07) **Mean percent blood glucose values <3.9 mmol/l (70.2 mg/dl)** Group 1: 9.1 (0.10) Group 2: 8.5 (0.01) Group 3: 7.7 (0.11) Group 4: 7.0 (0.12) Group 5: 6.3 (0.11) **Mean percent blood glucose values >10.0 mmol/l (180 mg/dl)** Group 1: 37.6 (0.27) Group 2: 37.3 (0.26) Group 3: 37.6 (0.33) Group 4: 37.7 (0.36) Group 5: 36.1 (0.36) **Mean percent blood glucose values ≥13.9 mmol/l (250.2 mg/dl)** Group 1: 16.2 (0.2) Group 2: 15.6 (0.19) Group 3: 15.3 (0.24) Group 4: 14.7 (0.25) Group 5: 13.0 (0.23) **Incidence rate ratio vs ≥75% sensor use group (95% CI), <2.8 mmol/l (50.4 mg/dl)**		

Study	N	Demographics	Inclusion/ exclusion criteria	Study purpose	Results	Conclusions	Funding
					Group 1: 1.64 (1.50 to 1.80), p<0.0001 Group 2: 1.49 (1.36 to 1.63), p<0.0001 Group 3: 1.31 (1.17 to 1.50), p<0.0001 Group 4: 1.17 (1.04 to 1.31), p=0.04 **Incidence rate ratio vs ≥75% sensor use group (95% CI), <3.3 mmol/l (59.4 mg/dl)** Group 1: 1.50 (1.39 to 1.61), p<0.0001 Group 2: 1.37 (1.28 to 1.48), p<0.0001 Group 3: 1.20 (1.10 to 1.31), p<0.0001 Group 4: 1.10 (1.01 to 1.20), p=0.04 **Incidence rate ratio vs ≥75% sensor use group (95% CI), <3.9 mmol/l (70.2 mg/dl)** Group 1: 1.36 (1.28 to 1.45), p<0.0001 Group 2: 1.27 (1.19 to 1.35), p<0.0001 Group 3: 1.12 (1.04 to 1.21), p=0.001 Group 4: 1.04 (0.96, 1.12), p=NS		

BMI, body mass index; CGM, continuous glucose monitoring; CI, confidence interval; HbA1c, hemoglobin A1c; mmol/l, millimoles per liter; NR, not reported; T1DM, type 1 diabetes mellitus;
* Value estimated from graph
† Events were self-rated and self-reported by patients
‡ 5 step scale is referring to the 5 group breakdown of the number of hypoglycemic events in the previous month (0 to <5, 5 to <10...etc)

Appendix Table F10. Study Characteristics, Patient Demographics and Results from Observational Studies Evaluating CGM versus SMBG in Pregnant Women with DM

Study	N	Demographics	Inclusion/ exclusion criteria	Study purpose	Results	Conclusions	Funding
Cordua 2013 *(Continuation of Secher 2013*)*	86	**CGM (n=27)** Age, median (range): 31 (25-40) years Duration of diabetes, median (range): 14 (1-36) years Pre-gestational BMI, median (range): 25.1 (20-34) HbA1c %, median (range): 6.6 (6.0-8.4) % **SMBG (n=59)** Age, median (range): 30 (19-43) years Duration of diabetes, median (range): 15 (1-38) years HbA1c %, median (range): 6.8 (5.6-10.7) %	**Inclusion criteria:** Pregestational diabetes, before 14 completed gestational weeks, one living intrauterine fetus **Exclusion criteria:** Present use of real-time CGM, severe mental or psychiatric barriers, nephropathy, severe concurrent comorbidity	To explore whether real-time CGM during labor and delivery supplementary to hourly self-monitored plasma glucose in women with Type 1 diabetes reduces the prevalence of neonatal hypoglycemia	**Neonatal hypoglycemia** *Moderate hypoglycemia*† CGM, n (%): 10 (37%) SMBG, n (%): 27 (46%) *Severe hypoglycemia*‡ CGM, n (%): 3 (11%) SMBG, n (%): 10 (17%) **Large for gestational age** CGM, n (%): 15 (56%) SMBG, n (%): 21 (36%) Women with infants with hypoglycemia (n=10), n (%): 7 (70%) Women with infants without hypoglycemia (n=17), n (%): 8 (47%) **Preterm delivery** CGM, n (%): 5 (19%) SMBG, n (%): 12 (20%) Women with infants with hypoglycemia (n=10), n (%): 1 (10%) Women with infants without hypoglycemia (n=17), n (%): 4 (24%) **Percent of measurements ≤3.9 mmol/l** Women with infants with hypoglycemia (n=10), median (range): 0% (0-50) [SMBG], 0% (0-66) [CGM] Women with infants without hypoglycemia (n=17), median (range): 14% (0-73) [SMBG], 2% (0-82) [CGM]	The use of real-time CGM supplementary to hourly self-monitored plasma glucose measurements during labor and delivery in did not reduce the prevalence of neonatal hypoglycemia.	European Foundation for the Study of Diabetes and LifeScan, Rigshospitalet's Research Foundation, The Capital Region of Denmark, The Medical Faculty Foundation of Copenhagen University, Aase and Ejnar Danielsen's Foundation, Master joiner Sophus Jacobsen and Astrid Jacobsen's Foundation, Novo Nordisk Foundation, Medtronic, Inc.

Study	N	Demographics	Inclusion/ exclusion criteria	Study purpose	Results	Conclusions	Funding
					Percent of measurements >7.0 mmol/l Women with infants with hypoglycemia (n=10), median (range): 26% (0-75) [SMBG], 17% (0-94) [CGM] Women with infants without hypoglycemia (n=17), median (range): 9% (0-70) [SMBG], 4% (0-46) [CGM]		
Fresa 2013 *Retrospective cohort*	65	**RT-CGM+CSII (n=18)** Age, mean (SD): 32 (6) years Duration of diabetes, mean (SD): 17 (10) years Pre-pregnancy BMI, mean (SD): 24 (2) HbA1c %, mean (SD): 6.3 (1)% **CSII (n=47)** Age, mean (SD): 30.5 (5) years Duration of diabetes, mean (SD): 15 (8) years Pre-pregnancy BMI, mean (SD): 25 (4) HbA1c %, mean (SD): 6.7 (1.4)%	**Inclusion criteria:** Pregnant women with T1DM **Exclusion criteria:** NR	To evaluate the efficacy and safety of CSII during delivery in pregnant women with T1DM. The secondary aim was to assess the impact of RT-CGM added to CSII versus CSII alone.	**HbA1c %, mean (SD)** *Third trimester* RT-CGM+CSII: 5.2 (0.4)% CSII: 6.2 (1.7)% **Cesarean section** RT-CGM+CSII: 83% CSII: 87% **Birth weight, mean (SD)** RT-CGM+CSII: 3664 (513) grams CSII: 3518 (698) grams **Percent with birth weight above 90th percentile** RT-CGM+CSII: 44% CSII: 42.5% **Number of admissions to neonatal intensive care unit** RT-CGM+CSII: 1 CSII: 7 **Events of neonatal hyperglycemia** RT-CGM+CSII: 1 CSII: 10	CSII is possible and safe in different types of delivery in selected and educated women. RT-CGM helps to obtain better outcomes in terms of maternal peripartum CBG levels. RT-CGM could be considered a useful tool in routine management of pregnancies complicated by diabetes.	NR
Secher 2014	28	Age: NR Female: 100%	**Inclusion criteria:** Women early in	To evaluate if routine use of RT-	**HbA1c %, median (range)** 9 weeks: 6.8 (5.4-8.5)	RT-CGM may have led to fewer severe	None

Study	N	Demographics	Inclusion/ exclusion criteria	Study purpose	Results	Conclusions	Funding
Prospective cohort		Duration of diabetes, median (range): 14 (6-18) Pre-pregnancy BMI, median (range): 25 (21-34) Pregestational HbA1c %, median (range): 7.0 (5.8-9.6) Diabetic retinopathy: 25% **CGM group (n=12)** Number of hypoglycemic events in year before pregnancy: 17.5 events/patient-year **Control group (n=16)** Number of hypoglycemic events in year before pregnancy: 1.6 events/patient-year	pregnancy with a history of severe hypoglycemia in the year before pregnancy or early in current pregnancy **Exclusion criteria:** NR	CGM from early pregnancy onwards could prevent severe hypoglycemia in women with T1DM who had had severe hypoglycemia the year before pregnancy.	21 weeks: 6.8 (5.4-8.5) 33-37 weeks: 6.2 (4.9-7.4) **Mild hypoglycemia events, median (range), CGM group** 9 weeks: 5 (0-14) 21 weeks: 4 (1-14) 33-37 weeks: 4 (0-10) **Number of hypoglycemic events** CGM group: 0.3 events/patient-year Control group: 5.0 events/patient-year **Percent of time in hypoglycemia, median % of time (range), CGM group** *6-13 weeks:* • ≤2.2 mmol/l: 0% (0-2) • ≤3.9 mmol/l: 13% (2-51) *17-20 weeks:* • ≤2.2 mmol/l: 0% (0-4) • ≤3.9 mmol/l: 15% (4-27) **Percent of time in hyperglycemia, median % of time (range), CGM group** *6-13 weeks:* • ≥8.0 mmol/l: 30% (5-68) *17-20 weeks:* • ≥8.0 mmol/l: 33% (14-56)	hypoglycemic events in early pregnancy in women with a documented high risk of severe hypoglycemia, but further evaluation is needed.	Conflict of interest: 1 or more authors are received fees or financial support from related industry companies. 1 or more authors are on the international advisory boards for related industry companies.

BMI, body mass index; CGM, continuous glucose monitoring; CI, confidence interval; CSII, continuous subcutaneous insulin infusion; HbA1c, hemoglobin A1c; mmol/l, millimoles per liter; NR, not reported; T1DM, type 1 diabetes mellitus;

* Randomization was broken, therefore study is considered observational

† Glucose values <2.5 mmol/l

‡ Glucose values <2.5 mmol/l requiring IV glucose infusion

APPENDIX G. Data Abstraction Tables: Efficacy Outcomes

Appendix Table G1. Efficacy Outcomes from RCTs Evaluating CGM versus SMBG in Children with Type 1 Diabetes Mellitus

			Results (mean±SD or %(n/N))			
Author	Outcome	F/U post-tx	Intervention	Control	Effect Estimate (95% CI)†	p-value†
Bergenstal 2010* **	*HbA1c %*					
	HbA1c %	Baseline	8.3±0.6 (n=78)	8.3±0.5(n=78)	NR	NR
	Δ from baseline, HbA1c %, mean (SD)	12 months	-0.4±0.9 (n=78)	+0.2±1.0 (n=78)	-0.5(-0.8 to -0.2)	<0.001‡
	% patients achieving target HbA1c < 7%	12 months	13% (10/78)	5% (4/78)	RR 2.5 (0.87 to 2.39) p=0.156††	0.150
	% patients achieving target HbA1c < 8% (6—12 year olds) or 7.5% (13—19 year olds)	12 months	44% (35/80)	20% (16/80)	RR 2.19 (1.15 to 2.43) p=0.005††	0.005
	Hypoglycemia					
	Rate of hypoglycemia at 1 year, person-year	12 months	8.9 per 100 person-years	4.95 per 100 person-years	NR	0.350
	Severe hypoglycemic events (n/N)	12 months	Events: 7 (4/78)	Events: 4 (4/81)	NR	0.530
	Incidence Rate	12 months	8.98 per 100 person-years	4.95 per 100 person-years	NR	0.350
	No. of Severe hypoglycemic events among children HbA1c < 7%	12 months	Events: 0	Events: 0	NR	NR
	AUC < 70 mg/dl*min, mean (SD)§	Baseline	0.26±0.40	0.23±0.40	NR	NR
		12 months	0.23±0.41	0.25±0.41	NR	0.790‡
	AUC < 50 mg/dl*min, mean±SD§	Baseline	0.01±0.04	0.02±0.05	NR	NR
		12 months	0.02±0.07	0.01±0.05	NR	0.640‡
	Hyperglycemia					
	AUC > 250 mg/dl*min, mean (SD)§	Baseline	13.89±11.04	16.23±10.46	NR	NR
		12 months	9.2±8.1	17.6±14.6	NR	<0.001‡
	AUC > 180 mg/dl*min, mean (SD)§	Baseline	39.36±21.70	44.68±20.34	NR	NR
		12 months	30.1±17.3	45.3±25.6	NR	<0.001‡
	Ketoacidosis.					
	Diabetic Ketoacidosis	12 months	Events: 1 (1/78)	Events: 2 (1/81)	NR	0.490

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)†	p-value†
	Rate of ketoacidosis at 1 year, person-year	12 months	0.02 (n=78)	0.02 (n=81)	NR	0.200
Hirsch 2008* **	*HbA1c %*					
	HbA1c %, mean (SD) (adolescents age 12 to <18)	Baseline	8.82(1.05) (n=17)	8.59(0.80) (n=23)	NR	NR
		3 mos.	7.86 (0.97) (n=16)	7.97 (0.59) (n=23)	NR	NR
		6 mos.	8.02 (1.11) (n=17)	8.21 (0.97) (n=23)	LSM (SE) 0.49(0.29)	0.101
	HbA1c %, Least Square Mean Δ (SE)	6 mos.	-0.617 (0.227) p=0.011 (n=23)	-0.127 (0.222) p=0.572 (n=17)		
	% achieving HbA1c of 7% (adolescents age 12 to <18)	3 mos.	NR	NR	NR	0.520
	Hypoglycemia					
	Severe hypoglycemic event§	6 mos.	11 (n=66)	3 (n=72)	NR	0.040
	Ketoacidosis					
	Number of patients experiencing ketoacidosis event§§	6 mos.	1 (n=66)	0 (n=72)	NR	NR
JDRF Trial 2008* ** Beck/Lawrence 2010	*HbA1c %*					
	HbA1c %, mean (SD)	Baseline	8.0 (0.7) (n=56)	7.9 (0.6) (n=58)	NR	NR
	Δ from baseline, HbA1c %, mean (SD)	6 mos.	-0.37 (0.9) (n=56)	-0.22 (0.54) (n=58)	MD 0.08 (−0.17 to 0.33)	0.290
	Relative decrease of HbA1c % by ≥10%	6 mos.	29% (16/56)	12% (7/58)	NR	0.040
	Absolute decrease of HbA1c % by ≥ 0.5%	6 mos.	54% (30/56)	31% (18/58)	NR	0.009
	Relative increase of HbA1c % by ≥ 10%	6 mos.	9% (5/56)	3% (2/58)	NR	0.240
	Absolute increase of HbA1c % by ≥ 0.5%	6 mos.	21% (12/56)	12% (7/58)	NR	0.180
	HbA1c % < 7%	6 mos.	27% (15/56)	12% (7/58)	NR	0.010
	HbA1c % < 7% without severe hypoglycemic events	6 mos.	25% (14/56)	10% (6/58)	NR	0.020
	Hypoglycemia					

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)†	p-value†
	Rate of severe hypoglycemia	6 mos.	17.9 per 100 person-years (n=56)	24.4 per 100 person-years (n=58)	NR	0.640
	> 1 severe hypoglycemic event	6 mos.	7% (4/56)	10% (6/58)	NR	0.740
	> 1 severe hypoglycemic event with seizure/coma	6 mos.	0% (0/56)	0% (0/58)	NA	NA
	Glucose Level (min/day) < 70 mg/dl, mean	Baseline	49 (n=56)	59 (n=58)	NR	NR
		6 mos.	47 (n=56)	59 (n=58)	NR	0.290
	Glucose Level (min/day) < 50 mg/dl, mean	Baseline	17 (n=56)	18 (n=58)	NR	NR
		6 mos.	10 (n=56)	13 (n=58)	NR	0.500
	Hyperglycemia					
	Glucose Level (min/day) > 180 mg/dl, mean	Baseline	745 (n=56)	671 (n=58)	NR	NR
		6 mos.	643 (n=56)	635 (n=58)	NR	0.580**
	Glucose Level (min/day) > 250 mg/dl, mean	Baseline	343 (n=56)	282 (n=58)	NR	NR
		6 mos.	242 (n=56)	268 (n=58)	NR	0.180**
	Ketoacidosis					
	Number of patients experiencing a ketoacidosis event	6 mos.	0 (n=56)	0 (n=58)	NA	NA
	QoL†††					
	HFS Worry (Participants <18 years)	Baseline	25.7±16.6 (n=107)	25.9±14.9 (n=111)	NR	NR
		6 mos.	20.8±13.1 (n=103)	22.6±14.4 (n=106)	NR	0.270
	HFS Worry (Participants <18 years with CGM use ≥6 days/week)	Baseline	24.9±15.2 (n=43)	NA	NA	NA
		6 mos.	18.8±11.8 (n=43)	NA	NA	NA
		Δ from baseline	-6.1±12.0 (n=43)	NA	NA	NA
	HFS Worry (Participants <18 years with CGM use <6 days/week)	Baseline	26.3±17.8 (n=60)	NA	NA	NA
		6 mos.	22.3±13.9 (n=60)	NA	NA	NA
		Δ from baseline	−4.0±12.6 (n=60)	NA	NA	NA
	PedsQL Generic (Participants <18 years)	Baseline	78.5±12.5 (n=107)	79.7±11.7 (n=111)	NR	NR
		6 mos.	80.5±12.4 (n=103)	81.4±12.0 (n=106)	NR	0.960

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)†	p-value†
	PedsQL Generic (Participants <18 years with CGM use ≥6 days/week)	Baseline	80.8±11.5 (n=43)	NA	NA	NA
		6 mos.	83.9±11.0 (n=43)	NA	NA	NA
		Δ from baseline	3.2±11.5 (n=43)	NA	NA	NA
	PedsQL Generic (Participants <18 years with CGM use <6 days/week)	Baseline	76.9 ± 13.1 (n=59)	NA	NA	NA
		6 mos.	78.1±12.8 (n=59)	NA	NA	NA
		Δ from baseline	+0.9±9.0 (n=59)	NA	NA	NA
	PedsQL Diabetes-Specific (Participants <18 years)	Baseline	82.2±12.2 (n=107)	81.6±12.9 (n=111)	NR	NR
		6 mos.	81.7±12.9 (n=103)	82.6±13.2 (n=106)	NR	0.280
	PedsQL Diabetes-Specific (Participants <18 years with CGM use ≥6 days/week)	Baseline	84.3 ± 11.6 (n=43)	NA	NA	NA
		6 mos.	85.1±10.4 (n=43)	NA	NA	NA
		Δ from baseline	+0.9±8.3 (n=43)	NA	NA	NA
	PedsQL Diabetes-Specific (Participants <18 years with CGM use <6 days/week)	Baseline	80.6 ± 12.5 (n=59)	NA	NA	NA
		6 mos.	79.1 ± 14.0 (n=59)	NA	NA	NA
		Δ from baseline	−1.8 ± 10.8 (n=59)	NA	NA	NA
	HFS Worry (parents of participants <18 years)	Baseline	41.5±16.0 (n=110)	42.2±19.8 (n=113)	NR	NR
		6 mos.	37.0±14.6 (n=107)	38.0±17.2 (n=107)	NR	0.880
	HFS Worry (parents of participants <18 years with CGM use ≥6 days/week)	Baseline	42.1 ± 13.9 (n=45)	NA	NA	NA
		6 mos.	37.0 ± 13.9 (n=45)	NA	NA	NA
		Δ from baseline	−5.2 ± 13.3 (n=45)	NA	NA	NA
	HFS Worry (parents of participants <18 years with CGM use <6 days/week)	Baseline	40.8 ± 17.5 (n=62)	NA	NA	NA
		6 mos.	37.0 ± 15.2 (n=62)	NA	NA	NA
		Δ from baseline	−3.5 ± 13.2 (n=62)	NA	NA	NA
	PAID-P (parents of participants <18 years)	Baseline	46.3±14.0 (n=110)	43.8±15.9 (n=113)	NR	NR
		6 mos.	47.1±12.7 (n=107)	43.8±17.0 (n=107)	NR	0.250
	PAID-P (parents of participants <18 years with CGM use ≥6 days/week)	Baseline	48.6 ± 12.3 (n=45)	NA	NA	NA
		6 mos.	47.0 ± 13.2 (n=45)	NA	NA	NA
		Δ from baseline	−1.6 ± 13.2 (n=45)	NA	NA	NA

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)†	p-value†
	PAID-P (parents of participants <18 years with CGM use <6 days/week)	Baseline	45.1 ± 14.8 (n=62)	NA	NA	NA
		6 mos.	47.3 ± 12.4 (n=62)	NA	NA	NA
		Δ from baseline	+2.6 ± 13.2 (n=62)	NA	NA	NA
	PedsQL Generic (parents of participants <18 years)	Baseline	76.7±11.8 (n=110)	77.2±13.7 (n=113)	NR	NR
		6 mos.	76.7±12.6 (n=107)	77.5±13.5 (n=107)	NR	0.700
	PedsQL Generic (parents of participants <18 years with CGM use ≥6 days/week)	Baseline	74.9 ± 11.1 (n=45)	NA	NA	NA
		6 mos.	77.3 ± 13.4 (n=45)	NA	NA	NA
		Δ from baseline	+2.4 ± 11.1 (n=45)	NA	NA	NA
	PedsQL Generic (parents of participants <18 years with CGM use <6 days/week)	Baseline	77.9 ± 12.2 (n=62)	NA	NA	NA
		6 mos.	76.4 ± 12.1 (n=62)	NA	NA	NA
		Δ from baseline	−1.6 ± 10.9 (n=62)	NA	NA	NA
	PedsQL Diabetes-Specific (parents of participants <18 years)	Baseline	76.0±12.1 (n=110)	75.7±14.2 (n=113)	NR	NR
		6 mos.	76.5±11.6 (n=107)	74.6±13.3 (n=107)	NR	0.280
	PedsQL Diabetes-Specific (parents of participants <18 years with CGM use ≥6 days/week)	Baseline	75.3 ± 11.0 (n=45)	NA	NA	NA
		6 mos.	77.9 ± 11.2 (n=45)	NA	NA	NA
		Δ from baseline	+2.6 ± 11.6 (n=45)	NA	NA	NA
	PedsQL Diabetes-Specific (parents of participants <18 years with CGM use <6 days/week)	Baseline	76.3 ± 12.9 (n=62)	NA	NA	NA
		6 mos.	75.4 ± 11.9 (n=62)	NA	NA	NA
		Δ from baseline	−1.4 ± 12.3 (n=62)	NA	NA	NA
Kordonouri 2010 (ONSET) 52 weeks	*HbA1c %*					
	% HbA1c all ages	Baseline	11.2±2.1 (n=76)	11.5±2.2 (n=78)	NA	0.472
		1.5 mos.	7.6±0.9 (n=76)	7.7±0.9 (n=78)	NR	0.561
		6 mos.	7.0±1.0 (n=76)	7.2±1.2 (n=78)	NR	0.368
		12 mos.	7.4±1.2 (n=76)	7.6±1.4 (n=78)	NR	0.451
	% HbA1c age 1-5	Baseline	11.2±2.0 (n=26)	10.5±1.9 (n=21)	NA	0.233
		1.5 mos.	7.8±0.8 (n=26)	7.7±1.0 (n=21)	NR	0.670
		6 mos.	7.1±0.7 (n=26)	7.3±1.2 (n=21)	NR	0.314
		12 mos.	7.3±0.9 (n=26)	7.6±1.0 (n=21)	NR	0.310

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)†	p-value†
	% HbA1c age 6-11	Baseline	10.7±2.3 (n=26)	11.5±2. (n=36)	NA	0.161
		1.5 mos.	7.6±0.9 (n=26)	7.6±0.8 (n=36)	NR	0.929
		6 mos.	6.9±1.0 (n=26)	7.1±1.1 (n=36)	NR	0.382
		12 mos.	7.2±1.0 (n=26)	7.4±1.2 (n=36)	NR	0.562
	% HbA1c age 12-16	Baseline	11.8±1.9 (n=24)	12.3±2.1 (n=21)	NA	0.412
		1.5 mos.	7.5±1.0 (n=24)	8.1±0.9 (n=21)	NR	0.073
		6 mos.	7.0±1.3 (n=24)	7.0±1.3 (n=21)	NR	0.953
		12 mos.	7.7±1.6 (n=24)	7.8±1.9 (n=21)	NR	0.847
	% with HbA1c <7.0%	12 mos.	39.5 (30/76)	33.8 (26/77)	RR 1.17 (0.84 to 1.66) p=0.345††	0.464
	Δ from baseline, HbA1c (%)	12 mos.	-3.8(n=76)	-3.9 (n=78)	NR	NR
	Glucose					
	Fasting Blood Glucose	Baseline	7.3±3.2 (n=76)	7.3±2.8 (n=78)	NR	0.737
	Glucose average, all ages (mmol/l)	12 mos.	8.14±1.55 (n=76)	8.15±1.75 (n=78)	NR	0.966
	Glucose SD (mmol/l)	12 mos.	1.46±0.71 (n=76)	1.76±1.05 (n=78)	NR	0.079
	Ratio of basal to bolus insulin (Number of daily boluses)	12 mos.	7.9±3.6 (n=76)	7.0±2.7 (n=78)	0.9 (-0.88 to 2.68) p=0.319††	0.097
	Ratio of basal to bolus insulin (Proportion of basal rate, %)	12 mos.	34.0±11.8 (n=76)	29.7±10.4 (n=78)	4.3(0.76 to 7.84) p=0.018††	0.021
	Hypoglycemia					
	Severe hypoglycemia (not further spec)	12 mos.	Events: 0 (0) (n=76)	Events: 4 (5%) (n=78)	NA	0.046
	DKA					
	Number of patients experiencing a ketoacidosis event	6 mos.	0	0	NA	NA
		12 mos.	7.4±1.2 (n=76)	7.6±1.4 (n=78)	-0.2 (-0.62 to 0.22) p=0.343††	0.451
	QoL					
	Mother's wellbeing (WHO-5)	Baseline	49.3±23.9 (n=76)	44.7±21.6 (n=78)	NR	0.217
		6 mos.	60.2±22.6 (n=76)	60.7±22.6 (n=78)	NR	0.892
		12 mos.	62.7±18.9 (n=76)	60.8±19.3 (n=78)	NR	0.528
		Baseline	40.4±9.7 (n=76)	38.7±9.2 (n=78)	NR	0.418

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)†	p-value†
	KIDSCREEN-27: Physical wellbeing Proxy/Parent Reported	6 mos.	49.4 ±9.0 (n=76)	46.8±8.8 (n=78)	2.6 (-0.23 to 5.43) p=0.072††	0.114
		12 mos.	50.0±8.1 (n=76)	50.3±9.7 (n=78)	-0.3 (-3.15 to 2.55); p=0.836††	0.879
	KIDSCREEN-27: Physical wellbeing Children Self-Reported	Baseline	43.7±9.4 (n=76)	39.8±8.2 (n=78)	NR	0.058
		6 mos.	49.1±8.5 (n=76)	49.6±9.0 (n=78)	-0.5 (-3.3 to 2.3); p=0.724††	0.685
		12 mos.	51.2±8.8 (n=76)	49.9±8.2 (n=78)	1.3 (-1.4 to 4.0); p=0.344††	0.359
	KIDSCREEN-27: Psychological wellbeing Proxy/Parent Reported	Baseline	40.3±10.5 (n=76)	40.4±10.9 (n=78)	NR	0.890
		6 mos.	48.4±10.4 (n=76)	48.3±10.2 (n=78)	0.1 (-3.18 to 3.38) p=0.952††	0.934
		12 mos.	47.8±9.3 (n=76)	48.6±10.3 (n=78)	-0.8 (-3.93 to 2.33) p=0.614††	0.826
	KIDSCREEN-27: Psychological wellbeing Children Self-Reported	Baseline	45.0±10.6 (n=76)	44.4±11.0 (n=78)	NR	0.847
		6 mos.	49.1±12.7 (n=76)	52.3±10.1 (n=78)	-3.2 (-6.8 to 0.4); p=0.085††	0.153
		12 mos.	50.4±9.2 (n=76)	50.3±10.8 (n=78)	0.1 (-3.1 to 3.3); p=0.951††	0.905
	KIDSCREEN-27: Autonomy and parents Proxy/Parent Reported	Baseline	50.3±10.4 (n=76)	49.5±8.6 (n=78)	NR	0.594
		6 mos.	51.4±11.2 (n=76)	50.4±8.9 (n=78)	1.0 (-2.22 to 4.22) p=0.540††	0.570
		12 mos.	52.6±11.2 (n=76)	50.9±10.1 (n=78)	1.7 (-1.69 to 5.09) p=0.324††	0.206
	KIDSCREEN-27: Autonomy and parents Children Self-Reported	Baseline	51.1±8.5 (n=76)	48.8±9.6 (n=78)	NR	0.313
		6 mos.	50.7±10.6 (n=76)	51.4±11.01 (n=78)	-0.7 (-4.14 to 2.74) p=0.688††	0.648
		12 mos.	52.5±10.0 (n=76)	50.2±9.9(n=78)	2.3 (-0.87 to 5.47); p=0.154††	0.158
	KIDSCREEN-27: Social support and peers Proxy/Parent Reported	Baseline	44.5±14.9 (n=76)	44.7±13.3 (n=78)	NR	0.998
		6 mos.	50.3±9.9 (n=76)	50.7±10.4 (n=78)	-0.4 (-3.63 to 2.83) p=0.807††	0.826
		12 mos.	51.1±10.2 (n=76)	51.3±8.9 (n=78)	-0.2 (-3.25 to 2.85) p=0.897††	0.860

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)†	p-value†
	KIDSCREEN-27: Social support and peers Children Self-Reported	Baseline	47.1±11.0 (n=76)	44.2±10.7(n=78)	NR	0.370
		6 mos.	53.3±9.2 (n=76)	50.9±9.6 (n=78)	2.4 (-0.60 to 5.40) p=0.115††	0.262
		12 mos.	52.4±9.6 (n=76)	50.8±9.0 (n=78)	1.6 (-1.36 to 4.56) p=0.288††	0.377
	KIDSCREEN-27: School environment Proxy/Parent Reported	Baseline	45.8±14.0 (n=76)	47.1±11.6 (n=78)	NR	0.511
		6 mos.	50.9±12.1 (n=76)	50.6±9.0 (n=78)	0.3 (-3.09 to 3.69) p=0.861††	0.854
		12 mos.	51.4±10.1 (n=76)	50.9±9.2 (n=78)	0.5 (-2.57 to 3.57) p=0.748††	0.792
	KIDSCREEN-27: School environment Children Self-Reported	Baseline	47.4±11.7 (n=76)	45.4±10.1 (n=78)	NR	0.612
		6 mos.	49.7±11.7 (n=76)	51.3±10.1 (n=78)	-1.6 (-5.08 to 1.88) p=0.365††	0.493
		12 mos.	52.8±9.8 (n=76)	51.3±10.2 (n=78)	1.5 (-1.69 to 4.69) p=0.354††	0.436
Mauras 2012 Study Period: 6 mos.	% who experienced ≥0.5% reduction in HbA1c with no severe hypoglycemic event	6 mos.	19.0% (13/69)	28.0% (19/68)	RR 0.67 (0.61 to 1.40) p=0.692††	0.170
	% who experienced ≥0.5% reduction in HbA1c	6 mos.	20.0% (14/69)	29.0% (20/68)	RR 0.68 (0.61 to 1.39) p=0.693††	0.170
	% who experienced ≥0.5% increase in HbA1c	6 mos.	16.0% (11/69)	22.0% (15/68)	RR 0.72 (0.63 to 1.51) p=0.901††	0.280
	% with <7.0% HbA1c level	6 mos.	16.0% (11/69)	15.0% (10/68)	RR 0.72 (0.63 to 1.51) p=0.901††	0.750
	Mean Δ from baseline, HbA1c	Baseline	7.9±0.8 (n=74)	7.9±0.8 (n=72)	NR	NR
		6 mos.	-0.1±0.6 (n=69)	-0.1±0.6 (n=68)	NR	0.790
	CGM glucose values (mg/dL) (% median) ≤60	Baseline	1.0 (n=74)	0.7 (n=72)	NR	NR
		6 mos.	0.4 (n=69)	0.6 (n=68)	NR	0.310
	CGM glucose values (mg/dL) (% median) ≤70	Baseline	2.2 (n=74)	2.5 (n=72)	NR	NR
		6 mos.	1.5 (n=69)	2.1 (n=68)	NR	0.780
	CGM glucose values (mg/dL) (% median) 71 to 180	Baseline	46 (n=74)	47 (n=72)	NR	NR
		6 mos.	48 (n=69)	49 (n=68)	NR	0.600
		Baseline	44 (n=74)	39 (n=72)	NR	NR

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)†	p-value†
	CGM glucose values (mg/dL) (% median) >200	6 mos.	39 (n=69)	41 (n=68)	NR	0.720
	CGM glucose values (mg/dL) (% median) >250	Baseline	23 (n=74)	22 (n=72)	NR	NR
		6 mos.	20 (n=69)	22 (n=68)	NR	0.180
	Severe Hypoglycemia	6 mos.	Events: 3 (n=69)	Events: 6 (n=68)	NR	NR
	Subjects with at least 1 event	6 mos.	4.0% (3/69)	7.0 (5/68)	RR 0.49 (0.60 to 1.70) p=0.969††	0.490
	Incidence rate of Severe Hypoglycemia per 100 person-years	6 mos.	8.6 (n=69)	17.6 (n=68)	NR	0.800
	Diabetic Ketoacidosis	6 mos.	Events: 0	Events: 0	IC	IC
	QoL					
	PAID	Baseline	52±15 (n=74)	55±16 (n=72)	NR	NR
		6 mos.	44±17 (n=69)	49±16 (n=68)	NR	0.420
	Hypoglycemia Fear Survey	Baseline	45±17 (n=74)	47±19 (n=72)	NR	NR
		6 mos.	38±17 (n=69)	42±19 (n=68)	NR	0.380
Rubin 2012 Follow-up trial of Bergenstal 2010 *also reports data on adults 6 mos.	*QoL*					
	Δ from baseline, Peds QL Psychosocial Health Summary Score (Participants <18 years)	Baseline	78.38±14.59 (n=77)	78.76±10.27 (n=70)	NR	NR
		Δ 12 mos.	3.39 (n=77)	3.64 (n=70)	Diff. -0.25 (NR)	NR
	Δ from baseline, Peds QL Physical Health Summary Score (Participants <18 years)	Baseline	86.99±12.93 (n=77)	88.37±11.16 (n=70)	NR	NR
		Δ 12 mos.	2.53 (n=77)	1.41 (n=70)	Diff. 1.12 (NR)	NR
	Δ from baseline, HFS Worry subscale (Participants <18 years)	Baseline	28.88±9.74 (n=77)	26.97±8.06 (n=70)	NR	NR
		Δ 12 mos.	-3.62 (n=77)	-2.43 (n=70)	Diff. 1.19 (NR)	NR
	Δ from baseline, HFS Avoidant subscale (Participants <18 years)	Baseline	30.60±5.43 (n=77)	29.70±**6**.04 (n=70)	NR	NR
		Δ 12 mos.	-4.01 (n=77)	-2.25 (n=70)	Diff. 1.76 (NR)	NR
	Δ from baseline, Peds QL Psychosocial Health Summary Score (Parents of participants <18 years)	Baseline	78.61±12.87 (n=77)	73.27±13.36 (n=70)	NR	NR
		Δ 12 mos.	4.06 (n=77)	3.06 (n=70)	Diff. 1.00 (NR)	NR
	Δ from baseline, Peds QL Physical Health Summary Score	Baseline	87.92±10.58 (n=77)	85.53±13.06 (n=70)	NR	NR
		Δ 12 mos.	0.94(n=77)	0.01 (n=70)	Diff. 0.93 (NR)	NR

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)†	p-value†
	(Parents of participants <18 years)					
	Δ from baseline, HFS Worry subscale (Parents of participants <18 years)	Baseline	42.49±10.11 (n=77)	43.21±12.28 (n=70)	NR	NR
		Δ 12 mos.	-3.64 (n=77)	-1.56 (n=70)	Diff. 2.08	NR
	Δ from baseline, HFS Avoidant subscale (Parents of participants <18 years)	Baseline	31.65±6.56 (n=77)	30.94±5.63 (n=70)	NR	NR
		Δ 12 mos.	-4.16 (n=77)	-1.07 (n=70)	3.09	<0.01
Slover 2012 Subset of the STAR3 trial (Bergenstal 2010) Study Period: 12 months	*HbA1c*					
	HbA1c (%) all ages	Baseline	8.26±0.54	8.30±0.53	NR	0.05
	HbA1c (%) (participants aged 7-12)	Baseline	8.21±0.56(n=43)	8.19±0.51(n=39)	NR	NR
		12 mos.	7.75 SEM (0.20) (n=43)	8.2 SEM (0.20) (n=39)	NR	NR
	HbA1c (%) (participants aged 13-18)	Baseline	8.33±0.53 (n=35)	8.40±0.54 (n=39)	NR	NR
		12 mos.	8.0 SEM (0.30) (n=35)	8.75 SEM (0.30) (n=39)	NR	NR
	% meeting HbA1c <8% (participants aged 7-12)	Baseline	39.0% (17/43)	35.0% (15/39)	NR	NR
		12 mos.	60.0% (26/43)	35.0% (15/39)	RR 1.57(0.95 to 1.98) p=0.085	NR
	% meeting HbA1c <7.5% (participants aged 13-18)	Baseline	5.0% (2/35)	0.0% (0/39)	NR	NR
		12 mos.	22.0% (8/35)	2.5%‡‡ (1/39)	RR 8.91 (0.94 to 2.72) p=0.081	NR
	AUC					
	AUC >250 mg/dL (participants aged 7-12) §	Baseline	15.47±11.39 (n=43)	19.72±9.87 (n=39)	NR	NR
		12 mos.	10.16 ± 8.56 (n=43)	16.35±9.61 (n=39)	NR	0.011
	AUC >250 mg/dL (participants aged 13-18) §	Baseline	11.96±10.43 (n=35)	12.64 ± 9.93 (n=39)	NR	NR
		12 mos.	8.09 ± 7.47 (n=35)	19.05 ± 18.67 (n=39)	NR	0.002
	AUC >180 mg/dL (participants aged 7-12) §	Baseline	43.08 ± 22.05 (n=43)	51.24 ± 18.46 (n=39)	NR	NR
		12 mos.	32.04 ± 17.75 (n=43)	44.05 ± 18.40 (n=39)	NR	0.012
	AUC >180 mg/dL (participants aged 13-18) §	Baseline	34.79 ± 20.66 (n=35)	37.95 ± 20.20 (n=39)	NR	NR
		12 mos.	27.88 ± 16.85 (n=35)	46.65 ± 31.84 (n=39)	NR	0.002

			Results (mean±SD or %(n/N))			
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**	Effect Estimate (95% CI)†	p-value†
	AUC <70 mg/dL (participants aged 7-12) §	Baseline	0.16 ± 0.29 (n=43)	0.12 ± 0.23 (n=39)	NR	NR
		12 mos.	0.23 ± 0.45 (n=43)	0.24 ± 0.38 (n=39)	NR	0.940
	AUC <70 mg/dL (participants aged 13-18)	Baseline	0.38 ± 0.48 (n=35)	0.35 ± 0.57 (n=39)	NR	NR
		12 mos.	0.23 ± 0.38 (n=35)	0.25 ± 0.44 (n=39)	NR	0.920
	AUC <60 mg/dL (participants aged 7-12) §	Baseline	0.04 ± 0.1 (n=43)	0.04 ± 0.09 (n=39)	NR	NR
		12 mos.	0.09 ± 0.24 (n=43)	0.07 ± 0.16 (n=39)	NR	0.500
	AUC <60 mg/dL (participants aged 13-18)	Baseline	0.11 ± 0.18 (n=35)	0.12 ± 0.25 (n=39)	NR	NR
		12 mos.	0.06 ± 0.13 (n=35)	0.07 ± 0.16 (n=39)	NR	0.870
	Standard Deviation of Sensor Glucose values (participants aged 7-12)	Baseline	77.34±16.23 (n=43)	83.79±13.70(n=39)	NR	NR
		12 mos.	70.12±16.13 (n=43)	80.61±12.59(n=39)	NR	0.009
	Standard Deviation of Sensor Glucose values (participants aged 13-18)	Baseline	75.66±16.23 (n=35)	66.01±14.67(n=39)	NR	NR
		12 mos.	74.35±12.54 (n=35)	81.81±18.29(n=39)	NR	<0.001

AUC, area under the curve; BMI, body mass index; CGM, continuous glucose monitoring; CI, confidence interval; CSII, continuous subcutaneous insulin infusion; IC, incalculable; HbA1c, hemoglobin A1c; mos., months; mmol/l, millimoles per liter; NR, not reported; T1DM, type 1 diabetes mellitus;

* Results are reported as either a mean or a percent. Confidence intervals or standard deviations are reported in parenthesis.

† As reported by the authors.

‡ Change from baseline to 12 months, pump therapy vs injection therapy.

§ AUC is a measure of duration and severity of hypoglycemia or hyperglycemia (units = mg/dL*min/day)

** Change from baseline to 26 weeks between arms

†† Calculated by AAI.

‡‡ Estimated from graph.

§§ Data not stratified by age

*** Includes data for an adult population —abstraction can be found in corresponding adult ages sections

††† Quality of life data taken from Lawrence 2010, a follow-up study to JDRF 2008. This data was only available for age <18 and their parents, and for >18 populations.

Appendix Table G2. Efficacy Outcomes from RCTs Evaluating CGM versus SMBG in Adults with Type 1 Diabetes Mellitus

			Results (mean±SD or %(n/N))			
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**	**Effect Estimate (95% CI)**	**p-value**
Beck 2017 (DIAMOND) Polonsky 2017	*HbA1c %*					
	HbA1c %, mean (SD)	Baseline	8.6±0.7 (n=105)	8.6±0.6 (n=53)	NR	NR
		3 mos.	7.6±0.7 % (n=103)	8.1±0.7 % (n=52)	NR	NR
		6 mos.	7.7±0.8 % (n=105)	8.2±0.8 % (n=53)	NR	NR
	Change in HbA1c levels	3 mos.	-1.1±0.7 %(n=103)	-0.5 ±0.7 % (n=52)	NR	NR
		6 mos.	-1.0 ±0.8 %(n=105)	-0.4 ±0.7 % (n=53)	Adj. MD -0.6% (-0.8% to -0.3%)	<0.001
	% HbA1c <7.0%, no (%)	3 mos.	14 (14%) (n=103)	2 (4%) (n=52)	NR	NR
		6 mos.	18 (18%) (n=105)	2 (4%) (n=53)	Adj. MD 15% (0% to 30%)*	0.1
	% HbA1c <7.5%, no (%)	3 mos.	49 (48%) (n=103)	6 (12%) (n=52)	NR	NR
		6 mos.	39 (38%) (n=105)	6 (11%) (n=53)	Adj. MD 31% (12% to 51%)*	<0.001
	Relative reduction in HbA1c ≥10%, no (%)	3 mos.	62 (60%) (n=103)	12 (23%) (n=52)	NR	NR
		6 mos.	58 (57%) (n=105)	10 (19%) (n=53)	Adj. MD 37% (16% to 58%)*	<0.001
	Reduction in % HbA1c ≥1%, no (%)	3 mos.	55 (53%) (n=103)	12 (23%) (n=52)	NR	NR
		6 mos.	53 (52%) (n=105)	10 (19%) (n=53)	Adj MD 33% (11% to 54%)*	<0.001
	Reduction in % HbA1c ≥1% or HbA1c <7.0%, no (%)	3 mos.	57 (55%) (n=103)	12 (23%) (n=52)	NR	NR

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)	p-value
		6 mos.	53 (52%) (n=105)	11 (21%) (n=53)	Adj MD 31% (9% to 52%)*	<0.001
	Hypoglycemia					
	Minutes per day <70 mg/dl, median (IQR)	Baseline	65 (33 to 103) (n=105)	72 (35 to 136) (n=53)	NR	NR
		3 mos.	49 (20-69) (n=102)	65 (29-124) (n=51)	NR	NR
		6 mos.	33 (14-72) (n=99)	55 (24-116) (n=53)	NR	0.002
	Minutes per day <60mg/dl, median (IQR)	Baseline	32 (15 to 61) (n=105)	39 (15 to 78) (n=53)	NR	NR
		3 mos.	21 (7-36) (n=102)	27 (9-86) (n=51)	NR	NR
		6 mos.	15 (4-29) (n=99)	31 (6-72) (n=53)	NR	0.002
	Minutes per day <50 mg/dl, median (IQR)	Baseline	13 (5 to 29) (n=105)	18 (4 to 39) (n=53)	NR	NR
		3 mos.	13 (5-29) (n=102)	18 (4-39) (n=51)	NR	NR
		6 mos.	4 (0-11) (n=99)	8 (1-33) (n=53)	NR	0.001
	Area above curve 70 mg/ml, median (IQR)	Baseline	0.5 (0.3 to 1.1) (n=105)	0.7 (0.2 to 1.4) (n=53)	NR	NR
		3 mos.	0.4 (0.1-0.6) (n=102)	0.4 (0.2-1.5) (n=51)	NR	NR
		6 mos.	0.3 (0.1-0.5) (n=99)	0.6 (0.1-1.1) (n=53)	NR	<0.001
	Hyperglycemia					
	Minutes per day >180 mg/dl, median (IQR)	Baseline	687 (554 to 810) (n=105)	725 (537 to 798) (n=53)	NR	NR

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)	p-value
		3 mos.	663 (486-809) (n=102)	666 (579-878) (n=51)	NR	NR
		6 mos.	604 (460-814) (n=99)	734 (626-896) (n=53)	NR	0.030
	Minutes per day >250 mg/dl, median (IQR)	Baseline	301 (190 to 401) (n=105)	269 (184 to 383) (n=53)	NR	NR
		3 mos.	226 (135-366) (n=102)	297 (197-419) (n=51)	NR	NR
		6 mos.	208 (112-352) (n=99)	352 (230-460) (n=53)	NR	<0.001
	Minutes per day >300 mg/dl, median (IQR)	Baseline	129 (66 to 201) (n=105)	109 (71 to 204) (n=53)	NR	NR
		3 mos.	70 (28-147) (n=102)	123 (47-219) (n=51)	NR	NR
		6 mos.	71 (30-140) (n=99)	171 (75-228) (n=53)	NR	<0.001
	Area under curve 180 mg/dl, median (IQR)	Baseline	34 (25 to 46) (n=105)	33 (26 to 45) (n=53)	NR	NR
		3 mos.	29 (18-41) (n=102)	34 (24-49) (n=51)	NR	NR
		6 mos.	26 (16-42) (n=99)	41 (27-54) (n=53)	NR	<0.001
	Severe hypoglycemic events (n/N)	6 mos.	1.9% (2/105)	3.8%(2/53)	NR	0.67
	Euglycemia					
	Minutes per day in range 70-180 mg/dl, mean (SD)	Baseline	660 ±179 (n=105)	650±170 (n=53)	NR	NR
		3 mos.	727±222 (n=102)	667±224 (n=51)	NR	NR
		6 mos.	740±223 (n=99)	639±210 (n=53)	NR	NR

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)	p-value
	Ketoacidosis					
	Diabetic ketoacidosis events (n/N)	6 mos.	0% (0/105)	0% (0/53)	IC	IC
	QoL measures†					
	World Health Organization (five) Well-Being Index (WHO-5), mean (SD)	Baseline	71.3±14.7 (n=102)	69.1±14.9 (n=53)	NR	NR
		6 mos.	70.5 ±16.7 (n=102)	67.3±16.9 (n=53)	Model 1: MD -1.3 (-5.4 to 2.9) Model 2: MD -1.6 (-5.9 to 2.6)	Model 1: 0.62 Model 2 : 0.50
	EQ-5D-5L, mean (SD)	Baseline	0.90±0.11 (n=102)	0.89±0.11 (n=53)	NR	NR
		6 mos.	0.89±0.10 (n=102)	0.88±0.10 (n=53)	Model 1: MD 0.00 (-0.03 to 0.03) Model 2: MD 0.00 (-0.03 to 0.03)	Model 1: 0.86 Model 2: 0.92
	Diabetes Distress Scale (DDS) Total, mean (SD)	Baseline	1.8±0.7 (n=102)	1.7±0.6 (n=53)	NR	NR
		6 mos.	1.6±0.5 (n=102)	1.8±0.7 (n=53)	Model 1: MD 0.22 (0.08 to 0.4) Model 2: MD 0.23 (0.09 to 0.4)	Model 1: 0.009 Model 2: 0.03
	DDS Regimen subscale, mean (SD)	Baseline	2.1±0.9 (n=102)	2.1±1.0 (n=53)	NR	NR
		6 mos.	1.8±0.7 (n=102)	2.1±0.9 (n=53)	Model 1: MD 0.25 (0.05 to 0.46)	Model 1: 0.04 Model 2: 0.04

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)	p-value
					Model 2: MD 0.26 (0.05 to 0.47)	
	DDS Emotional Burden subscale, mean (SD)	Baseline	2.1±0.9 (n=102)	1.9±0.8 (n=53)	NR	NR
		6 mos.	1.9±0.8 (n=102)	2.0±1.0 (n=53)	Model 1: MD 0.21 (0.01 to 0.41) Model 1: MD 0.21 (0.00 to 0.41)	Model 1: 0.08 Model 2: 0.09
	DDS Interpersonal subscale, mean (SD)	Baseline	1.5±0.8 (n=102)	1.5±0.7 (n=53)	NR	NR
		6 mos.	1.4±0.6 (n=102)	2.0±1.0 (n=53)	Model 1: MD 0.37 (0.16 to 0.56) Model 2: MD 0.37 (0.16 to 0.58)	Model 1: 0.009 Model 2: 0.01
	DDS Physician subscale, mean (SD)	Baseline	1.2±0.6 (n=102)	1.1±0.3 (n=53)	NR	NR
		6 mos.	1.1±0.3 (n=102)	1.2±0.7 (n=53)	Model 1: MD 0.10 (-0.04 to 0.25) Model 2: MD 0.12 (-0.03 to 0.27)	Model 1: 0.12 Model 2: 0.18
	Hypoglycemic Confidence Scale (HCS), mean (SD)	Baseline	3.3±0.6 (n=102)	3.2±0.6 (n=53)	NR	NR
		6 mos.	3.5±0.6 (n=102)	3.2±0.6 (n=53)	Model 1: MD 0.2 (0.06 to 0.4) Model 2: MD 0.2 (0.05 to 0.4)	Model 1: 0.03 Model 2: 0.03

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)	p-value
	Hypoglycemic Fear Survey (HFS-II), mean (SD)	Baseline	15.8±12.3 (n=102)	17.3±13.2 (n=53)	NR	NR
		6 mos.	13.5±10.6 (n=102)	17.7±14.9 (n=53)	Model 1: MD 3.2 (0.2 to 6.1) Model 2: MD 2.5 (-0.6 to 5.5)	Model 1: 0.07 Model 2: 0.15
	Clarke Hypoglycemia Unawareness Questionnaire, mean (SD)	Baseline	2.1±1.8 (n=102)	2.7 ±2.1 (n=53)	NR	NR
		6 mos.	2.0±1.8 (n=102)	2.5 ±2.1 (n=53)	NR	NR
	Usage					
	Average number of days of usage per week, median (IQR)	1 month	7.0 (7.0-7.0)	NA	NA	NA
		3 mos.	7.0 (7.0-7.0)	NA	NA	NA
		6 mos.	7.0 (7.0-7.0)	NA	NA	NA
	% of subjects with zero use, no (%)	1 month	0 (0%)	NA	NA	NA
		3 mos.	1 (<1)	NA	NA	NA
		6 mos.	2 (2)	NA	NA	NA
	% of subjects with < 1 day of use, no (%)	1 month	0 (0%)	NA	NA	NA
		3 mos.	0 (0%)	NA	NA	NA
		6 mos.	0 (0%)	NA	NA	NA
	% of subjects with 1 to < 2 days of use, no (%)	1 month	0 (0%)	NA	NA	NA

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)	p-value
		3 mos.	0 (0%)	NA	NA	NA
		6 mos.	0 (0%)	NA	NA	NA
	% of subjects with 2 to < 3 days of use, no (%)	1 month	0 (0%)	NA	NA	NA
		3 mos.	0 (0%)	NA	NA	NA
		6 mos.	0 (0%)	NA	NA	NA
	% of subjects with 3 to < 4 days of use, no (%)	1 month	1 (1%)	NA	NA	NA
		3 mos.	0 (0%)	NA	NA	NA
		6 mos.	0 (0%)	NA	NA	NA
	% of subjects with 4 to < 5 days of use, no (%)	1 month	0 (0%)	NA	NA	NA
		3 mos.	0 (0%)	NA	NA	NA
		6 mos.	1 (1%)	NA	NA	NA
	% of subjects with 5 to < 6 days of use, no (%)	1 month	0 (0%)	NA	NA	NA
		3 mos.	3 (3%)	NA	NA	NA
		6 mos.	4 (4%)	NA	NA	NA
	% of subjects with 6 to < 7 days of use, no (%)	1 month	11 (11%)	NA	NA	NA

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)	p-value
		3 mos.	7 (7%)	NA	NA	NA
		6 mos.	12 (12%)	NA	NA	NA
	% of subjects with 7 days of use, no (%)	1 month	88 (88%)	NA	NA	NA
		3 mos.	92 (89%)	NA	NA	NA
		6 mos.	79 (81%)	NA	NA	NA
	% of subjects with < 6 days of use, no (%)	1 month	1 (1%)	NA	NA	NA
		3 mos.	4 (4%)	NA	NA	NA
		6 mos.	7 (7%)	NA	NA	NA
	% of subjects with ≥ 6 days of use, no (%)	1 month	99 (99%)	NA	NA	NA
		3 mos.	99 (96%)	NA	NA	NA
		6 mos.	91 (93%)	NA	NA	NA
Bergenstal 2010‡	*HbA1c %*					
	HbA1c %, mean (SD)§	Baseline	8.3±0.5 % (n=166)	8.3±0.5 % (n=163)	NR	NR
		3 mos.	7.26% (n=166)	7.79% (n=163)	NR	<0.001
		6 mos.	7.32% (n=166)	7.83% (n=163)	NR	<0.001
		9 mos.	7.32% (n=166)	7.83% (n=163)	NR	<0.001

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)	p-value
		12 mos.	7.31% (n=166)	7.92% (n=163)	NR	<0.001
	Δ from baseline, HbA1c %, mean (SD)	12 mos.	-1.0 ±0.7 % (n=166)	-0.4 ±0.8 % (n=163)	-0.6 (-0.8 to -0.4)	<0.001
	% patients achieving target HbA1c < 7%	12 mos.	34% (n=166)	12% (n=163)	NR	<0.001
	Change in HbA1c % based on frequency (% of time) of sensor use**	0-20% frequency	-0.43%	NA	NA	NA
		21-40% frequency	-0.19%	NA	NA	NA
		41-60% frequency	-0.64%	NA	NA	NA
		61-80% frequency	-0.79%	NA	NA	NA
		81-100% frequency	-1.21%	NA	NA	NA
	Hypoglycemia					
	Rate of hypoglycemia at 1 year, person-year	12 mos.	15.31/100 (n=169)	17.62/100 (n=167)	NR	0.66
	AUC < 70 mg/dl*min, mean (SD)	Baseline	0.28 ±0.54 (n=169)	0.31±0.49 (n=167)	NR	NR
		12 mos.	0.25 ±0.44 (n=169)	0.29±0.55 (n=167)	NR	0.63
	AUC < 50 mg/dl*min, mean (SD)	Baseline	0.02 ±0.10 (n=169)	0.02±0.07 (n=167)	NR	NR
		12 mos.	0.02 ±0.04 (n=169)	0.03±0.09 (n=167)	NR	0.16
	Hyperglycemia					
	AUC > 250 mg/dl*min, mean (SD)	Baseline	8.16±8.31 (n=169)	7.98±7.98 (n=167)	NR	NR

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)	p-value
		12 mos.	3.74±5.01 (n=169)	7.38±8.62 (n=167)	NR	<0.001
	AUC > 180 mg/dl*min, mean (SD)	Baseline	28.92±17.80 (n=169)	28.04±17.03 (n=167)	NR	NR
		12 mos.	16.06±12.84 (n=169)	26.01±19.52 (n=167)	NR	<0.001
	Ketoacidosis					
	Rate of ketoacidosis at 1 year, person-year	12 mos.	0.01/100 (n=169)	0 (n=167)	NR	NR
	QoL measures					
	Δ from baseline, SF-36 PCS (Participants ≥18 years)	Baseline	49.86±9.64 (n=166)	49.50±9.09 (n=168)	NR	NR
		12 mos.	0.05 (n=166)	-1.26 (n=168)	Diff. -1.31 (NA)	NR
	Δ from baseline, SF-36 MCS (Participants ≥18 years)	Baseline	50.61±7.12 (n=166)	50.97±7.86 (n=168)	NR	NR
		Δ 12 mos.	1.22 (n=166)	0.26 (n=168)	Diff. -0.96 (NA)	NR
	Δ from baseline, HFS Worry subscale (Participants ≥18 years)	Baseline	21.96±14.34 (n=166)	21.52±13.37 (n=168)	NR	NR
		Δ 12 mos.	-6.36 (n=166)	-1.87 (n=168)	Diff. 4.49 (NA)	<0.001
	Δ from baseline, HFS Avoidant subscale (Participants ≥18 years)	Baseline	16.38±8.24 (n=166)	16.70±8.00 (n=168)	NA	NR
		Δ 12 mos.	-2.30 (n=166)	-0.52 (n=168)	Diff. 1.78 (NA)	<0.01
Bolinder 2016	*HbA1c %*					
	HbA1c %, mean (SD)	Baseline	6.79 (0.52)	6.78 (0.64)	NR	NR
		3 mos	6.85 (0.65)	6.92 (0.67)	Adj MD -0.06 (0.05)	0.232

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)	p-value
		6 mos	6.94 (0.65)	6.95 (0.66)	Adj MD 0.00 (0.06)	0.956
	Hypoglycemia					
	Hypoglycemia <70 mg/dL hours/day	Baseline	3.38 (2.31)	3.44 (2.62)	NR	NR
		3 mos	1.91 (1.42)	3.03 (2.21)	Adj MD -1.09 (0.18)	<0.0001
		6 mos	2.03 (1.93)	3.27 (2.58)	Adj MD -1.24 (0.24)	<0.0001
	Hypoglycemic events <70 mg/dL	Baseline	1.81 (0.90)	1.67 (0.80)	NR	NR
		3 mos	1.30 (0.77)	1.59 (0.83)	Adj MD -0.35 (0.09)	<0.0001
		6 mos	1.32 (0.81)	1.69 (0.83)	-0.45 (0.09)	<0.0001
	AUC <70 mg/dL hours/day	Baseline	53.42 (43.56)	58.34 (57.22)	NR	NR
		3 mos	NR	NR	NR	NR
		6 mos	28.58 (31.15)	54.67 (60.08)	Adj MD -25.14 (5.32)	<0.0001
	Nocturnal hypoglycemia <70 mg/dL hours/day	Baseline	1.32 (1.07)	1.48 (1.29)	NR	NR
		3 mos	0.72 (0.70)	1.26 (0.99)	Adj MD -0.48 (0.10)	<0.0001
		6 mos	0.68 (0.97)	1.23 (1.10)	Adj MD -0.47 (0.12)	<0.0001
	Nocturnal hypoglycemic events <70 mg/dL	Baseline	0.47 (0.32)	0.46 (0.29)	NR	NR
		3 mos	0.31 (0.28)	0.42 (0.28)	Adj MD -0.11 (0.03)	0.0010

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)	p-value
		6 mos	0.27 (0.23)	0.40 (0.29)	Adj MD -0.14 (0.03)	<0.0001
	Hypoglycemia <55 mg/dL hours/day	Baseline	1.59 (1.42)	1.77 (1.86)	NR	NR
		3 mos	0.74 (0.75)	1.48 (1.57)	Adj MD -0.68 (0.13)	<0.0001
		6 mos	0.80 (0.96)	1.65 (1.97)	Adj MD -0.82 (0.175)	<0.0001
	AUC <55 mg/dL hours/day	Baseline	16.04 (17.46)	18.94 (23.22)	NR	NR
		3 mos	NR	NR	NR	NR
		6 mos	7.59 (10.25)	17.69 (26.34)	Adj MD -9.67 (2.29)	<0.0001
	Nocturnal hypoglycemia <55 mg/dL hours/day	Baseline	0.62 (0.60)	0.75 (0.83)	NR	NR
		3 mos	NR	NR	NR	NR
		6 mos	0.31 (0.43)	0.66 (0.08)	Adj MD -0.32 (0.07)	<0.0001
	Nocturnal hypoglycemic events <55 mg/dL	Baseline	0.34 (0.27)	0.36 (0.34)	NR	NR
		3 mos	NR	NR	NR	NR
		6 mos	0.19 (0.24)	0.30 (0.28)	Adj MD -0.11 (0.03)	0.0005
	Hypoglycemia <45 mg/dL hours/day	Baseline	0.85 (1.03)	1.04 (1.36)	NR	NR
		3 mos	NR	NR	NR	NR
		6 mos	0.38 (0.58)	0.96 (1.57)	Adj MD -0.55 (0.14)	<0.0001
	AUC <45 mg/dL hours/day	Baseline	3.99 (5.36)	5.00 (7.10)	NR	NR
		3 mos	NR	NR	NR	NR
		6 mos	1.74 (2.91)	4.73 (8.66)	Adj MD -2.88 (0.75)	0.0002
	Nocturnal hypoglycemia <45 mg/dL hours/day	Baseline	0.36 (0.44)	0.48 (0.66)	NR	NR
		3 mos	NR	NR	NR	NR

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)	p-value
		6 mos	0.15 (0.25)	0.43 (0.65)	Adj MD -0.25 (0.06)	<0.0001
	Hypoglycemia <40 mg/dL hours/day	Baseline	0.59 (0.85)	0.75 (1.11)	NR	NR
		3 mos	0.23 (0.34)	0.60 (1.02)	Adj MD -0.33 (0.09)	0.0003
		6 mos	0.26 (0.47)	0.73 (1.41)	Adj MD -0.46 (0.12)	0.0003
	Hypoglycemic events <40 mg/dL	Baseline	0.39 (0.43)	0.44 (0.51)	NR	NR
		3 mos	0.17 (0.23)	0.36 (0.50)	Adj MD -0.18 (0.05)	<0.0001
		6 mos	0.19 (0.29)	0.43 (0.55)	Adj MD -0.22 (0.05)	<0.0001
	Events of severe hypoglycemia	6 months	2% (2/119) (2 events)	3% (3/120) (4 events)	0.67 (0.11 to 3.95)††	0.65††
	Hyperglycemia					
	Hyperglycemia >180 mg/dL hours/day	Baseline	5.62 (2.48)	5.80 (3.11)	NR	NR
		3 mos	NR	NR	NR	NR
		6 mos	6.16 (3.05)	6.08 (3.20)	Adj MD 0.19 (0.329)	0.5623
	Hyperglycemia >240 mg/dL hours/day	Baseline	1.85 (1.44)	1.91 (1.70)	NR	NR
		3 mos	1.73 (1.41)	2.36 (2.06)	Adj MD -0.60 (0.19)	0.0016

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)	p-value
		6 mos	1.67 (1.36)	2.06 (1.61)	Adj MD -0.37 (0.16)	0.025
	Hyperglycemia >300 mg/dL hours/day	Baseline	0.48 (0.58)	0.49 (0.69)	NR	NR
		3 mos	NR	NR	NR	NR
		6 mos	0.34 (0.46)	0.44 (0.54)	Adj MD -0.11 (0.06)	0.0684
	Target Glycemic Range					
	Time with glucose 70-180 mg/dL hours/day	Baseline	15.0 (2.5)	14.8 (2.8)	NR	NR
		3 mos	16.0 (2.8)	14.3 (3.1)	Adj MD 1.6 (0.30)	<0.0001
		6 mos	15.8 (2.9)	14.6 (2.9)	Adj MD 1.0 (0.30)	0.0006
	QoL‡‡					
	DTSQ total treatment satisfaction, mean (95% CI) PP population	6 mos	13.9 (12.2 to 14.6)	6.8 (5.4 to 8.1)	NR	<0.0001
	DTSQ perceived frequency of hyperglycemia, mean (95% CI) PP population	6 mos	-0.52 (-0.20 to -0.82)	0.46 (0.16 to 0.81)	NR	<0.0001
	DTSQ perceived frequency of hypoglycemia, mean (95% CI) PP population	6 mos	-0.26 (-0.61 to 0.02)	0.13 (-0.22 to 0.45)	NR	0.0629
	DTSQ total treatment satisfaction, mean (95% CI) full analysis population	6 mos	13.3 (12.0 to 14.4)	7.3 (5.6 to 8.5)	Adj MD 6.1 (0.84)	<0.0001
	DTSQ perceived frequency of hyperglycemia, mean (95% CI) full analysis population	6 mos	-0.60 (-0.24 to -0.86)	0.40 (0.08 to 0.76)	Adj MD-1.0 (0.22)	<0.0001

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
			Intervention	Control		
	DTSQ perceived frequency of hypoglycemia, mean (95% CI) full analysis population	6 mos	-0.32 (0.0 to -0.64)	0.08 (-0.28 to 0.42)	NR	0.0713
	DQoL total scale, mean (95% CI), PP population	6 mos	1.96 (1.90 to 2.02)	2.04 (1.98 to 2.10)	NR	0.0466
	DQoL satisfaction with treatment subscale, mean (95% CI), PP population	6 mos	1.87 (1.80 to 1.95)	2.11 (2.02 to 2.20)	NR	<0.0001
	DQoL social worry subscale, mean (95% CI), PP population	6 mos	1.78 (1.67 to 1.89)	1.75 (1.63 to 1.87)	NR	0.7661
	DQoL diabetes worry subscale, mean (95% CI), PP population	6 mos	1.96 (1.86 to 2.10)	2.07 (1.94 to 2.20)	NR	0.2504
	DQoL impact of treatment subscale, mean (95% CI), PP population	6 mos	2.11 (2.05 to 2.18)	2.12 (2.07 to 2.19)	NR	0.5041
	DQoL total scale, mean (95% CI), full analysis population	6 mos	1.95 (189 to 2.01)	2.03 (1.97 to 2.09)	Adj MD -0.08 (0.039)	0.0524
	DQoL satisfaction with treatment subscale, mean (95% CI), full analysis population	6 mos	1.83 (1.77 to 1.90)	2.08 (2.01 to 2.17)	NR	<0.0001
	DQoL social worry subscale, mean (95% CI), full analysis population	6 mos	1.77 (1.68 to 1.96)	1.71 (1.60 to 1.82)	NR	0.3794
	DQoL diabetes worry subscale, mean (95% CI), full analysis population	6 mos	1.97 (1.86 to 2.08)	2.04 (1.92 to 2.16)	NR	0.4055
	DQoL impact of treatment subscale, mean (95% CI), full analysis population	6 mos	2.10 (2.04 to 2.16)	2.13 (2.08 to 2.19)	NR	0.4057
	HFS behavior subscale, mean (95% CI), PP population	6 mos	13.7 (12.6 to 14.8)	13.4 (12.3 to 14.6)	NR	0.8203
	HFS worry subscale, mean (95% CI), PP population	6 mos	14.7 (12.3 to 17.0)	15.9 (13.6 to 18.2)	NR	0.4294

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)	p-value
	HFS behavior subscale, mean (95% CI), full analysis population	6 mos	13.8 (12.8 to 14.9)	13.8 (12.7 to 15.0)	Adj MD 0.0 (0.72)	0.9834
	HFS worry subscale, mean (95% CI), full analysis population	6 mos	14.9 (12.7 to 17.1)	16.0 (13.8 to 18.3)	Adj MD -1.2 (1.48)	0.4154
	DDS total score, mean (95% CI), PP population	6 mos	1.81 (1.67 to 1.96)	1.84 (1.70 to 1.89)	NR	0.7233
	DDS emotional burden subscale, mean (95% CI), PP population	6 mos	1.92 (1.75 to 2.09)	1.98 (1.81 to 2.15)	NR	0.5621
	DDS physician distress, mean (95% CI), PP population	6 mos	1.68 (1.48 to 1.88)	1.62 (1.41 to 1.83)	NR	0.6765
	DDS regimen distress, mean (95% CI), PP population	6 mos	1.90 (1.75 to 2.06)	1.97 (1.80 to 2.11)	NR	0.5378
	DDS interpersonal distress, mean (95% CI), PP population	6 mos	1.63 (1.48 to 1.78)	1.67 (1.51 to 1.82)	NR	0.6900
	DDS total score, mean (95% CI), full analysis population	6 mos	1.80 (1.76 to 1.94)	1.82 (1.68 to 1.97)	Adj MD -0.03 (0.089)	0.7634
	DDS emotional burden subscale, mean (95% CI), full analysis population	6 mos	1.91 (1.76 to 2.07)	1.95 (1.80 to 2.10)	NR	0.6727
	DDS physician distress, mean (95% CI), full analysis population	6 mos	1.64 (1.45 to 1.93)	1.60 (1.40 to 1.80)	NR	0.7130
	DDS regimen distress, mean (95% CI), full analysis population	6 mos	1.89 (1.73 to 2.04)	1.95 (1.80 to 2.10)	NR	0.4777
	DDS interpersonal distress, mean (95% CI), full analysis population	6 mos	1.63 (1.49 to 1.77)	1.64 (1.50 to 1.79)	NR	0.8698
Hermanides 2011	*HbA1c %*					
	HbA1c (%), mean (SD)	Baseline	8.46±0.95 (n=41)	8.59±0.82 (n=36)	NR	NR

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)	p-value
		3 mos.	7.29±0.71 (n=41)	8.55±1.21 (n=36)	Diff 1.25 (0.79 to 1.72)	<0.001
		6 mos.	7.23±0.65 (n=41)	8.46±1.04 (n=36)	MD 1.23 (0.83–1.63)	<0.001
	HbA1c mmol/mol, mean (SD)	Baseline	69±10 (n=41)	70±9 (n=36)	NR	NR
		3 mos.	56±NR (n=41)	70±NR (n=36)	NR	<0.001
		6 mos.	56±NR (n=41)	69 ±NR (n=36)	NR	<0.001
	LSM Δ in HbA1c % from baseline, mean (SD)	3 mos.	-1.17±0.93 (n=41)	-0.05±0.73 (n=36)	Diff -1.13 (-1.51 to -0.74)	<0.001
		6 mos.	-1.23±1.01 (n=41)	-0.13±0.56 (n=36)	Diff -1.10 (-1.47 to -0.73)	<0.001
	Proportion of patients with HbA1c % <7%	6 mos.	34% (n=41)	0% (n=36)	NR	<0.001
	Hypoglycemia					
	Severe hypoglycemia events	6 mos.	4 (n=41)	1 (n=36)	NR	0.210
	% of time in hypoglycemia	Baseline	3.9±4.7 % (n=40)	2.5±2.8 % (n=31)	NR	NR
		6 mos.	2.7±3.4 % (n=40)	2.5±3.6 % (n=31)	0.2 (-1.4 to 1.9)	0.790
	Number of hypoglycemic events (defined as <4.0 mmol/l) per day, mean (SD)	Baseline	0.7±0.1 (n=40)	0.5±0.5 (n=31)	NR	NR
		6 mos.	0.7±0.7 (n=40)	0.6±0.7 (n=31)	Diff -0.1 (-0.2 to 0.5)	0.40
	LSM Δ from baseline hyperglycemia (%)	6 mos.	NA	NA	0.0 (-1.6 to 1.7)	0.96
	Hyperglycemia					

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)	p-value
	% of time in hyperglycemia	Baseline	38 ±17.4 (n=40)	40.1±18.4 (n=31)	NA	NR
		6 mos.	21.6±12.2 (n=40)	38.2±21.5 (n=31)	Diff 16.5 (7.8–25.2)	<0.001
	Number of hyperglycemic events (defined as >11.1 mmol/l) per day, mean (SD)	Baseline	2.4±0.6 (n=40)	2.5±0.6 (n=31)	NR	NR
		6 mos.	2.1±0.8 (n=40)	2.2±0.7 (n=31)	Diff 0.2 (-0.2 to 0.5)	0.300
	LSM Δ from baseline hyperglycemia (%)	6 mos.	NA	NA	-17.3 (-25.1 to -9.5)	<0.001
	QoL measures					
	Hypoglycemia Fear Survey, mean (SD)	Baseline	29.8±19.2 (n=30)	21.0±17.7 (n=24)	NR	NA
		6 mos.	24.1±20.2 (n=30)	20.3±16.9 (n=24)	3.9 (-5.7 to 13.4)	0.420
	SF-36 Physical Functioning	Baseline	89.4±14.5 (n=42)	90.5±14.3 (n=33)	NR	NR
		6 mos.	92.7±11.2 (n=42)	91.4±12.7 (n=33)	1.4 (-4.1 to 6.9)	0.620
	SF-36 Role-Physical	Baseline	76.8±23.8 (n=42)	84.4±19.3 (n=33)	NR	NR
		6 mos.	85.7±20.7 (n=42)	87.3±20.4 (n=33)	1.6 (-11.2 to 8.0)	0.740
	SF-36 Bodily Pain	Baseline	78.9±25.4 (n=42)	78.7±23.0 (n=33)	NA	NR
		6 mos.	79.9±24.4 (n=42)	78.7±22.6 (n=33)	1.3 (-9.7 to 12.2)	0.820
	SF-36 General Health	Baseline	55.5±20.3 (n=42)	59.8±22.3 (n=33)	NR	NR
		6 mos.	67.7±21.6 (n=42)	63.1±19.1 (n=33)	4.5 (-5.0 to 14.1)	0.350

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)	p-value
	SF-36 Vitality	Baseline	53.9±20.0 (n=42)	61.0±23.7 (n=33)	NR	NR
		6 mos.	66.7±20.2 (n=42)	65.2±19.3 (n=33)	1.5 (-7.7 to 10.7)	0.740
	SF-36 Social Functioning	Baseline	81.5±20.3 (n=42)	86.4±21.0 (n=33)	NR	NR
		6 mos.	89.3±16.0 (n=42)	82.2±25.2 (n=33)	7.1 (-3.0 to 17.2)	0.170
	SF-36 Role-emotional	Baseline	84.9±20.4 (n=42)	89.6±16.7 (n=33)	NR	NR
		6 mos.	87.1±19.6 (n=42)	88.0±16.0 (n=33)	0.9 (-7.6 to 9.4)	0.830
	SF-36 Mental Health	Baseline	72.6±14.8 (n=42)	77.9±20.2 (n=33)	NR	NR
		6 mos.	79.2±12.5 (n=42)	76.8±16.5 (n=33)	2.3 (-4.3 to 9.0)	0.490
	Usage					
	Mean days/week of sensor use, mean (SD)	6 mos.	4.5 (1.0)	NA	NA	NA
	% of patients using sensor >60% of the time	6 mos.	79%	NA	NA	NA
Hirsch 2008‡	*HbA1c %*					
	HbA1c %, mean (SD)	Baseline	8.4±0.6 % (n=49)	8.3±0.5 (n=49)	NR	NR
		3 mos.	7.6±0.9 % (n=49)	7.7±0.6 (n=49)	NR	NR
		6 mos.	7.7 ±0.8 % (n=49)	7.7 ±0.7 (n=49)	NR	NR
	HbA1c %, Least Square Mean Δ (SE)	6 mos.	-0.77±0.15 (n=49)	-0.73±0.14 (n=49)	LSM -0.04(0.14)	0.800
	Hypoglycemia					

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)	p-value
	AfUC <70 mg/dL*min **	Δ from baseline 6 mos.	0	NR	LSM(SE) 0.47 (0.12)	<0.001
	Severe hypoglycemic events**	6 mos.	11 (n=66)	3 (n=72)	NR	0.040
	Hyperglycemia					
	AUC >180 mg/dL*min**	Δ from baseline 6 mos.	–11.3±19.3	-9.7±16.5	Diff. in Δ 2.800	0.291
	Ketoacidosis					
	Number of patients experiencing ketoacidosis event**	6 mos.	0 (n=66)	1 (n=72)	NR	NR
JDRF 2008†† Beck/Lawrence 2010	*HbA1c %*					
	HbA1c %, mean (SD)	Baseline	7.6±0.5 % (n=52)	7.6±0.5 % (n=46)	NR	NR
	Δ from baseline HbA1c %, mean (SD)	6 mos.	-0.50 (0.56) %	0.02 (0.45) %	NR	<0.001
	Relative decrease of HbA1c % by > 10%, no (%)	6 mos.	26% (13/52)	4% (2/46)	NR	0.003
	Absolute decrease of HbA1c % by > 0.5%, no (%)	6 mos.	48% (24/52)	11% (5/46)	NR	<0.001
	Relative increase of HbA1c % by > 10%, no (%)	6 mos.	0% (0/52)	2% (n=1/46)	NR	0.480
	Absolute increase of HbA1c % by > 0.5%, no (%)	6 mos.	0% (0/52)	11% (5/46)	NR	0.020
	HbA1c % < 7%,	6 mos.	34% (17/52)	9% (4/46)	NR	0.005
	HbA1c % < 7% w/o severe hypoglycemic events, no (%)	6 mos.	30% (15/52)	7% (3/46)	NR	0.006
	Hypoglycemia					

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)	p-value
	Rate of severe hypoglycemia	6 mos.	43.4/100 person-year	26.3/100 person-year	NR	0.660
	> 1 severe hypoglycemic event, no (%)	6 mos.	10 (5/52)	9 (4/46)	NR	1.000
	> 1 severe hypoglycemic event with seizure/coma, no (%)	6 mos.	1 (2) (1/52)	1 (2) (n=46)	NR	1.000
	Minutes/day < 70 mg/dl, mean	Baseline	89 (n=52)	60 (n=46)	NR	NR
		6 mos.	60 (n=52)	81 (n=46)	NR	0.410
	Minutes/day < 50 mg/dl, mean	Baseline	32 (n=52)	22 (n=46)	NR	NR
		26 wks	11 (n=52)	23 (n=46)	NR	0.100
	Hyperglycemia					
	Minutes/day > 180 mg/dl, mean	Baseline	497(n=52)	548 (n=46)	NR	0.002
		6 mos.	394(n=52)	519 (n=46)	NR	0.002
	Minutes/day > 250 mg/dl, mean	Baseline	149(n=52)	181 (n=46)	NR	NR
		6 mos.	101(n=52)	161 (n=46)	NR	<0.001
	Ketoacidosis					
	Number of patients experiencing a ketoacidosis event	6 mos.	0 (n=52)	0 (n=46)	IC	IC
	Euglycemia					
	Minutes/day 71-180 mg/dl, mean	Baseline	854 (n=52)	811 (n=46)	NR	NR
		6 mos.	986 (n=52)	840 (n=46)	NR	<0.001

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)	p-value
	QoL measures					
	SF-12 PCS (Participants ≥18 years), mean (SD)	Baseline	54.1±5.9 (n=122)	54.1±7.2 (n=106)	NR	NR
		6 mos.	55.5±4.9 (n=120)	54.1±6.9 (n=106)	NR	0.030
	SF-12 MCS (Participants ≥18 years), mean (SD)	Baseline	49.5±8.4 (n=122)	48.2±10.0 (n=106)	NR	NR
		6 mos.	48.4±10.1 (n=120)	48.7±9.6 (n=106)	NR	0.350
	PAID (Participants ≥18 years), mean (SD)	Baseline	22.7±15.3 (n=122)	21.7±18.0 (n=106)	NR	NR
		6 mos.	18.1±14.1 (n=120)	18.2±14.6 (n=106)	NR	0.500
	HFS Total (Participants ≥18 years), mean (SD)	Baseline	37.4±12.8 (n=122)	37.8±14.3 (n=106)	NR	NR
		6 mos.	33.3±11.5 (n=120)	36.0±13.6 (n=106)	NR	0.040
	HFS Worry (Participants ≥18 years), mean (SD)	Baseline	30.1±18.3 (n=122)	30.6±18.3 (n=106)	NA	NR
		6 mos.	25.3±15.8 (n=120)	27.7±17.3 (n=106)	NR	0.120
	HFS Behavior (Participants ≥18 years), mean (SD)	Baseline	46.9±11.0 (n=122)	47.3±13.1 (n=106)	NR	NR
		6 mos.	43.8±11.2 (n=120)	46.8±13.3 (n=106)	NR	0.030
	Usage					
	Hours per week of CGM glucose readings‡‡, mean	1-4 wks	132 hrs/week	NA	NA	NA
		5-8 wks	123 hrs/week	NA	NA	NA

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)	p-value
		9-13 wks	126 hrs/week	NA	NA	NA
		14-17 wks	122 hrs/week	NA	NA	NA
		18-21 wks	120 hrs/week	NA	NA	NA
		22-26 wks	118 hrs/week	NA	NA	NA
New 2015 (GLADIS)	*HbA1c*					
	HbA1c %, mean (SD)	Baseline	8.1 (0.8) % CGM no alarms (n=45) 8.2 (1.3) % CGM w/alarms (n=44)	8.0 (1.0) % (n=39)	NR	NR
		11.4-14.3 wks.	8.0 (0.8) % CGM no alarms (n=45) 8.1 (1.2) % CGM w/alarms (n=44)	8.0 (1.0) % (n=39)	NR	NS
	Percent of patients with reduction in HbA1c ≥0.5%	14.3 wks.	27.1% CGM no alarms (n=45) 24.5% CGM w/alarms (n=44)	10.6% (n=39)	NR	0.065§§
	Hypoglycemia					
	Hours/day with blood glucose < 70 mg/dl	11.4-14.3 wks	1.3 hrs/day CGM no alarms (n=45) 1.0 hrs/day CGM w/alarms (n=44)	1.6 hrs/day (n=39)	(95% CI -0.8 to 0.3) §§ (95% CI -1.2 to -0.1)***	0.349§§ 0.030***
	Hypoglycemia/hyperglycemia					
	Hours/day spent outside target range (70-180 mg/dl), mean (SD)	Baseline	10.0 (3.5) CGM w/no alarms (n=45) 10.3 (3.3) CGM w/alarms (n=44)	10.5 (3.2) (n=39)	NR	NR
		11.4-14.3 wks	9.6 (4.1) CGM w/no alarms (n=45) 9.6 (3.7) CGM w/no alarms (n=44)	10.8 (3.7) (n=39)	NR	NR

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)	p-value
		11.4-14.3	9.9 CGM w/no alarms (n=45) 9.7 CGM w/alarms (n=44)	10.6 (n=39)	Adj MD 0.7††† (-1.86 to 0.35) ‡‡‡ Adj MD 0.8††† (-2.10 to 0.13) §§§§	0.180 0.080
	Quality of life measures					
	Diabetes Distress Scale (DDS)	14.3 wks	NR	NR	NR	NS
	SF-8 mental component score CGM no alarms vs SMBG, mean (SD)	Baseline	49.1 ± 9.4 (n=44)	49.0 ± 10.4 (n=39)	NR	NR
		14.3 wks	50.9 ± 9.4 (n=44)	49.3 ± 10.7 (n=39)	MD NR (-2.2 to 5.2)	0.440
	SF-8 mental component score CGM w/alarms vs SMBG, mean (SD)	Baseline	47.6 ± 11.2 (n=43)	49.0 ± 10.4 (n=39)	NR	NR
		14.3 wks	48.9 ± 11.4(n=43)	49.3 ± 10.7 (n=39)	MD NR (-3.5 to 4.0)	0.890
	SF-8 physical component score CGM no alarms vs SMBG, mean (SD)	Baseline	48.6 ± 9.7 (n=44)	49.1± 7.9 (n=39)	NR	NR
		14.3 wks	49.0 ± 9.8 (n=44)	47.5 ± 8.5 (n=39)	MD NR (-1.3, 4.9)	0.260
	SF-8 physical component score CGM no alarms vs SMBG, mean (SD)	Baseline	46.7 ± 8.8 (n=43)	49.1 ± 7.9 (n=39)	NR	NR
		14.3 wks	49.4 ± 9.6 (n=43)	47.5 ± 8.5 (n=39)	MD NR (-0.5 to 6.7)	0.025
Peyrot 2009	*HbA1c %*					
	HbA1c (%)	Baseline	8.87±0.89 % (n=14)	8.32±1.05 % (n=14)	NR	NR
		4 mos.	7.16±0.75 (n=14)	7.3±0.92 % (n=14)	NR	NR
	Δ from baseline, HbA1c (%)	4 mos.	-1.7 % (n=14)	-1.0 % (n=14)	Diff. -0.7	0.071
	Hypoglycemia					

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
			Intervention	Control		
	Severe Hypoglycemic events	4 mos.	0 (n=14)	3 (n=14)	IC	IC
	Ketoacidosis					
	Diabetic Ketoacidosis events	4 mos.	0 (n=14)	1 (n=14)	IC	IC

HbA1c, hemoglobin A1c; HFS, Hypoglycemia Fear Survey; mg/dl, milligrams per deciliter; mmol/l, millimole per liter; NA, not applicable; NR, not reported; wks., weeks;

*99% confidence interval
†Model 1 values are adjusted for baseline values of each outcome. Model 2 values are adjusted for the demographic factors of age, sex, and number of years since diagnosis
‡Includes data for a pediatric population—abstraction can be found in corresponding pediatric sections
§ All HbA1c % values besides the baseline were estimated from a graph
**Data not stratified by age
††Calculated by AAI
‡‡Footnote: All values estimated from figures with the exception adjusted mean differences and effect sizes of "DTSQ total treatment satisfaction", "DTSQ perceived frequency of hyperglycemia", "DQoL total scale", "HFS behavior subscale", "HFS worry subscale", and "DDS total score"
§§1 event of diabetic ketoacidosis was reported in the CGM group, but it was caused by pump failure and therefore categorized as an adverse event
***Includes data for a pediatric population and a mixed ages population—abstraction can be found in corresponding pediatric and mixed ages sections
††† Values estimated from graph
‡‡‡Includes data for a type 2 and mixed type 1 and 2 population—abstraction can be found in corresponding sections
§§§Footnote: MDs calculated by AAI using adjusted means reported by the study (95% CIs and p values given by study)
****CGM no alarms vs SMBG (0.059 p value)
††††CGM alarms vs SMBG (0.015 p value)

Appendix Table G3. Efficacy Outcomes from RCTs Evaluating CGM versus SMBG in Mixed Adults and Children with Type 1 Diabetes Mellitus

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**		
Parallel Trials						
Battelino 2011 6 months	HbA1c (%)	At screening	6.83±0.44 (n=62)	6.90±0.47 (n=54)	NR	NR
		Baseline	6.92±0.56(n=62)	6.91±0.67 (n=54)	NR	NR
		6 mos.	6.69% (n=62)	6.95% (n=54)	Adj. MD -0.27 (95%CI -0.47 to -0.07)	0.008
	Mean blood glucose in 1 month run-in period (mg/dL)	Baseline	147±23 (n=62)	148±28 (n=54)	NR	NR
	Low Blood Glucose Index	6 mos.	1.18±0.82 (n=62)	1.74±1.62 (n=54)	Ratio of Means 0.68 (0.49-0.89)	0.020
	High Blood Glucose Index	6 mos.	5.1±3.1 (n=62)	6.0±3.2 (n=54)	Ratio of Means 0.85 (0.70-1.05)	0.050
	Hours per day in hyperglycemia >180 mg/dL	6 mos.	5.5±3.2 (n=62)	6.4±3.4 (n=54)	Ratio of Means 0.86 (0.71-1.06)	0.080
	Hours per day in hyperglycemia >250 mg/dL	6 mos.	1.14±1.46 (n=62)	1.66±1.53 (n=54)	Ratio of Means 0.69 (0.48-1.07)	0.060
	Hours per day in normoglycemia 90-180 mg/dL	6 mos.	15.1±2.7 (n=62)	13.5±3.1 (n=54)	Ratio of Means 1.12 (1.04-1.21	0.003
	Hours per day in normoglycemia 70-180 mg/dL	6 mos.	17.6±3.2 (n=62)	16.0±3.4 (n=54)	Ratio of Means 1.10 (1.02-1.18)	0.009
	Hours per day in hypoglycemia <70 mg/dL	6 mos.	0.91±0.81(n=62)	1.60±2.02 (n=54)	Ratio of Means 0.57 (0.36-0.80)	0.010
	number of hypoglycemia excursions per day <63 mg/dL)	6 mos.	0.53±0.6 (n=62)	0.76±0.94 (n=54)	Ratio of Means 0.70 (95%CI 0.43-1.03)	0.08
	Hours per day in hypoglycemia (<63 mg/dL)	6 mos.	0.48±0.57 (n=62)	0.97±1.55 (n=54)	Ratio of Means 0.49 (0.26-0.76)	0.030

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**		
	Median hours per day in hypoglycemia (<63 mg/dL) (IQR)	6 mos.	0.54(0.23-1.31) (n=62)	0.26(0.14-0.54) (n=54)	NR	NR
	Integrated Glucose Excursion Index (AUC) <63 mg/dL	6 mos.	5.4±7.6(n=62)	11.1±14.2 (n=54)	Ratio of Means 0.49 (0.29-0.79)	0.020
	number of Hypoglycemic excursions per day <55 mg/dL)	6 mos.	0.28±0.54 (n=62)	0.37±0.4 (n=54)	Ratio of Means 0.76 (95%CI 0.47-1.43)	0.070
	No. of Nocturnal Hypoglycemic Excursions below <55 mg/dL	6 mos.	0.13(0.30) (n=62)	0.19(0.19) (n=54)	NR	0.010
	No. of Nocturnal Hypoglycemic Excursions below <63 mg/dL	6 mos.	0.21(0.32) (n=62)	0.30(0.31) (n=54)	NR	0.009
	Record of Severe Hypoglycemia in the prior year, number (%)	Baseline	5(8)	7(12)	NR	NR
	Severe Hypoglycemia	6 mos.	Events: 0 (n=62)	Events: 0 (n=54)	NR	NR
	Mild Diabetic Ketoacidosis (unrelated to study participation)	6 mos.	Events: 1 (n=62)	Events: 0 (n=54)	NR	NR
Deiss 2006 G1 – CGM full time G2 – CGM biweekly G3 – SMBG 3 months	HbA1c (%)	Baseline	G1: 9.5±1.1 (n=50) G2: 9.6±1.2 (n=52)	G3: 9.7±1.3 (n=54)	NR	NR
	Δ from baseline, HbA1c (%)	3 mos	G1: -1.0±1.1 (n=50) G2: -0.7±1.3 (n=52)	G3: -0.4±1.0 (n=54)	G1-G3: 0.6(0.19 to 1.00) p=0.004 G2-G3: 0.3 (-0.15 to 0.75) p=0.185	G1-G3:0.003 G2-G3: <.001
	% patients with reduction in HbA1c ≥1%	3 mos.	G1: 50.0%(25/50) G2: 37.0% (19/52)	G3: 15.0% (8/54)	G1-G3: RR 3.38 (1.22 to 2.87) p=0.003 G2-G3: RR 2.47 (1.02 to 2.49) p=0.037	NR
	% patients with reduction in HbA1c ≥2%	3 mos.	G1: 26.0% (13/50) G2:9.0% (5/52)	G3: 4.0% (2/54)	G1-G3: RR 7.02 (1.07 to 2.97) p=0.023	NR

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**		
					G2-G3: RR 2.60 (0.781 to 2.29) p=0.288	
	Severe hypoglycemia(not further spec) G1-G3	3 mos.	G1: Events: 1 (1/50) G2: Events: 1 (1/52)	G3: 0 (0/54)	NA	NR
JDRF 2009a Separate concurrent trial to JDRF 2008	*HbA1c*					
	HbA1c %, mean (SD)	Baseline	6.4 (0.5) % (n=67)	6.5 (0.3) %	NR	NR
	Δ from baseline, HbA1c %, mean (SD)	6 mos.	+0.02 (0.45) (n=67)	+0.33 (0.43)	-0.34 (-0.49 to -0.20)	<0.001
	Decrease of HbA1c % by ≥ 0.3%, % (n/N)	6 mos.	31% (21/67)	5% (3/62)	NR	<0.001
	Increase of HbA1c % by ≥ 0.3%, % (n/N)	6 mos.	28% (19/67)	52% (31/62)	NR	0.002
	Subjects who maintained HbA1c % <7.0, % (n/N)	6 mos.	88% (54/67)	63% (38/62)	NR	<0.001
	Absolute rate of glucose level change (mg/dL per min), median (IQR)	Baseline	0.60 (0.50–0.71) (n=67)	0.65 (0.56–0.80) (n=62)	NR	NR
		3 mos.	0.65 (0.50–0.73) (n=67)	0.63 (0.54–0.79) (n=58)	NR	NR
		6 mos.	0.66 (0.53–0.76) (n=66)	0.66 (0.54–0.87) (n=60)	NR	0.350, 0.510, 0.510*
	Normoglycemia					
	Glucose Level (minutes/day) 71-180 mg/dL, median (IQR)	6 mos.	1,063(921-1,174) (n=67)	972(809-1,089) (n=62)	NR	NR
		6 mos.	1,092 (947–1,200) (n=67)	951 (778–1,079) (n=58)	NR	NR
		6 mos.	1,063 (948–1,185) (n=66)	949 (784–1,106) (n=60)	NR	0.003, 0.002, 0.004*
	Standard Deviation of Glucose Level values, median (IQR)	6 mos.	48 (42–58) (n=67)	63 (27–118) (n=62)	NR	NR
		3 mos.	49 (40–58) (n=67)	58 (48–69) (n=58)	NR	NR
		6 mos.	50 (41–63) (n=66)	60 (46–67) (n=60)	NR	0.170, 0.130, 0.210*
	Hypoglycemia					

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**		
	Event rate per 24 h	6 mos.	0.25±0.40	0.47±0.68	NR	0.070
	AUC < 70 mg/dl, median (IQR)	6 mos.	0.64(0.19-1.24) (n=67)	0.60(0.18-1.88) (n=62)	NR	NR
		6 mos.	0.32 (0.09-0.80) (n=67)	0.48 (0.17-1.80) (n=58)	NR	NR
		6 mos.	0.26 (0.11-0.64) (n=66)	0.49 (0.13-1.73) (n=60)	NR	0.030, 0.010, 0.008*
	Glucose Level (minutes/day) ≤ 70 mg/dl, median (IQR)	Baseline	91(40-147) (n=67)	96(37-225) (n=62)	NR	NR
		3 months	61 (24-118) (n=67)	89 (33-198) (n=58)	NR	NR
		6 months	54 (28-108) (n=66)	91 (27-188) (n=60)	NR	0.160, 0.040, 0.060*
	Median decrease in minutes/day < 70 mg/dl from baseline	6 months	-37 min/day(n=66)	-5 min/day(n=60)	NR	0.430
	Glucose Level (minutes/day) ≤60 mg/dL, median (IQR)	Baseline	40(9-73) (n=67)	37(12-100) (n=62)	NR	NR
		3 months	21 (3-52) (n=67)	37 (12-100) (n=58)	NR	NR
		6 months	18 (5-40) (n=66)	37 (7-116) (n=60)	NR	0.050, 0.020, 0.020*
	Glucose Level (minutes/day) ≤70 mg/dL, median (IQR)	Baseline	7(0-38) (n=67)	9(0-45) (n=62)	NR	NR
		3 months	3 (0-18) (n=67)	7 (0-51) (n=58)	NR	NR
		6 months	4 (0-15) (n=66)	8 (0-55) (n=60)	NR	0.050, 0.030, 0.010*
	Proportion of participants who experienced ≥1 serious hypoglycemic event	6 months	10% (7/66)	11% (7/60)	NR	NS
	Hyperglycemia					
	Glucose Level (minutes/day) > 180 mg/dl, median(IQR)	Baseline	255(151-420) (n=67)	331(206-489) (n=62)	NR	NR
		3 months	268 (179-410) (n=67)	362 (221-527) (n=58)	NR	NR

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**		
		6 months	283 (173-423) (n=66)	341 (232-502) (n=60)	NR	0.100, 0.090, 0.130*
	Glucose Level (minutes/day) > 250 mg/dl, median(IQR)	Baseline	10(10-101) (n=67)	63(27-118) (n=62)	NR	NR
		3 months	42 (8-77) (n=67)	76 (29-173) (n=58)	NR	NR
		6 months	48 (11-103) (n=66)	82 (22-149) (n=60)	NR	0.120, 0.050, 0.100*
JDRF 2008	*HbA1c %*					
	HbA1c %, mean (SD)	Baseline	8.0 (0.7) % (n=57)	7.9 (0.8) % (n=53)	NR	NR
	Δ from baseline, HbA1c %, mean (SD)	6 mos.	-0.18 (0.65) % (n=57)	-0.21 (0.61) % (n=53)	NR	0.520
	Relative decrease of HbA1c % by > 10%, no (%)	6 mos.	8 (14%) (n=57)	5 (10%) (n=53)	NR	0.460
	Absolute decrease of HbA1c % by > 0.5%, no (%)	6 mos.	20 (36%) (n=57)	19 (37%) (n=53)	NR	0.570
	Relative increase of HbA1c % by > 10%, no (%)	6 mos.	2 (4%) (n=57)	2 (4%) (n=53)	NR	0.980
	Absolute increase of HbA1c % by > 0.5%, no (%)	6 mos.	7 (13%) (n=57)	7 (14%) (n=53)	NR	0.840
	HbA1c % < 7%, no (%)	6 mos.	8 (14%) (n=57)	9 (18%) (n=53)	NR	0.800
	HbA1c % < 7% w/o severe hypoglycemic events, no (%)	6 mos.	7 (13%) (n=57)	7 (14%) (n=53)	NR	0.670
	Hypoglycemia					
	Rate of severe hypoglycemic event	6 mos.	17.9/100 person-year (n=57)	23.9/100 person-year (n=53)	NR	0.640
	Rate of severe hypoglycemic event with seizure or coma, no (%)	6 mos.	3.6/100 person-year	11.9/100 person-year (n=53)	NR	0.140
	≥ 1 severe hypoglycemic event, no (%)	6 mos.	3 (5%) (n=57)	5 (9%) (n=53)	NR	0.480
	≥ 1 severe hypoglycemic event with seizure/coma, no (%)	6 mos.	1 (2%) (n=57)	3 (6%) (n=53)	NR	0.350
	Minutes/day < 70 mg/dl, mean	6 mos.	99 (n=57)	102 (n=53)	NR	NR
		6 mos.	88 (n=57)	88 (n=53)	NR	0.790
	Minutes/day < 50 mg/dl, mean	Baseline	37 (n=57)	42 (n=53)	NR	NR
		6 mos.	29 (n=57)	31 (n=53)	NR	0.990

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**		
	Hyperglycemia					
	Minutes/day > 180 mg/dl, mean, adults ≥25	Baseline	650 (n=57)	641 (n=53)	NR	NR
		6 mos.	591 (n=57)	591 (n=53)	NR	0.002
	Minutes/day > 250 mg/dl, mean, adults ≥25	Baseline	271 (n=57)	265 (n=53)	NR	NR
		6 mos.	215 (n=57)	242 (n=53)	NR	0.440
	Ketoacidosis					
	Number of patients experiencing a ketoacidosis event	6 mos.	1 (n=57)	0 (n=53)	NR	NR
	Euglycemia					
	Minutes/day 71-180 mg/dl, mean	Baseline	691 (n=57)	697 (n=53)	NR	NR
		6 mos.	761 (n=57)	761 (n=53)	NR	0.790
O'Connell 2009 3 months	HbA1c (%)	Baseline	7.3±0.6 (n=26)	7.5±0.7 (n=29)	NR	NR
		3 mos	7.1±0.8 (n=26)	7.8±0.9 (n=29)	Adj. Diff. -0.43 (-0.19 to -0.75)	0.009
	% of patients who achieved end-of-study HbA1c levels ≤7%	3 mos	53.8% (14/26)	17.2% (5/29)	RR 3.12 (1.01 to 2.57) p=0.041	0.004
	% of time in euglycemia (4-10 mmol/l)	Baseline	62.1±12.5 (n=26)	58.0±9.4 (n=29)	NR	NR
		3 mos	57.2±11.3 (n=26)	53.9±15.0 (n=29)	1.72 (−5.37 to 8.81)	0.630
	% of time in hypoglycemia (≤3.9 mmol/l)	Baseline	9.3±5.9 (n=26)	10.3±7.6 (n=29)	NR	NR
		3 mos	9.2±8.7 (n=26)	9.1±6.9 (n=29)	Adj. Diff. 0.54 (-3.48 to 4.55)	0.790
	% of time in hyperglycemia (≥10.1 mmol/l)	Baseline	28.6±13.5 (n=26)	31.7±13.0 (n=29)	NR	NR
		3 mos	33.6±12.7 (n=26)	37.0±17.3 (n=29)	Adj. Diff. -2.18 (-10.0 to 5.69)	0.580
	Severe Hypoglycemia	3 mos.	Events: 0 (n=26)	Events: 0 (n=29)	IC	IC
	Diabetic Ketoacidosis	3 mos.	Events: 0 (n=26)	Events: 0 (n=29)	IC	IC
Raccah 2009	Mean Δ from baseline, HbA1c (%)	Baseline	9.11±1.28 (n=46)	9.28±1.19 (n=54)	NR	NR

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**		
Study period: 6 months		6 mos.	-0.81±1.09 (n=46)	-0.57±0.94 (n=54)	-0.24	p=0.087
	Δ from baseline, Blood Glucose (mg/dL)	6 mos.	-30.6±54.0 (n=46)	-10.8±39.6 (n=54)	Diff. -19.8 (-38.42 to -1.18) p =0.037	p<0.005
	Glycemic Levels					
	Δ from baseline, Hyperglycemia >190 mg/dL (h/day)	6 mos.	-3.5±4.8 (n=46)	-0.7±3.8 (n=54)	Diff. 2.8 (1.09 to 4.50) p=0.002‡	<0.005
	Δ from baseline, Hyperglycemia AUC	6 mos.	-17.1±31.7 (n=46)	-5.8±26.7 (n=54)	Diff. 11.3 (-0.29 to 22.89) p=0.559‡	<0.05
	Δ from baseline, Hyperglycemia (episodes/day)	6 mos.	-0.2±0.7 (n=46)	-0.2±0.7 (n=54)	Diff. 0 (-0.28 to 0.28) p=1.00‡	NS
	Δ from baseline, Hypoglycemia frequency <70 mg/dl, (episodes/day)	6 mos.	0.1±0.9 (n=46)	0.1±0.7 (n=54)	Diff. 0 (-0.32 to 0.32) p=1.00‡	NS
	Δ from baseline, Hypoglycemia frequency <70 mg/dL (h/day)	6 mos.	0.3±1.4 (n=46)	0±1.2 (n=54)	Diff. 0.3 (-0.22 to 0.82) p=0.251‡	NR
	Δ from baseline, Hypoglycemia AUC	6 mos.	0.4±1.3 (n=46)	0.0±1.8 (n=54)	Diff. 0.4 (-0.23 to 1.03) p=0.213‡	NR
	Ratio of basal to bolus insulin (Number of daily boluses)	6 mos.	4.7±1.4 (n=46)	3.9±1.4 (n=54)	Diff. 0.8 (0.24 to 1.36) p=0.005‡	0.005
	DKA					
	Diabetic Ketoacidosis (%)	6 mos.	Events: 2 (n=46)	Events: 3 (n=54)	NR	NR
	Incidence Rate of Diabetic Ketoacidosis	6 mos.	3.2 per 100 patient-years	3.2 per 100 patient-years	IC	IC
	Severe hypoglycemia, not further spec. (%)	6 mos.	Events: 1 (n=46)	Events: 0 (n=54)	NR	NR
	Incidence Rate of Severe Hypoglycemia	6 mos.	0.64 per 100 patients years (n=100)		IC	IC

AUC, area under the curve; HbA1c, hemoglobin A1c; IC, incalculable; mg/dl, milligrams per deciliter; mos., months; mmol/l, millimole per liter; NR, not reported; NS, not significant;

* P-values provided are: ranks (first), outliers truncated (second), and square root transformation (third).

† Only a 'brief report' was available for Deiss 2006

‡ Calculated by AAI.

Appendix Table G4. Efficacy Outcomes from RCTs Evaluating CGM versus SMBG in Adults with Type 2 Diabetes Mellitus

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**		
Beck 2017b (DIAMOND)	*HbA1c %*					
	HbA1c %, mean (SD) or (95%CI)(	Baseline	8.5 (0.6) (n=79)	8.5 (0.7) (n=79)	NR	NR
		3 mos.	7.5 (7.4 to 7.7) (n=77)	7.9 (7.7 to 8.1) (n=75)	NR	NR
		6 mos.	7.7 (7.5 to 7.8) (n=79)	8.0 (7.8 to 8.2) (n=79)	NR	NR
	Change in HbA1c levels	3 mos.	−1.0 (−1.2 to −0.8)	−0.6 (−0.8 to −0.4)	Adj. MD −0.3 (−0.6 to −0.1) **	0.005**
		6 mos.	−0.8 (−1.0 to −0.7)	−0.5 (−0.7 to −0.3)	Adj. MD −0.3 (−0.5 to 0.0) **	0.022**
	% HbA1c <7.0%	3 mos.	22% (17/77)	12% (9/75)	Adj. MD 10% (−2% to 23%)**	0.260**
		6 mos.	14% (11/77)	12% (9/75)	Adj. MD 3% (−9% to 14%)**	0.880**
	% HbA1c <7.5%	3 mos.	45% (35/77)	29% (22/75)	Adj. MD 17% (−3% to 37%) **	0.054**
		6 mos.	35% (27/77)	28% (21/75)	Adj. MD 8% (−11% to 26%) **	0.630**
	Relative reduction in HbA1c ≥10%	3 mos.	57% (44/77)	35% (26/75)	Adj. MD 25% (3% to 46%) **	0.016**
		6 mos.	52% (40/77)	32% (24/75)	Adj. MD 22% (0% to 42%)**	0.028**
	Reduction in % HbA1c ≥1%	3 mos.	52% (40/77)	33% (25/75)	Adj. MD 20% (−1% to 41%)**	0.044**
		6 mos.	39% (30/77)	28% (21/75)	Adj. MD 12% (−7% to 30%)**	0.210**
	Reduction in % HbA1c ≥1% or HbA1c <7.0%	3 mos.	53% (41/77)	33% (25/75)	Adj. MD 22% (0% to 43%)**	0.034**
		6 mos.	43% (33/77)	29% (22/75)	Adj. MD 15% (−5% to 34%)**	0.146**
	Reduction in HbA1c level ≥0.5%	3 mos.	79% (61/77)	51% (38/75)	Adj. MD 31% (5% to 57%)**	0.002**
		6 mos.	73% (56/77)	49% (37/75)	Adj. MD 26% (0% to 50%) **	0.007**

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)	p-value
	Euglycemia					
	Time per day in range of 70–180 mg/dL, min	Baseline	802 (604–974) (n=79)	794 (665–976) (n=78)	NR	NR
		3 mos.	937 (664–1083) (n=77)	822 (537–1025) (n=74)	NR	NR
		6 mos.	882 (647–1077) (n=74)	836 (551–965) (n=72)	NR	NR
	Hypoglycemia					
	Minutes per day <70 mg/dl, median (IQR)	Baseline	11 (1–33) (n=79)	12 (3–39) (n=78)	NR	NR
		3 mos.	9 (1–25) (n=77)	11 (0–37) (n=74)	NR	NR
		6 mos.	4 (0–17) (n=74)	12 (0–34) (n=72)	NR	NR
	Minutes per day <60mg/dl, median (IQR)	Baseline	3 (0–15) (n=79)	4 (0–17) (n=78)	NR	NR
		3 mos.	1 (0–7) (n=77)	1 (0–12) (n=74)	NR	NR
		6 mos.	0 (0–6) (n=74)	2 (0–12) (n=72)	NR	NR
	Minutes per day <50 mg/dl, median (IQR)	Baseline	0 (0–8) (n=79)	0 (0–7) (n=78)	NR	NR
		3 mos.	0 (0–0) (n=77)	0 (0–3) (n=74)	NR	NR
		6 mos.	0 (0–1) (n=74)	0 (0–5) (n=72)	NR	NR
	Area above curve 70 mg/ml, median (IQR)	Baseline	0.1 (0.0–0.3) (n=79)	0.1 (0.0–0.3) (n=78)	NR	NR
		3 mos.	0.0 (0.0–0.1) (n=77)	0.0 (0.0–0.3) (n=74)	NR	NR
		6 mos.	0.0 (0.0–0.1) (n=74)	0.1 (0.0–0.2) (n=72)	NR	NR
	Nocturnal Hypoglycemia					
	Minutes per day <70 mg/dl, median (IQR)	Baseline	0.6 (0.0-3.4) (n=79)	1.0 (0.0-3.2) (n=78)	NR	NR
		3 mos.	0.2 (0.0-1.8) (n=77)	0.0 (0.0-1.8) (n=74)	NR	NR
		6 mos.	0.0 (0.0-1.6) (n=74)	0.0 (0.0-2.9) (n=72)	NR	NR
	Minutes per day <60mg/dl, median (IQR)	Baseline	0.0 (0.0-1.6) (n=79)	0.2 (0.0-1.1) (n=78)	NR	NR
		3 mos.	0.0 (0.0-0.1) (n=77)	0.0 (0.0-0.3) (n=74)	NR	NR
		6 mos.	0.0 (0.0-0.2) (n=74)	0.0 (0.0-<0.1) (n=72)	NR	NR
	Minutes per day <50 mg/dl, median (IQR)	Baseline	0.0 (0.0–0.2) (n=79)	0 (0.0–0.4) (n=78)	NR	NR
		3 mos.	0 (0–0) (n=77)	0 (0–0) (n=74)	NR	NR
		6 mos.	0 (0–0) (n=74)	0 (0–0) (n=72)	NR	NR
	Area above curve 70 mg/ml, median (IQR)	Baseline	0.0 (0.0–0.4) (n=79)	0.1 (0.0–0.3) (n=78)	NR	NR
		3 mos.	0.0 (0.0–0.1) (n=77)	0.0 (0.0–0.1) (n=74)	NR	NR
		6 mos.	0.0 (0.0–0.1) (n=74)	0.0 (0.0–0.2) (n=72)	NR	NR
	Hyperglycemia					
	Minutes per day >180 mg/dl, median (IQR)	Baseline	612 (411–809) (n=79)	607 (392–775) (n=78)	NR	NR

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**		
		3 mos.	501 (323–746) (n=77)	560 (382–818) (n=74)	NR	NR
		6 mos.	549 (353–789) (n=74)	571 (422–883) (n=72)	NR	NR
	Minutes per day >250 mg/dl, median (IQR)	Baseline	150 (68–265) (n=79)	154 (66–281) (n=78)	NR	NR
		3 mos.	100 (37–180) (n=77)	137 (53–251) (n=74)	NR	NR
		6 mos.	105 (37–246) (n=74)	118 (48–288) (n=72)	NR	NR
	Minutes per day >300 mg/dl, median (IQR)	Baseline	33 (9–77) (n=79)	42 (9–96) (n=78)	NR	NR
		3 mos.	19 (0–56) (n=77)	33 (1–95) (n=74)	NR	NR
		6 mos.	23 (0–66) (n=74)	18 (0–83) (n=72)	NR	NR
	Area under curve 180 mg/dl, median (IQR)	Baseline	22 (13–32) (n=79)	21 (11–33) (n=78)	NR	NR
		3 mos.	14 (7–26) (n=77)	18 (11–34) (n=74)	NR	NR
		6 mos.	16 (8–30) (n=74)	18 (12–34) (n=72)	NR	NR
	Diabetic Ketoacidosis	6 mos.	0 (n=79)	0 (n=79)	IC	IC
	Severe hypoglycemic events (n/N)	6 mos.	0 (n=79)	0 (n=79)	IC	IC
	Quality of Life					
	EQ-5D-5L	Baseline	0.82 ± 0.15 (n=79)	0.82 ± 0.14 (n=79)	NR	NR
		6 mos.	0.82 ± 0.14 (n=77)	0.82 ± 0.16 (n=73)	NR	NR
	World Health Organization (five) Well-Being Index (WHO-5)	Baseline	16 ± 4 (n=79)	17 ± 4 (n=79)	NR	NR
		6 mos.	16 ± 5 (n=77)	17 ± 4 (n=73)	NR	NR
	Diabetes Distress Scale (DDS) Total,	Baseline	1.9 ± 0.8 (n=79)	2.0 ± 0.8 (n=79)	NR	NR
		6 mos.	1.8 ± 0.9 (n=77)	1.8 ± 0.6 (n=73)	NR	NR
	DDS Regimen subscale	Baseline	2.2 ± 0.9 (n=79)	2.4 ± 1.0 (n=79)	NR	NR
		6 mos.	2.0 ± 0.9 (n=77)	2.1 ± 0.9 (n=73)	NR	NR
	DDS Emotional Burden subscale	Baseline	2.3 ± 1.2 (n=79)	2.3 ± 1.1 (n=79)	NR	NR
		6 mos.	2.2 ± 1.2 (n=77)	2.1 ± 1.0 (n=73)	NR	NR
	DDS Interpersonal subscale	Baseline	1.8 ± 1.0 (n=79)	2.0 ± 1.2 (n=79)	NR	NR
		6 mos.	1.7 ± 1.1 (n=77)	1.7 ± 0.8 (n=73)	NR	NR
	DDS Physician subscale	Baseline	1.3 ± 0.6 (n=79)	1.3 ± 0.8 (n=79)	NR	NR

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N)) Intervention	Control	Effect Estimate (95% CI)	p-value
		6 mos.	1.3 ± 0.9 (n=77)	1.1 ± 0.3 (n=73)	NR	NR
	Hypoglycemia Fear Survey, worry subscale,	Baseline	0.8 ± 0.7 (n=79)	0.8 ± 0.6 (n=79)	NR	NR
		6 mos.	0.8 ± 0.6 (n=77)	0.7 ± 0.5 (n=73)	NR	NR
	Hypoglycemia Confidence Scale, worry subscale,	Baseline	3.2 ± 0.7 (n=79)	3.4 ± 0.6 (n=79)	NR	NR
		6 mos.	3.3 ± 0.6 (n=77)	3.4 ±0.6 (n=73)	NR	NR
Ehrhardt 2011, Vigersky 2012	*HbA1c*					
	HbA1c %, mean (SD)	Baseline	8.4 (1.3) % (n=50)	8.2 (1.1) % (n=50)	NR	0.240
		3 mos.	7.4 (1.0) % (n=47)	7.7 (1.2) % (n=47)	NR	0.230
		6 mos.	7.3 (1.1) % (n=50)	7.6 (1.3) % (n=50)	NR	NR
		9 mos.	7.6 (1.2) % (n=50)	7.7 (1.3) % (n=50)	NR	NR
		12 mos.	7.7 (1.1) % (n=50)	7.9 (1.4) % (n=50)	NR	NR
	Change from baseline in HbA1c %, mean (SD)	3 mos.	-1.0 (1.1)% (n=47)	-0.5 (0.8)% (n=47)	NR	0.006
		6 mos.	-1.2 (1.7)% (n=50)	-0.5 (1.0)% (n=50)	NR	NR
		9 mos.	-0.8 (1.7)% (n=50)	-0.5 (1.1)% (n=50)	NR	NR
		12 mos.	-0.8 (1.5)% (n=50)	-0.2 (1.3)% (n=50)	NR	NR
	Hypoglycemia					
	Percent glucose readings <50 mg/dl	3 mos.	0.2% (n=47)	2.1% (n=47)	NR	NR
	Percent glucose readings <70 mg/dl	3 mos.	2.1% (n=47)	2.7% (n=47)	NR	NR

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**		
	Hyperglycemia					
	Percent glucose readings >180 mg/dl	3 mos.	22.6% (n=47)	28.7% (n=47)	NR	NR
	Percent glucose readings >240 mg/dl	3 mos.	6.1% (n=47)	12.1% (n=47)	NR	NR
	Quality of life measures					
	Problem Areas in Diabetes (PAID) questionnaire, mean (SD)	Baseline	23.9 (22.3) (n=50)	25.7 (20.8) (n=50)	NR	NR
		3 mos.	17.1 (18.0) (n=50)	19.9 (17.1) (n=50)	NR	NR
		12 mos.	18.4 (20.5) (n=50)	19.6 (20.5) (n=50)	NR	NR
	Euglycemia					
	% of patients within target range (> 70 mg/dl, <180 mg/dl)	3 mos.	75.3% (n=47)	68.6% (n=47)	NR	NR
	Usage					
	Proportion of patients using CGM ≥48 days, no (%)	3 mos.	34 (68%) (n=47)	NA (n=47)	NA	NA
	Change from baseline in HbA1c % by usage, mean (SD)	3 mos.	-1.2 (1.1) % CGM ≥48 days (n=16) -0.6 (1.1) % CGM <48 days (n=34)	-0.5 (0.8) (n=50)	Adj MD -0.60*	0.003† 0.002*
	Change from baseline in HbA1c % by usage, median	3 mos.	-0.95% CGM ≥48 days (n=16) -0.45% CGM <48 days (n=34)	-0.40%‡ (n=50)	NR	NR
Haak 2016††	*HbA1c*					
	HbA1c %, mean (SD)	Baseline	8.65 (1.01) (n=149)	8.75 (0.98) (n=75)	NR	NR
		6 mos.	8.37 (0.83) (n=149)	8.34 (1.14) (n=75)	0.3 (1.25)	0.826

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**		
	Eugylcemia					
	Time with glucose 3.9–10.0 mmol/L (70–180 mg/dL), hours	Baseline	13.9 (4.5) (n=149)	13.5 (5.2) (n=75)	NR	NR
		6 mos.	13.6 (4.6) (n=149)	13.2 (4.9) (n=75)	0.2 (0.58)	0.793
	Hypoglycemia					
	Glucose <3.9 mmol/L (70 mg/dL) within 24 h, events	Baseline	0.64 (0.63) (n=149)	0.63 (0.66) (n=75)	NR	NR
		6 mos.	0.38 (0.45) (n=149)	0.53 (0.59) (n=75)	-0.16 (0.065)	0.016
	Glucose <3.9 mmol/L (70 mg/dL) within 24 h, hours	Baseline	1.30 (1.78) (n=149)	1.08 (1.58) (n=75)	NR	NR
		6 mos.	0.59 (0.82) (n=149)	0.99 (1.29) (n=75)	-0.47 (0.134)	p<0.005
	AUC <3.9 mmol/L (70 mg/dL) (h x mg/dL)	Baseline	20.15 (35.21) (n=149)	14.05 (26.35) (n=75)	NR	NR
		6 mos.	7.23 (12.35) (n=149)	13.59 (22.31) (n=75)	-7.80 (2.20)	p<0.005
	Glucose<3.1 mmol/L (55 mg/dL) within 24 h, events	Baseline	0.34 (0.50) (n=149)	0.27 (0.44) (n=75)	NR	NR
		6 mos.	0.14 (0.24) (n=149)	0.24 (0.36 (n=75)	-0.12 (0.037)	p<0.005
	Glucose <3.1 mmol/L (55 mg/dL) within 24 h, hours	Baseline	0.59 (1.13) (n=149)	0.38 (0.83) (n=75)	NR	NR
		6 mos.	0.19 (0.37) (n=149)	0.37 (0.69) (n=75)	-0.22 (0.068)	p<0.005
	AUC (h x mg/dL) <3.1 mmol/L (55 mg/dL)	Baseline	6.02 (13.23) (n=149)	3.40 (9.16) (n=75)	NR	NR
		6 mos.	1.64 (3.85) (n=149)	3.66 (7.97) (n=75)	-2.51 (0.76)	p<0.005
	Glucose <2.5 mmol/L (45 mg/dL) within 24 h, events	Baseline	0.19 (0.37) (n=149)	0.13 (0.34) (n=75)	NR	NR
		6 mos.	0.06 (0.13) (n=149)	0.11 (0.25) (n=75)	-0.06 (0.02)	p<0.005
	Glucose <2.5 mmol/L (45 mg/dL) within 24 h, hours	Baseline	0.32 (0.74) (n=149)	0.17 (0.54) (n=75)	NR	NR
		6 mos.	0.08 (0.21) (n=149)	0.19 (0.45) (n=75)	-0.14 (0.04)	p<0.005
	AUC(h x mg/dL) <2.5 mmol/L (45 mg/dL) within 24 h	Baseline	1.52 (3.77) (n=149)	0.77 (2.63) (n=75)	NR	NR
		6 mos.	0.35 (1.11) (n=149)	0.93 (2.23) (n=75)	-0.70 (0.22)	p<0.005
	Glucose <2.2 mmol/L (40 mg/dL) within 24 h, events	Baseline	0.13 (0.30) (n=149)	0.10 (0.30) (n=75)	NR	NR
		6 mos.	0.05 (0.13) (n=149)	0.09 (0.22) (n=75)	-0.05 (0.02)	p=0.020
	Glucose <2.2 mmol/L (40 mg/dL) within 24 h, hours	Baseline	0.22 (0.57) (n=149)	0.12 (0.43) (n=75)	NR	NR
		6 mos.	0.05 (0.17) (n=149)	0.14 (0.34) (n=75)	-0.10 (0.03)	p<0.005
	Nocturnal Hypoglycemia					
		Baseline	0.25 (0.28) (n=149)	0.27 (0.32) (n=75)	NR	NR

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**		
	Glucose<3.9 mmol/L (70 mg/dL) at night (23.00–06.00) within 7 h, events	6 mos.	0.14 (0.20) (n=149)	0.27 (0.33) (n=75)	-0.12 (0.03)	p<0.005
	Glucose<3.9 mmol/L (70 mg/dL) at night (23.00–06.00) within 7 h, hours	Baseline	0.55 (0.84) (n=149)	0.49 (0.71) (n=75)	NR	NR
		6 mos.	0.23 (0.43) (n=149)	0.51 (0.72) (n=75)	-0.29 (0.08)	p<0.005
	Glucose <3.1 mmol/L (55 mg/dL) at night (23.00–06.00) within 7 h, events	Baseline	0.15 (0.23) (n=149)	0.13 (0.20) (n=75)	NR	NR
		6 mos.	0.06 (0.13) (n=149)	0.13 (0.21) (n=75)	-0.07 (0.02)	p<0.005
	Glucose <3.1 mmol/L (55 mg/dL) at night (23.00–06.00) within 7 h, hours	Baseline	0.27 (0.58) (n=149)	0.18 (0.35) (n=75)	NR	NR
		6 mos.	0.09 (0.22) (n=149)	0.19 (0.40) (n=75)	-0.12 (0.04)	p<0.005
	Glucose <2.5 mmol/L (45 mg/dL) at night (23.00–06.00) within 7 h, events	Baseline	0.08 (0.17) (n=149)	0.06 (0.14) (n=75)	NR	NR
		6 mos.	0.03 (0.08) (n=149)	0.07 (0.16) (n=75)	-0.04 (0.02)	p=0.009
	Glucose <2.5 mmol/L (45 mg/dL) at night (23.00–06.00) within 7 h, hours	Baseline	0.16 (0.42) (n=149)	0.08 (0.23) (n=75)	NR	NR
		6 mos.	0.04 (0.12) (n=149)	0.11 (0.28) (n=75)	-0.08 (0.03)	p<0.005
	Glucose <2.2 mmol/L (40 mg/dL) at night (23.00-06.00) within 7 h, events	Baseline	0.23 (0.53)	0.16 (0.43)	NR	NR
		6 mos.	0.07 (0.24)	0.19 (0.51)	-0.13 (0.05)	p=0.009
	Glucose <2.2 mmol/L (40 mg/dL) at night (23.00-06.00) within 7 h, hours	Baseline	0.41 (1.20)	0.18 (0.69)	NR	NR
		6 mos.	0.09 (0.29)	0.27 (0.79)	-0.22 (0.07)	p<0.003
	Hyperglycemia					
	Time with glucose >10.0 mmol/L (180 mg/dL), hours	Baseline	8.8 (5.0) (n=149)	9.4 (5.8) (n=75)	NR	NR
		6 mos.	9.8 (4.8) (n=149)	9.8 (5.4) (n=75)	0.3 (0.63)	p=0.597
	Time with glucose >13.3 mmol/L (240 mg/dL) (h)	Baseline	3.1 (3.3) (n=149)	3.9 (4.5) (n=75)	NR	NR
		6 mos.	3.5 (3.7) (n=149)	3.9 (4.2) (n=75)	0.1 (0.46)	p=0.873
	Diabetic Ketoacidosis	6 mos.	0 (n=149)	0 (n=75)	IC	IC
	Participants (%) with adverse or serious adverse events	6 mos.	77% (114/149)	63% (47/75)	RR 1.22 (1.00 to 1.48) p=0.042	NR
	Number of adverse events (excluding serious events)	6 mos.	316 (n=149)	157 (n=75)	NR	NR

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**		
	Participants (%) with serious adverse events	6 mos.	10.7% (16/149)	16.0% (12/75)	RR 0.67 (0.61 to 1.46) p=0.787‡‡	NR
	Number of Serious Adverse Events	6 mos.	20 (n=149)	22 (n=75)	NR	NR
	Participants with hypoglycemic serious adverse events	6 mos.	2.0% (3/149)	1% (1/75)	RR 1.51 (0.70 to 2.12 p=0.493	NR
	Number of hypoglycemic serious adverse events	6 mos.	3 (n=149)	1 (n=75)	NR	NR
	Participants (%) with hypoglycemic events	6 mos.	7% (1/149)	9% (7/75)	RR 0.07 (0.481 to 1.32) p=0.380	NR
	Number of hypoglycemic adverse events	6 mos.	27 (n=149	30 (n=75)	NR	NR
	Serious adverse event related to device or study procedure	6 mos.	0 (n=149)	0 (n=75)	IC	IC
	Device related adverse events	6 mos.	Events: 9 (6/149)	NA	NA	NA
	Serious Adverse Event leading to withdrawal	6 mos.	<1.0% (1/149)	2.6% (2/75)	RR 0.25 (0.62 to 1.85) p=0.819‡‡	NR
Yoo 2008	*HbA1c*					
	HbA1c %, mean (SD)	Baseline	9.1 (1.0) % (n=50)	8.7 (0.7) % (n=50)	NR	0.120
		3 mos.	8.0 (1.2)% (n=47)	8.3 (1.1)% (n=47)	NR	0.004
	Hypoglycemia					
	% of time spent <60 mg/dl	Baseline	0%	NR	NR	NR
		3 mos.	0.6%	NR	NR	NR
	Change from baseline in percent of time glucose readings <60 mg/dl	3 mos.	+0.6%‡	NR	NR	NR
	Hyperglycemia					
	% of times spent >250 mg/dl	Baseline	17.8%	NR	NR	NR

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**		
		3 mos.	9.0%	NR	NR	NR
	Change from baseline in percent of time glucose readings >250 mg/dl	3 mos.	-8.8%	NR	NR	NR
	Glucose levels					
	Fasting blood glucose (mmol/l), mean (SD)	Baseline	6.3 (1.3)	6.5 (1.3)	NR	0.570
		3 mos.	6.5 (1.2) (n=47)	7.2 (2.2) (n=47)	NR	0.480
	Postprandial blood glucose (mmol/l), mean (SD)	Baseline	11.3 (2.8) (n=50)	11.5 (3.6) (n=50)	NR	0.870
		3 mos.	10.0 (2.5) (n=47)	10.9 (4.1) (n=47)	NR	0.480
	Euglycemia					
	% of time >80 mg/dl and <250 mg/dl	Baseline	61.6% (n=50)	NR (n=50)	NR	NR
		3 mos.	71.6% (n=47)	NR (n=47)	NR	NR
	Change from baseline in percent of time >80 mg/dl and <250 mg/dl	3 mos.	10% (n=47)	NR (n=47)	NR	NR
Tildesley 2013 Tang 2014	*HbA1c %*					
	HbA1c %, mean (SD)	Baseline ITT	8.80 (1.37) % (n=25)	8.79 (1.25) % (n=25)	NR	0.500
		6 mos. ITT	7.49 (0.70) % (n=25)	7.96 (1.30) % (n=25)	NR	0.081
		Baseline PP	8.4 (1.08) % (n=25)	8.8 (1.28) (n=25)	NR	NR
		Baseline PP	7.9 (1.32) % (n=25)	7.3 (0.75) % (n=25)	NR	0.312

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**		
	HbA1c mmol/mol, mean (SD)	Baseline PP	68 (12) (n=25)	73 (14) (n=25)	NR	NR
		6 mos. PP	63 (15) (n=25)	57 (8) (n=25)	NR	0.312
	QoL measures					
	Diabetes Treatment Satisfaction Questionnaire, mean (SD)	6 mos. PP	24.80 (7.10) (n=25)	33.41 (2.65) (n=25)	NR	<0.001

Adj., adjusted; MD, mean difference; mmol/l, millimole per liter; mos, months; NR, not reported; wks., weeks
*P value is based on comparison of CGM use ≥ 48 days vs SMBG
†P value is based on ANCOVA for all three groups
‡Value estimated from graph
§Includes data for a type 2 and mixed type 1 and 2 population—abstraction can be found in corresponding sections
**P value for change in HbA1c level is from a mixed-effects linear model adjusting for baseline HbA1c level and accounting for clinical site. For the binary outcomes, P values are from mixed-effects logistic regression models adjusting for baseline HbA1c level and accounting for clinical site. Confidence bounds for adjusted differences for the binary outcomes were calculated using bootstrap methods.
††Effect sizes from Haak 2016 are difference in adjusted means in intervention vs control (Standard Error) unless otherwise noted.
‡‡Calculated by AAI.

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
			Intervention	Control		
Feig 2017 (Pregnancy trial) Study period: length of pregnancy	*HbA1c%*					
	Mean HbA1c (%)	Baseline	6.83 ± 0.67 (n=108)	6.95 ± 0.66 (n=107)	NR	NR
		24 wks. gestation	6.23 ± 0.53	6.40 ± 0.68 (n=96)	NR	NR
		34 wks. gestation	6.35 ± 0.57 (n=95)	6.53 ± 0.70 (n=92)	NR	NR
	Change from baseline in HbA1c %	24 wks. gestation	-0.67 ± 0.58	-0.52 ± 0.55		0.037
		34 wks. gestation	-0.54±0.62	-0.35±0.65		0.037
	Proportion who achieved HbA1c ≤ 6.5%	34 wks. gestation	66.0% (63/95)	52.0% (48/92)	RR 1.27 (0.99 to 1.58) p=0.06	0.060
	Hours of CGM data per week, median (IQR)	Baseline	158 (143-168) (n=107)	150 (139-165) (n=107)	NR	NR
		24 wks. gestation	168 (147, 182)	160 (144, 165)	NR	NR
		34 wks. gestation	159 (143-177) (n=77)	156(143-166) (n=77)	NR	NR
	Mean Glucose Level mmol/L	Baseline	7.3 ± 1.2 (n=107)	7.6 ± 1.1 (n=107)	NR	NR
		24 wks. gestation	7.6 ± 1.2 (n=90)	7.8 ± 1.3 (n=90)	NR	0.530
		34 wks. gestation	6.7 ± 0.9 (n=77)	7.0 ± 1.1 (n=77)	NR	0.140
	% Time in target (3.5-7.8 mmol/L)	Baseline	52±13(n=107)	52±14 (n=107)	NR	NR
		24 wks. gestation	53% ± 15% (n=90)	50% ± 15% (n=90)	NR	0.140
		34 wks. gestation	68±13 (n=77)	61±15 (n=77)	NR	0.003
	Hyperglycemia					
	% Time > 6.7 mmol/L,	Baseline	51% (40%, 61%) (n=107)	53% (46%, 63%) (n=107)	NR	NR
		24 wks. gestation	58% (44%, 70%) (n=90)	60% (49%, 69%) (n=90)	NR	0.510
		34 wks. gestation	45% (34%, 57%) (n=77)	48% (42%, 55%) (n=77)	NR	0.140
	AUC > 6.7 mmol/L,	Baseline	30 (18, 39) (n=107)	31 (21, 44) (n=107)	NR	NR
		24 wks. gestation	27 (17, 42) (n=90)	31 (20, 40) (n=90)	NR	0.460
		34 wks. gestation	15 (9, 21) (n=77)	18 (13, 26) (n=77)	NR	0.049
	% Time > 7.8 mmol/L,	Baseline	39% (28%, 49%) (n=107)	40% (32%, 51%) (n=107)	NR	NR

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**		
		24 wks. gestation	43% (29%, 54%) (n=90)	45% (33%, 54%) (n=90)	NR	0.760
		34 wks. gestation	27% (19-37) (n=77)	32% (25-39) (n=77)	NR	0.028
	AUC >7.8 mmol/L	Baseline	20 (11, 29) (n=107)	22 (13, 32) (n=107)	NR	NR
		24 wks. gestation	17 (10, 30) (n=90)	21 (11, 28) (n=90)	NR	0.470
		34 wks. gestation	8 (4, 13) (n=77)	10 (7, 16) (n=77)	NR	0.087
	High Blood Glucose Index	Baseline	4.2 (2.3-6.2) (n=107)	4.6 (2.8-6.7) (n=107)	NR	NR
		24 wks. gestation	3.6 (2.2, 6.3) (n=90)	4.4 (2.5, 5.9) (n=90)	NR	0.440
		34 wks. gestation	1.8 (1.1-2.8) (n=77)	2.3 (1.5-3.4) (n=77)	NR	0.067
	Hypoglycemia					
	% Time <3.5 mmol/L,	Baseline	8% (4-14) (n=107)	6% (3-11) (n=107)	NR	NR
		24 wks. gestation	3% (1%, 6%) (n=90)	4% (1%, 8%) (n=90)	NR	0.420
		34 wks. gestation	3% (1-6) (n=77)	4% (2-8) (n=77)	NR	0.100
	AUC <3.5 mmol/L	Baseline	0.8 (0.3, 1.7) (n=107)	0.5 (0.2, 1.3) (n=107)	NR	NR
		24 wks. gestation	0.3 (0.1, 0.6) (n=90)	0.4 (0.1, 0.8) (n=90)	NR	0.380
		34 wks. gestation	0.2 (0.1, 0.6) (n=77)	0.2 (0.1, 0.9) (n=77)	NR	0.170

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**		
	% Time <2.8 mmol/L,	Baseline	2% (0%, 6%) (n=107)	1% (0%, 4%) (n=107)	NR	NR
		24 wks. gestation	0% (0%, 2%) (n=90)	1% (0%, 3%) (n=90)	NR	0.320
		34 wks. gestation	0% (0%, 2%) (n=77)	1% (0%, 3%) (n=77)	NR	0.440
	AUC <2.8 mmol/L	Baseline	0.1 (0.0, 0.4) (n=107)	0.1 (0.0, 0.3) (n=107)	NR	NR
		24 wks. gestation	0.0 (0.0, 0.1) (n=90)	0.0 (0.0, 0.2) (n=90)	NR	0.450
		34 wks. gestation	0.0 (0.0, 0.1) (n=77)	0.0 (0.0, 0.2) (n=77)	NR	0.570
	Low Blood Glucose Index	Baseline	2.8 (1.6-4.6) (n=107)	2.4 (1.5-3.6) (n=107)	NR	NR
		24 wks. gestation	1.5 (0.9, 2.4) (n=90)	1.7 (0.9, 2.7) (n=90)	NR	0.420
		34 wks. gestation	1.7(1.1-2.8) (n=77)	2.1(1.4-2.8) (n=77)	NR	0.180
	Hypoglycemia	Baseline	0.8 (0.6-1.0) (n=107)	0.7 (0.4-0.9) (n=107)	NR	NR
		24 wks. gestation	0.5 (0.3, 0.8) (n=90)	0.5 (0.3, 0.8) (n=90)	NR	0.960
		34 wks. gestation	0.5 (0.3-0.8) (n=77)	0.5 (0.3-0.8) (n=77)	NR	0.730
	Nocturnal Glucose Measures (23.00-07.00hr)					
	Mean Glucose mmol/L	Baseline	6.9 ± 1.5	7.2 ± 1.4		NR
		34 weeks gestation	6.3 ±0.9	6.4 ± 1.2		NR
	% time in target	Baseline	51 ± 16	53 ± 16		NR
		34 weeks gestation	72 ± 15	65 ± 17		NR
	% time > 7.8 mmol/L, median (IQR)	Baseline	31 (20-48)	37 (22-49)	NR	NR
		34 weeks gestation	19 (10-32)	24 (11-35)	NR	NR

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**		
	% Time <3.5 mmol/L, median (IQR)	Baseline	9 (3-23)	9 (4-15)	NR	NR
		34 weeks gestation	3 (1-9)	7 (1-15)	NR	NR
	Episodes of Nocturnal Hypoglycemia, median (IQR)	Baseline	1.3 (0.5-1.8)	1.0 (0.5-1.6)	NR	NR
		34 weeks gestation	0.6 (0.4-1.2)	0.8 (0.4-1.3)	NR	NR
	Severe Hypoglycemia					
	Number of episodes of severe hypoglycemia	Baseline	11 (7/107)	5 (4/107)	NR	NR
		34 wks. gestation	18 (11/77)	21 (12/77)	RR 0.92 (0.68 to 1.70) p=0.745	1.00
	Diabetic Ketoacidosis	Baseline	NR	NR	NR	NR
		34 wks. gestation	2% (2/77)	2% (2/77)	N	1.00
	Maternal Outcomes					
	Preeclampsia	34 wks. gestation	9.0% (9/100)	18.0% (18/102)	RR 1.0 (0.68 to 2.04) p=0.572	0.100
	Caesarian Section	34 wks. gestation	63.0% (63/100)	73.0% (74/102)	RR 0.87 (0.77 to 1.13) p=0.462	0.180
	Weight gain (kg) from baseline (IQR)	34 wks. gestation	13.1 (9.9-16.6) (n=100)	13.7 (10.9-17.6) (n=102)	NR	0.220
	Neonatal Outcomes					
	Pregnancy Loss < 20 weeks, %	End of Pregnancy	5.0% (5/105)	4.0% (4/106)	RR 1.26 (0.71 to 2.04) p=0.486	1.00
	Stillbirth, n	End of Pregnancy	0 (n=105)	1 (n=106)		NR

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**		
	Termination, n	End of Pregnancy	0 (n=105)	1 (n=106)		NR
	Congenital Anomaly†, n	End of Pregnancy	2 (n=105)	3 (n=106)		NR
	Preterm births <37 weeks	End of Pregnancy	38% (38/100)	42% (43/100)	RR 0.88 (0.73 to 1.30) p=0.848	0.570
	Early preterm births <34 weeks	End of Pregnancy	5.0% (5/100)	11.0% (11/100)	RR 0.45 (0.55 to 1.47)	0.190
	Gestational Age at Delivery, median (IQR)	End of Pregnancy	37.4 (36.7-38.1)	37.3 (36.0-38.0)	NR	0.50
	Birthweight (g)	End of Pregnancy	3545.4 (649.0) (n=100)	3582 (777.0) (n=100)	NR	0.370
	Small for gestational age (<tenth centile)	End of Pregnancy	2.0% (2/100)	2.0% (2/100)	RR 1 (0.68 to 2.04) p=0.572	1.00
	Large for Gestational Age (> 90th centile)	End of Pregnancy	53.0% (53/100)	69.0% (69/100)	RR 0.77 (0.68 to 1.06)	0.021
	Extremely Large for Gestational Age (>97.7th centile), %	End of Pregnancy	36.0% (36/100)	44.0% (44/100)	RR 0.82 (0.69 to 1.24) p=0.596	0.310
	Macrosomia (≥4000 g), %	End of Pregnancy	23.0% (23/100)	27.0% (27/100)	RR 0.85 (0.68 to 1.42) p=0.932	0.620
	Birth injury, %	End of Pregnancy	1% (1/100)	0	IC	1.000

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**		
	Shoulder dystocia, %	End of Pregnancy	1% (1/100)	0	IC	1.000
	Neonatal hypoglycemia requiring intravenous dextrose, %	End of Pregnancy	15.0% (15/100)	28.0% (28/100)	RR 0.54 (0.53 to 1.16) p=0.226	0.025
	Hyperbilirubinaemia, %	End of Pregnancy	25.0% (25/100)	31.0% (31/100)	RR 0.80 (0.66 to 1.34) p=0.748	0.430
	Respiratory distress, %	End of Pregnancy	9.0% (9/100)	9.0% (9/100)	RR 1.0 (0.70 to 1.82) p=0.629	1.000
	High-level neonatal care (NICU) >24 h, %	End of Pregnancy	27.0% (27/100)	43.0% (43/100)	RR 0.63 (0.57 to 1.09) p=0.145	0.016
	Infant length of hospital stay, median (IQR)	End of Pregnancy	3.1 (2.1-5.7) (n=105)	4.0 (2.4-7.0) (n=106)	NR	0.009
	Composite neonatal Outcomes‡	End of Pregnancy	42.9% (45/105)	52.8% (56/106)	RR 0.81 (0.70 to 1.17) p=0.428	0.170
Feig 2017 Pregnancy Planning Trial (concurrent trial with subpopulation of participants planning to become pregnant) Study period: 6 mos. or duration of pregnancy	*HbA1c, %*					
	Mean HbA1c (%)	Baseline	7.57±0.77 (n=46)	7.57±0.58 (n=52)	NR	NR
		3 mos.	7.30±0.70 (n=42)	7.34±0.61 (n=46)	NR	NR
		6 mos.	7.12±0.64 (n=42)	7.35±0.87 (n=46)	NR	NR
	Change from baseline in HbA1c %	3 mos.	-0.35±0.72 (n=42)	-0.22±0.39 (n=46)	NR	0.440
		6 mos.	-0.41±0.72 (n=42)	-0.23±0.65 (n=46)	NR	0.170
	Proportion of participants who achieved HbA1c ≤ 7.0%	6 mos.	52.1% (25/48)	40.4% (21/52)	NR	0.440

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
			Intervention	Control		
	Glycemic Measures					
	Hours of CGM data per week, median (IQR)	Baseline	166 (149-172) (n=53)	157 (142-166) (n=57)	NR	NR
		6 mos.	159 (142-168) (n=39)	152 (139-165) (n=52)	NR	NR
	Mean Glucose Level mmol/L	Baseline	8.8±1.3 (n=53)	9.0±1.5 (n=57)	NR	NR
		6 mos.	8.0±1.3 (n=39)	8.6±1.6 (n=52)	NR	0.140
	% Time in target (3.5-7.8 mmol/L)	Baseline	42±13 (n=53)	41±13 (n=57)	NR	NR
		6 mos.	48±13 (n=39)	43±16 (n=52)		0.300
	Hypoglycemia					
	% Time < 3.5mmol/l, median (IQR)	Baseline	3 (1-7) (n=53)	2 (0-4) (n=57)	NR	NR
		6 mos.	4 (1-8) (n=39)	3 (1-6) (n=52)	NR	0.150
	Low Blood Glucose Index, median (IQR)	Baseline	1.3 (0.7-2.5) (n=53)	1.0 (0.4-1.7) (n=57)	NR	NR
		6 mos.	1.8 (0.9-2.5) (n=39)	1.3 (0.7-2.2) (n=52)	NR	0.410
	Hypoglycemia event	Baseline	0.5 (0.1-0.7) (n=53)	0.3 (0.1-0.6) (n=57)	NR	NR
		6 mos.	0.6 (0.2-0.8) (n=39)	0.5 (0.1-0.7) (n=52)	NR	0.340
	Hyperglycemia					
	% Time > 7.8mmol/l, median (IQR)	Baseline	54 (45-62) (n=53)	57 (44-65) (n=57)	NR	NR
		6 mos.	49 (40-57) (n=39)	52 (39-65) (n=52)	NR	0.230
	High Blood Glucose Index, median (IQR)	Baseline	7.5 (4.8-9.7) (n=53)	7.0 (4.8-10.2) (n=57)	NR	NR
		6 mos.	5.9 (3.3-7.2) (n=39)	6.7 (3.9-8.7) (n=52)	NR	0.180
	Nocturnal (23.00-07.00hr) Glycemic Measures					
	Mean Glucose mmol/L	Baseline	8.7±1.9 (n=53)	8.9±2.1 (n=57)	NR	NR
		6 mos.	7.8±1.6 (n=39)	8.4±2.0 (n=52)	NR	NR

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
			Intervention	Control		
	% time in target	Baseline	41±17 (n=53)	41±17 (n=57)	NR	NR
		6 mos.	49±19 (n=39)	45±21 (n=52)	NR	NR
	% time Hyperglycemia > 7.8 mmol/L, median (IQR)	Baseline	50 (40-66) (n=53)	54 (38-68) (n=57)	NR	NR
		6 mos.	41 (32-59) (n=39)	50 (35-64) (n=52)	NR	NR
	% Time Hypogylcemia <3.5 mmol/L, median (IQR)	Baseline	3 (0-8) (n=53)	1 (0-8) (n=57)	NR	NR
		6 mos.	6 (1-9) (n=39)	3 (0-8) (n=52)	NR	NR
	Episodes of Nocturnal Hypoglycemia, median (IQR)	Baseline	0.4 (0.0-1.0) (n=53)	0.4 (0.0-0.9) (n=57)	NR	NR
		6 mos.	0.5 (0.0-1.0) (n=39)	0.4 (0.0-0.9) (n=52)	NR	NR
	Adverse Events					
	Severe Hypoglycemia, episodes	Baseline	7	11	NR	NR
		6 mos.	12	6	NR	NR
	Proportion who experienced Severe Hypoglycemia, %	Baseline	5.7% (3/53)	12.3% (7/57)	NR	NR
		6 mos.	13.5% (7/52)	8.8% (5/57)	NR	0.540
	Proportion who experienced Diabetic Ketoacidosis	Baseline	NA	NA	NR	NR
		6 mos.	22.6% (12/53)	36.8% (21/57)	NR	NR
	Maternal Outcomes					
	Hypertensive Disorders	24 wks.	1 (n=10)	5 (n=15)	NR	NR
	Preeclampsia, n	24 wks.	0 (n=10)	1 (n=15)	NR	NR
	Caesarian Section, n	24 wks.	7 (n=10)	11 (n=15)	NR	NR

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**		
	Maternal Weight Gain (kg), median (IQR)	34 wks. gestation	10.4 (7.3-13.9) (n=10)	13.4 (9.9-16.2) (n=15)	NR	NR
	Neonatal Outcomes					
	Pregnancy Loss < 20 weeks	20 wks.	28.6% (4/14)	11.8% (2/17)	NR	NR
	Stillbirth, %	End of pregnancy	0 (0/10)	0 (0/17)	NR	NR
	Termination, %	End of pregnancy	0 (0/10)	0 (0/17)	NR	NR
	Congenital anomaly, %	End of pregnancy	0 (0/10)	0 (0/17)	NR	NR
	Gestational Age at delivery, weeks median (IQR)	End of pregnancy	37.0 (35.8-37.4)	37.6 (36.9-38.0)	NR	NR
	Preterm birth	End of pregnancy	5	4	NR	NR
	Early preterm births <34 weeks	End of pregnancy	0	0	NR	NR
	Birthweight (g)	End of pregnancy	3544.2±582.9	3871.5±620.4	NR	NR
	Small for gestational age (<tenth centile)	End of pregnancy	0	0	NR	NR
	Large for Gestational Age (> 90th centile)	End of pregnancy	6	11	NR	NR
	Extremely Large for Gestational Age (>97.7th centile), %	End of pregnancy	4	9	NR	NR

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**		
	Macrosomia (≥4000 g), %	End of pregnancy	2	7	NR	NR
	Birth injury, %	End of pregnancy	0	0	NR	NR
	Shoulder dystocia, %	End of pregnancy	0	0	NR	NR
	Neonatal hypoglycemia requiring intravenous dextrose, %	End of pregnancy	7	7	NR	NR
	Hyperbilirubinaemia, %	End of pregnancy	3	3	NR	NR
	Respiratory distress, %	End of pregnancy	0	1	NR	NR
	High-level neonatal care (NICU) >24 h, %	End of pregnancy	7	6	NR	NR
	Infant length of hospital stay, median (IQR)	End of pregnancy	5.3 (4.2-10.0)	3.0 (2.8-6.3)	NR	NR
	Composite neonatal Outcomes‡	End of pregnancy	78.6% (11/14)	70.6% (12/17)	NR	NR
Wei 2016 Study period: Length of pregnancy	Mean HbA1c	At OGTT	5.7 ± 0.34 (n=51)	5.8 ± 0.29 (n=55)	NR	0.096
		End of Pregnancy	5.5% ± 0.39% (n=51)	5.6% ± 0.35% (n=55)	MD -0.10 (-0.24 to 0.42) p=0.167*	0.089
	Oral Glucose Tolerance Test	Baseline 0 h	5.69 ± 0.58 (n=51)	5.67 ± 0.29 (n=55)	NR	0.859
		Baseline 1 h	10.86 ± 1.01 (n=51)	10.90 ± 0.85 (n=55)	NR	0.843
		Baseline 2 h	8.23 ± 1.78 (n=51)	8.29 ± 0.94 (n=55)	NR	0.833
	Birth Weight (g)	End of Pregnancy	3275.88±519.72 (n=51)	3451.09±514.05 (n=55)	MD -175.21 (-374.43 to 24.01) p=0.084*	0.084

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**		
	Gestational Weeks at Birth	End of Pregnancy	37.44±0.99 (n=51)	37.47±1.32 (n=55)	MD -0.03 (-0.48 to 0.42) p=0.896*	0.922
	Apgar Score 5 min	End of Pregnancy	9.40±0.56 (n=51)	9.49±0.50 (n=55)	MD -0.09 (-0.29 to 0.11) p=0.384*	0.390
	Neonatal Hypoglycemia	End of Pregnancy	7.8% (4/51)	12.7% (7/55)	RR 0.61 (95% CI 0.19 to 1.98)*	0.410
	Treated Medically	End of Pregnancy	31.3% (16/51)	12.7% (7/55)	RR 2.46 (0.98 to 2.46) p=0.06*	0.020
	Macrosomia	End of Pregnancy	7.8% (4/51)	12.7% (7/55)	RR 0.61 (95% CI 0.19 to 1.98)*	0.410
	Large for gestational age (≥90th percentile):	End of Pregnancy	35.3% (18/51)	52.7% (29/55)	RR 0.67 (95% CI 0.43 to 1.05)	0.071
	Extremely large for gestational age (≥97.7th percentile)	End of Pregnancy	17.6% (9/51)	30.9% (17/55)	RR 0.57(95% CI 0.28 to 1.16)	0.113
	Caesarian Section	End of Pregnancy	60.0% (31/55)	69.0% (38/55)	RR 0.88 (95% CI 0.66 to 1.17)*	0.370
	Congenital Malformation	End of Pregnancy	4.8% (3/60)	10.3% (6/62)	OR 0.075 (2.535 to 2.886)	0.421
	Respiratory Distress Syndrome	End of Pregnancy	7.1% (4/60)	10.6% (6/62)	OR 0.646 (0.145 to 2.885)	0.717

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
			Intervention	Control		
	NICU admission	End of Pregnancy	34.8% (21/60)	30.0% (19/62)	OR 1.244 (0.502 to 3.087)	0.653
Secher 2013 Study period: Length of pregnancy	Mothers with Type 1 DM					
	HbA1c (%), median (range)	Baseline (8 wks.)	6.6 (5.4-10.0) (n=60)	6.8 (5.6-10.7) (n=59)	NR	0.960
		12 wks.	6.3 (5.0-8.3) (n=60)	6.3 (5.1-8.3) (n=59)	NR	0.570
		21 wks.	6.0 (5.2-7.4) (n=60)	6.2 (4.9-7.7) (n=59)	NR	0.260
		27 wks.	6.0 (4.9-7.1) (n=60)	6.1 (4.8-7.4) (n=59)	NR	0.440
		33 wks.	6.1 (5.1-7.8) (n=60)	6.2 (4.8-8.2) (n=59)	NR	0.220
		36 wks.	6.0 (5.1-7.7) (n=60)	6.2 (4.7-8.4) (n=59)	NR	0.370
	Median SMPG values (mmol/l), median (range)	Baseline (8 wks.)	6.9 (5.7-8.9) (n=60)	6.8 (4.9-10.2) (n=59)	NR	0.960
		12 wks.	6.7 (4.5-8.9) (n=60)	6.7 (5.1-9.5) (n=59)	NR	0.590
		21 wks.	6.5 (5.1-8.8) (n=60)	6.9 (5.2-10.5) (n=59)	NR	0.080
		27 wks.	6.5 (4.9-8.3) (n=60)	6.5 (5.2-8.9) (n=59)	NR	0.420
		33 wks.	6.3 (4.7-7.9) (n=60)	6.2 (4.9-7.9) (n=59)	NR	1.000
	≤3.9 mmol/l SMPG Values throughout pregnancy, median (range)	End of pregnancy	14 (0-25) (n=60)	14 (0-25) (n=59)	NR	0.960
	4.0-7.9 mmol/l SMPG Values throughout pregnancy, median (range)	End of pregnancy	58 (40-91) (n=60)	58 (35-96) (n=59)	NR	0.870

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**		
	≥8.0 mmol/l SMPG Values throughout pregnancy, median (range)	End of pregnancy	28 (4-44) (n=60)	28 (4-48) (n=59)	NR	0.700
	2-hour plasma glucose (mmol/l)	End of pregnancy	2.8 (0.5-4.7) (n=57)	2.6 (1.1-5.9) (n=60)	NR	0.750
	Large-for-gestational-age infants	End of pregnancy	30 (50%) (n=63)	21 (36%) (n=60)	RR 1.36 (95% CI 0.88 to 2.09)*	0.110
	Birth weight (g)	End of pregnancy	3,591 (1,829-4,356) (n=63)	3,440 (2,045-4,424) (n=60)	NR	0.570
	Birth weight z-score	End of pregnancy	1.18 (-1.90-3.78) (n=63)	0.66 (-1.06-3.45) (n=60)	NR	0.180
	Neonatal Hypoglycemia	End of pregnancy	21 (37%) (n=57)	27 (46%) (n=60)	RR 0.82 (95% CI 0.53 to 1.27)*	0.330
	Severe Neonatal Hypoglycemia	End of pregnancy	9 (16%) (n=57)	10 (17%) (n=60)	RR 0.95 (0.69 to 1.77)*	0.870
	Preterm delivery and/or severe neonatal hypoglycemia	End of pregnancy	18 (32%) (n=57)	16 (27%) (n=60)	RR 1.18 (0.79 to 1.78)	0.600
	Caesarian Section	End of pregnancy	20 (33%) (n=63)	27 (46%) (n=60)	RR 0.71 (95% CI 0.45 to 1.11)*	0.170
	Miscarriage	End of pregnancy	3 (5%) (n=63)	1 (2%) (n=60)	RR 2.86 (0.31 to 26.72)*	0.620
	Mothers with Type 2 DM					
	HbA1c (%), median (range)	Baseline (8 wks.)	6.4 (5.3-8.1) (n=16)	6.5 (5.3-9.0) (n=14)	NR	0.560
		12 wks.	6.2 (5.6-7.8) (n=16)	6.2 (5.1-7.7) (n=14)	NR	0.900
		21 wks.	5.7 (5.2-6.9) (n=16)	5.6 (4.6-6.3) (n=14)	NR	0.240
		27 wks.	5.8 (5.0-7.7) (n=16)	5.7 (4.8-6.6) (n=14)	NR	0.280

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**		
		33 wks.	6.0 (5.1-7.0) (n=16)	5.9 (5.2-6.8) (n=14)	NR	0.440
		36 wks.	6.0 (5.1-6.5) (n=16)	5.9 (5.2-6.7) (n=14)	NR	0.310
	Median SMPG values (mmol/l), median (range)	Baseline (8 wks.)	6.2 (5.3-7.3) (n=16)	7.0 (4.8-10.3) (n=14)	NR	0.040
		12 wks.	6.2 (5.4-7.5) (n=16)	6.7 (4.6-7.4) (n=14)	NR	0.500
		21 wks.	5.9 (5.2-6.9) (n=16)	5.9 (5.1-7.8) (n=14)	NR	0.640
		27 wks.	5.8 (5.3-8.2) (n=16)	6.5 (5.6-7.3) (n=14)	NR	0.070
		33 wks.	5.8 (5.0-7.0) (n=16)	6.3 (5.0-7.7) (n=14)	NR	0.300
	≤3.9 mmol/l SMPG Values throughout pregnancy, median (range)	End of pregnancy	5 (0-19) (n=16)	4 (0-15) (n=14)	NR	0.790
	4.0-7.9 mmol/l SMPG Values throughout pregnancy, median (range)	End of pregnancy	80 (63-98) (n=16)	78 (60-95) (n=14)	NR	0.310
	≥8.0 mmol/l SMPG Values throughout pregnancy, median (range)	End of pregnancy	15 (0-31) (n=16)	18 (0-35) (n=14)	NR	0.250
	2-hour plasma glucose (mmol/l), median (range)	End of pregnancy	2.8 (1.8-5.5) (n=13)	3.5 (2.2-6.7) (n=15)	NR	0.070
	Large-for-gestational-age infants, median (range)	End of pregnancy	4 (25%) (n=16)	4 (29%) (n=15)	RR 0.94 (95% CI 0.28 to 3.09)*	1.000
	Birth weight (g) , median (range)	End of pregnancy	3,371 (1,070-4,260) (n=16)	3,343 (2,773-3,818) (n=15)	NR	0.700
	Birth weight z-score, median (range)	End of pregnancy	0.27 (-2.32-3.18) (n=16)	0.22 (-1.13-2.19) (n=15)	NR	0.650

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**		
	Neonatal Hypoglycemia, n (%)	End of pregnancy	4 (31%) (n=13)	2 (14%) (n=15)	RR 2.31 (95% CI 0.40 to 8.78)*	0.390
	Severe Neonatal Hypoglycemia, n (%)	End of pregnancy	0 (0%) (n=13)	0 (0%) (n=15)	IC	IC
	Preterm delivery and/or severe neonatal hypoglycemia, n (%)	End of pregnancy	2 (15%) (n=13)	0 (0%) (n=15)	RD 0.15 (-0.05 to 0.16)*	0.220
	Caesarian Section, n (%)	End of pregnancy	8 (50%) (n=16)	6 (43%) (n=15)	RR 1.25 (95% CI 0.57 to 2.75) *	0.700
	Miscarriage, n (%)	End of pregnancy	0 (0%) (n=16)	1 (7%) (n=15)	RD -6.7% (95% CI -19.3% to 6.0%)*	0.480

IC, incalculable; NR, not reported; OR, odds ratio; RR, risk ratio;
*Calculated by AAI.
†Congenital anomalies included aortic stenosis and hypospadias grade 1 (CGM group) and hypoplastic right heart syndrome (termination of pregnancy), aberrant right subclavian artery, and bilateral hydronephrosis (control group).
‡Composite outcome comprises pregnancy loss (miscarriage, stillbirth, and neonatal death); birth injury; neonatal hypoglycaemia; hyperbilirubinaemia; respiratory distress; and high-level neonatal care for more than 24 h.

Appendix Table G6. Results from Cost Effectiveness Studies

Type 1 Studies:	Chaugule 2017[1]	Huang 2010[2]	McQueen 2011[3]	Roze 2014[4]
Population	Adult only (avg. age = 46) Baseline HbA1c = 8.6% Type I Diabetes 53% Male MDI	Included two cohorts: Baseline HbA1c = 7.6 and 7.1%: for SMBG and CGM groups respectively with avg. age = 43 (25-73) 57% Female HbA1c <7.0% avg. age = 31 (8-65) Both MDI and CSII included	Adult only (avg. age 40) with Baseline HbA1c = 7.6% Type 1 Diabetes Assumed 20 yrs. since diagnosis Both MDI and CSII included	Adult only (avg. age =27) Baseline HbA1c = 8.6% 54.5% Female Assumed 13 yrs. since diagnosis CSII
Intervention(s)	CGM	CGM	CGM	CGM
Comparator(s)	SMBG	SMBG	SMBG	SMBG
Country	Canada	United States	United States	Sweden
Funding	Dexcom Inc.	JDRF Grant	Reports no funding received	Medtronic
Study design	CUA	CUA	CUA	CUA
Perspective	Canadian societal	Societal	Societal	Swedish societal
Time horizon	50 years	Lifetime	33 years	70 years
Analytic model	CORE Diabetes Model Cohort-based Monte Carlo Incorporating Markov sub-models	Recycled predictions for Immediate outcomes Markov model extrapolated from trial based utilities	Markov Cohort Analysis constructed in decision analysis format. Holds similarities to CORE	CORE Diabetes Model Cohort-based Monte Carlo Incorporating Markov sub-models
Effectiveness outcome	QALY	QALWeeks and QALY	QALY	QALY
Effectiveness outcome components	Assumed 0.6% HbA1c greater reduction[8] Key health states/ complications: Angina pectoris, myocardial infarction, congestive heart failure, stroke, peripheral vascular disease, DM retinopathy, cataracts, hypoglycemia, DM ketoacidosis, nephropathy, neuropathy, foot ulcer/ amputation, macular edema, and	Assumed 0.5% HbA1c reduction of 0.53% Health states divided into modules: Retinopathy, Nephropathy, Neuropathy, Ischemic Heart, Myocardial Infarction, Congestive Heart Failure, Stroke	Assumed 0.5% HbA1c reduction[14] Key health states/ complications: Retinopathy, nephropathy, neuropathy, Coronary Heart Disease, continue with diabetes and no complications, or death. With additional sub-diseases associated with each disease state.	Assumed 0.3% HbA1c reduction[15] with greater reduction for every extra day of sensor use per week. Key health states/ complications: Angina pectoris, myocardial infarction, congestive heart failure, stroke, peripheral vascular disease, DM retinopathy, cataracts, hypoglycemia, DM ketoacidosis,

Type 1 Studies:	Chaugule 2017[1]	Huang 2010[2]	McQueen 2011[3]	Roze 2014[4]
	depression			nephropathy, neuropathy, foot ulcer/ amputation, macular edema, and depression
Source for effectiveness data	DIAMOND RCT[8] IMS CORE Diabetes Model	JDRF Trial[14] Health Utility Index DCCT[9] Published literature[16-18]	Modeled after the C.D.C. Cost-Effectiveness Group analysis, CDM, relied on professional expertise, and DCCT[9] published literature[19-22], Associated utilities taken from EQ-5D catalog	IMS CORE Diabetes Model DCCT[9] Published literature[20, 23]
Costing year	2016	2010	2007	2011
Currency	1 USD = 1.3 CAD[6]	USD	USD	1 USD = 6.4 Swedish SEK[6]
Discounting	1.5%	3%	3%	3%
Components of cost data	Management cost, card complications, renal complications, acute events, eye disease, neuro/foot ulcer/amputations	Direct costs divided between personnel (staff time for training) and medical care costs (device and usage costs) Indirect cost, work/school performance. Hours devoted to diabetes care	Hospital inpatient visits, nursing/residential facility visits, physician's office visits, emergency department trips, hospital outpatient visits, home health care, hospice care, podiatry care, insulin, DM supplies, oral agents, retail prescriptions, other supplies, and patient time. Included indirect cost such as lost wages.	Intervention (Enlite sensor, test strips, and others), complication (Cardiovascular, renal, hypoglycemia, eye disease, others) and indirect cost (including production loss)
Cost sources	Canadian Formulary health.gov Published literature	Bureau of Labor Statistics Averaged device manufacturer retail prices Redbook Published Literature	Costs were derived from evidence published by the ADA and device manufacture retail prices.	Swedish Pharmaceutical Benefits Board Published Literature[9, 24]
Sensitivity analysis	One-way sensitivity analyses discount rate, baseline HbA1c level, hypoglycemia-related disutility, HbA1c reduction	Isolated benefit to include only improved glucose control, HbA1c difference range, number of test strips 2 vs 10, daily cost of CGM	Conducted one-way and multivariate probabilistic analysis. Included varying all assumed parameters by	One-way sensitivity analysis: Increasing frequency of CGM from 48 to 51 sensors / yr.

Type 1 Studies:	Chaugule 2017[1]	Huang 2010[2]	McQueen 2011[3]	Roze 2014[4]
	conferred by CGM vs SMBG, percentage reduction in NSHEs and SHEs, starting utility of patients in the simulation cohort, and fingersticks per day Probabilistic sensitivity analysis used to derive the acceptability curve.		15%.The top 10 most influential variables then underwent additional testing and were varied by 50%.	Number of SMBG test from 2.1 to 7.1 Baseline HbAc1 level from 7.2 to 9% Rate of severe hypoglycemia Discount rates from 0 to 5% Complication costs from ±10%
QHES	**86/100**	**85/100**	**92/100**	**93/100**
Results:				
Cost / QALY of CGM	$440,955/ 8.38 = $52,620/QALY	$659,837 / 14.35 QALY= $45,982/QALY	$494,135 / 10.81 QALY= $45,710/QALY	$448,832 / 13.05QALY= $34,393/QALY
Cost / QALY of comparator(s)	$293,621/ 5.03 = $58,374/QALY	$601,070 / 13.75 QALY = $43,714/QALY	$470,583 / 10.29 QALY= $45,732 /QALY	$405,088 / 12.29QALY= $32,961/QALY
ICER	$43,926/ QALY	$98,679 / QALY	$45,033 / QALY	$57,433 / QALY
One-way SA	Hypoglycemia disutility decrease by 50% caused ICER to increase to 84,972 Otherwise, results stable and within original CI: • Varying baseline HbA1c from 7.6 to 9.5 ICER remained between $43,848 and $45,215 • % HbA1c reduction CGM vs SMBG =0.3 and 0.9 were $45,159and $42,552	ICER increased to $701,397 if benefit restricted to lowering glucose. If daily costs of CGM reduced from $13.85 to $9.89 the ICER drops below $70,000 If 2 test strips used per day CGM would be cost saving	Utility of diabetes with no complications, the annual cost of CHD, and the probability of going from diabetes with no complications to the CHD disease state, had the largest impact on the model. The utility of diabetes with no complications was decreased (increased) by 50%, the ICER over $300,000 ($30,000) /QALY. Annual cost of CHD also had a large impact on the model results, and when decreased (increased) by 50%, the ICER was US$86,000 ($12,000) /	Increasing the CGM sensor use to 51 sensors/year $58,044 Varying the number of SMBG tests/day from 7.1, though 6.1, to 2.1 resulted in the ICER of $74,292, $68,183, $43,751 / QALY Altering the baseline HbA1c value from 8.6% to 7.2% to 9% changed the ICER to $92,759 $53,693 /QLY respectively

Type 1 Studies:	Chaugule 2017[1]	Huang 2010[2]	McQueen 2011[3]	Roze 2014[4]
			QALY.	Increasing the rate of severe hypoglycemic events reduced the ICER to $46,349 /QALY.
Other SA	Presents an acceptability curve built from probabilistic model.	NR	Results from Monte Carlo Probabilistic model CGM: $494,135 (420,381 - 571,631) QALY=10.812 (9.894 - 11.887) SMBG: $470,583 (397,782 - 550,598) QALY=10.289 (9.615 - 10.957) 48% of the Monte Carlo simulations were under US$50,000/QALY, while 70% were under US$100,000/QALY	NR
Author's Conclusion	With a WTP threshold of $50,000 CGM was found to be a robustly, cost effective alternative to SMBG	Wide uncertainty with CI that included CGM dominating and being dominated by SMBG The immediate quality-of-life effect of CGM was responsible for the majority of projected lifetime benefits of the technology.	CGM was found to be cost effective in more circumstances than not, given a WTP of $100,000.	CGM is a cost–effective option in the treatment of Type 1 diabetes in Sweden
Limitations	Canadian societal perspective Industry funded	Cardiovascular complications relied on type 2 diabetes cardiovascular models. High baseline utilities effectively placed a ceiling on the potential quality-of-life benefit of CGM	Some costs were extrapolated from studies that include all age groups.	Swedish societal perspective Industry ties

Type 2 Studies:	Fonda 2016[5]
Population	Adults avg. age= 57.8 years. Diagnosis with type 2 diabetes for at least 3 months. Not taking prandial insulin. Initial A1C of between 7% and 12% Both MDI and CSII
Intervention(s)	CGM (intervention was short-term and intermittent)
Comparator(s)	SMBG
Country	USA (w/UK trial data)
Funding	Dexcom Grant
Study design	CUA
Perspective	Third-party payer (direct costs only)
Time horizon	Lifetime
Analytic model	Markov based (CORE Diabetes Model), Scenario analysis
Effectiveness outcome	Life expectancy (LE) QALY
Effectiveness outcome components	Assumed HbA1c reduction of 1.1 (±1.5) and 0.5 (±1.3) for CGM and SMBG respectively Hypoglycemia, amputation, a myocardial infarction, etc.), the progression of A1C, systolic blood pressure, lipids.
Source for effectiveness data	Risk adjustments are derived from the United Kingdom Prospective Diabetes Study (UKPDS)[10], the Diabetes Control and Complications Trial (DCCT), the Framingham Heart Study, and other published literature. CORE Diabetes Model
Costing year	2011
Currency	USD
Discounting	3%
Components of cost data	Intervention costs of CGM, SMBG, antidiabetic oral medications, insulin, routine management such as recommended screening, exams, and treatment for depression, and treatment of diabetes complications. cardiovascular disease complications, renal complications, acute events, eye disease, and neuropathy
Cost sources	Provided by Dexcom Inc. and published literature[10-13]
Sensitivity analysis	Both univariate and probabilistic sensitivity conduct. Minimal details reported.
QHES	**75**/100
Results:	
Cost / QALY of CGM	$66,094 /6.03 QALY =10,961

Type 2 Studies:	Fonda 2016[5]
Cost / QALY of comparator(s)	$65,441 / 5.96 QALY = 10,980
ICER	$8,898 / QALY
One-way SA	Results not discussed
Other SA	Probabilistic cost-effectiveness analysis suggests that the likelihood of the intervention being cost-effective is 70% at the willingness-to-pay threshold of $100,000 per QALY.
Author's Conclusion	CGM offers a cost-effective alternative to populations matching that the trial specifically: short-term, intermittent use in people with type 2 diabetes.
Limitations	Small sample size of trial (n = 100) to estimate effectiveness parameters. Used older CGM device that has since been update.

Appendix Table G7. Summary of extension study reporting on frequency of CGM use among Children initially randomized to SMBG with A1C >7.0% at the time of initiation of CGM in the JDRF 2008 trial

JDRF (2010) Prospective Cohort LoE II	Use 0 days/week in month 12 (6th month CGM) (n = 11)	Use > 0 to < 4 days/week in month 12 (6th month CGM) (n = 15)	Use 4 to < 6 days/week in month 12 (6th month CGM) (n = 10)	Use ≥ 6 days/week in month 12 (6th month CGM) (n=11)	P-value
A1C (%), mean					
Baseline*	7.8	7.6	7.9	7.8	NR
Change, 6 months	-0.1 ± 0.6	+0.2 ± 0.6	-0.2 ± 0.9	0.0 ± 0.6	NR
Improved ≥ 0.5%, n(%)	3 (27)	2 (13)	4 (40)	3 (27)	NR
Worsened ≥ 0.5%, n(%)	3 (27)	7 (47)	2 (20)	2(18)	NR
A1C < 7.0%, n (%)	2 (18)	1 (7)	3 (30)	2 (18)	NR

*Baseline refers to the time of initiation of CGM use after the 6 months in the JDRF RCT SMBG group

Appendix Table G8. Summary of extension study reporting on frequency of CGM use among Mixed Adults and Children initially randomized to SMBG with A1C >7.0% at the time of initiation of CGM in the JDRF 2008 trial

JDRF (2010) Prospective Cohort LoE II	Use 0 days/week in month 12 (6th month CGM) (n = 11)	Use > 0 to < 4 days/week in month 12 (6th month CGM) (n = 15)	Use 4 to < 6 days/week in month 12 (6th month CGM) (n = 10)	Use ≥ 6 days/week in month 12 (6th month CGM) (n=11)	P-value
A1C (%), mean					
Baseline*	8.1	7.9	8.1	7.7	NR
Change, 6 months	+0.4 ± 1.2	0.0 ± 0.5	-0.6 ± 0.3	0.0 ± 0.3	NR
Improved ≥ 0.5%, n(%)	4 (36)	4 (15)	5 (71)	1 (8)	NR
Worsened ≥ 0.5%, n(%)	4 (36)	5 (19)	0	1 (8)	NR
A1C < 7.0%, n (%)	0	2 (8)	3 (43)	1 (8)	NR

*Baseline refers to the time of initiation of CGM use after the 6 months in the JDRF RCT SMBG group

Appendix Table G9. Summary of extension study reporting on frequency of CGM use among Adults initially randomized to SMBG with A1C >7.0% at the time of initiation of CGM in the JDRF 2008 trial

JDRF (2010) Prospective Cohort LoE II	Use 0 days/week in month 12 (6th month CGM) (n = 11)	Use > 0 to < 4 days/week in month 12 (6th month CGM) (n = 15)	Use 4 to < 6 days/week in month 12 (6th month CGM) (n = 10)	Use ≥ 6 days/week in month 12 (6th month CGM) (n=11)	P-value
A1C (%), mean					
Baseline*	8.0	7.6	7.5	7.6	NR
Change, 6 months	+0.1 ± 0.9	-0.4 ± 0.7	-0.5 ± 0.3	-0.4 ± 0.4	NR
Improved ≥ 0.5%, n(%)	1 (25)	2 (50)	4 (67)	16 (43)	NR
Worsened ≥ 0.5%, n(%)	1 (25)	1 (25)	0	1 (3)	NR
A1C < 7.0%, n (%)	0	2 (50)	3 (50)	10 (27)	NR

*Baseline refers to the time of initiation of CGM use after the 6 months in the JDRF 2008 RCT SMBG group

APPENDIX H. Data Abstraction Tables: Safety Outcomes

Appendix Table H1. Safety outcomes related to CGM device or procedure reported in included RCTs

RCT	Trial length	Outcome	n/N (%)	Events
AE leading to discontinuation*				
Battelino 2011	6 mos	Alarms too frequent	3/62 (5%)	3
		Alarms too frequent/too difficult to operate device	1/62 (2%)	1
		Device too big	2/62 (4%)	2
		Too busy to use device	1/62 (2%)	1
		Too difficult to operate device	1/62 (2%)	1
		Too frequent of adhesive failure	1/62 (2%)	1
		Any reason for discontinuation	9/62 (14.5%)	9
Deiss 2006	3 mos	Difficulties with sensor use and/or alarms	6/108 (6%)	6
Hermanides 2011	6.5 mos	Intolerant of SAP intensity	1/44 (2%)	1
		Intolerant of sensor use	4/87 (5%)	4
		Any reason for discontinuation	5/87 (6%)	5
Lind 2017	6.5 mos	Allergic reaction to sensor	1/142 (1%)	1
O'Connell 2009	3 mos	Burden of alarms	2/31 (6%)	2
		Difficulty maintaining transmitter adhesion	1/31 (3%)	1
		Skin irritation	2/31 (6%)	2
		Any reason for discontinuation	5/31 (16%)	5
Tildesley 2013	6 mos	Treatment discomfort or inconvenience	5/25 (20%)	5
		Subcutaneous infection	1/25 (4%)	1
		Any reason for discontinuation	6/25 (24%)	6
Van Beers 2016	4 mos	Could not upload CGM data	5/52 (4%)	2
Wei 2016	3 mos†	Site discomfort	1/58 (2%)	1
Technical/mechanical issues				
Langeland 2012 (cross-over trial)	1 month	Technical problems with sensor (all readings were lost)	4/27 (15%)	4
Lind 2017 (cross-over trial)	6.5 mos	Device issue	1/156 (1%)	1
O'Connell 2009	3 mos	Failure of insulin pump	1/31 (3%)	1
		Radiofrequency transmitter replacement needed	4/31 (13%)	4
		Any mechanical problems related to device	5/31 (16%)	5
Feig 2017		Problems encountered with device	83/103 (81%)	204

RCT	Trial length	Outcome	n/N (%)	Events
	6 mos to 8.5 mos	Reasons for not using device	80/103 (78%)	274
Device-related AE				
Feig 2017	6 mos to 8.5 mos	Skin changes	46/103 (45%)	103
Hermanides 2011	6.5 mos	Skin-related problems at the sensor or insulin infusion site related to device	17/83 (20%)	NR
	6.5 mos	Any device-related AE, possible or probable	20/83 (24%)	26
Lind 2017 (cross-over trial)	6.5 mos	Allergic reaction to sensor	1/156 (1%)	1
		Inflammation‡	1/156 (1%)	1
		Itching (pruritus) at application site	1/156 (1%)	1
		Rash at application site	1/156 (1%)	2
		Any device related AE	4/156 (3%)	5
New 2015	3.3 mos	Any sensor insertion AE	12/157 (8%)	13
Tildesley 2013	6 mos	Cyst from sensor	1/25 (4%)	1
Wei 2016	3 mos†	Mild erythema, itchiness, and inflammation at sensor insertion site§	NR	NR
		Skin infection at sensor insertion site	0/58 (0%)	0
Yoo 2008	3 mos	Skin reaction	0/29 (0%)	0
Serious device-related AE				
Bergenstal 2010	12 mos	Cellulitis from insertion site infection (requiring hospital admission)	2/244 (1%)	2
Feig 2017	6 mos to 8.5 mos	Severe skin change	3/49 (6%)	3**
Hermanides 2011	6.5 mos	Serious device related AE (hospitalization for DKA because of pump failure)	1/44 (2%)	1
Hirsch 2008	6 mos	Skin abscess at infusion site	1/72 (1%)††	2
Hommel 2014 (cross-over trial)	6 mos	Hospitalization, diabetes-related	(3%)‡‡	NR
JDRF 2008	6.5 mos	Cellulitis related to sensor use	2/165 (1%)	2
JDRF 2009a	6.5 mos	Serious AE related to device or study procedures	0/66 (0%)	0
Lind 2017 (cross-over trial)	6.5 mos	Retinal detachment	1/156 (1%)	1
Maurus 2012	6.5 mos	Serious device or study related adverse events	0/74 (0%)	0
		Serious skin reactions	0/74 (0%)	0

RCT	Trial length	Outcome	n/N (%)	Events
Tumminia 2015 (cross-over trial)	6 mos	Hospitalization for ketoacidosis	1/14 (7%)	1
Van Beers 2016	4 mos	Serious adverse events related to device or intervention	0/52 (0%)	0

AE, adverse event; NR, not reported; RCT, randomized controlled trial

*Percentages of patients discontinuing reported in safety tables in the report represents the total sum of patients discontinuing. Meaning, for studies reporting more than one adverse event that caused discontinuation, the "any reason for discontinuation" percentage was reported

†Patients were enrolled between 24-36 gestational weeks and were followed until the participants gave birth. Follow-up was estimated to be 3 months

‡Location and cause of inflammation was not reported by authors

§ Authors only state that these events occurred "often" but no data was provided

**Authors reported that there were 3 "severe" skin changes reported; this was interpreted to mean three patients experienced three events

††Authors reported that 1 patient experienced a skin abscess (twice) at the infusion site; although both groups received pump therapy and the group was not explicitly stated, the assumption was made that the patient was in the CGM group

‡‡2.5% in the sensor-on group, 0.6% in the sensor off group

Appendix Table H2. Safety outcomes on any adverse event or any serious adverse event reported from included RCTs

RCT	Trial length	Outcome	CGM n/N (%)	CGM events	SMBG n/N (%)	SMBG events
Any AE (≥1 event; not necessarily related to device, procedure or study)						
Battelino 2012 (cross-over trial)	6 mos.	Non-serious adverse events (not otherwise specified)	NR/153	80	NR/153	98
Feig 2017	6 mos to 8.5 mos.	Participants with adverse events (not further specified)	51/107 (48%)	109	40/107 (43%)	78
Hommel 2014 (cross-over trial)*	6 mos.	AE (any, ≥1 event)	69/153 (45%)	NR	77/153 (50%)	NR
Langeland 2012 (cross-over trial)	1 month	Any adverse event	0/30 (0%)	0	0/30 (0%)	0
Lind 2017 (cross-over trial)	6.5 mos.	Retinopathy	1/156 (1%)	1	0/151 (0%)	0
		Infection	2/156 (2%)	1	0/151 (0%)	0
		Localized infection	1/156 (1%)	1	1/156 (1%)	1
		post-procedural infection	1/156 (1%)	1	0/151 (0%)	0
		DVT	1/156 (1%)	1	0/151 (0%)	0
		thrombophlebitis	1/156 (1%)	1	0/151 (0%)	0
		AE (any, ≥1 event)	77/156 (49%)	137	67/151 (44%)	122
Any serious AE (≥1 event; not necessarily related to device, procedure or study)						
Beck 2017a	6 mos.	Any serious adverse event	2/105 (2%)	3	0/53 (0%)	0
Beck 2017b	6 mos	Any serious adverse event	3/74 (4%)	3	0/72 (0%)	0
Feig 2017	6 to 8.5 mos	Any serious adverse event	7/107 (7%)	7	5/107 (5%)	7
Hermanides 2011	6.5 mos.	Any severe adverse event	2/44 (5%)	2	5/39 (13%)	5
Lind 2017 (cross-over trial)	6.5 mos.	Serious AE (any, ≥1 event)	7/156 (5%)	9	3/151 (2%)	9
Secher 2013	8.25 mos.	Severe adverse events	0/79 (0%)	0	NR	NR

*Hommel 2014 reports on the same patient population as Battelino 2012

Appendix Table H3. Safety Outcomes Reported in Included Observational Studies

Observational study	Trial length	Outcome	n/N (%)	Events
Discontinuation				
Rachmiel 2015	12 mos	Skin reactions	2/83 (2%)	2
	12 mos	Pain at insertion site*	NR	NR
	12 mos	Discrepancy between CGM and SMBG*	NR	NR
	12 mos	Annoyance from frequent alerts*	NR	NR
Wong 2014	12 mos	Sensor uncomfortable to wear	307/1724 (18%)	307
	12 mos	Problems inserting sensor	242/1724 (14%)	242
	12 mos	Problems with adhesive holding sensor	215/1724 (12%)	215
	12 mos	Problems with CGM working properly	204/1724 (12%)	204
	12 mos	Too many alarms from CGM	197/1724 (11%)	197
	12 mos	Concerns about CGM accuracy	183/1724 (11%)	183
	12 mos	CGM interfered with sports/activities	132/1724 (8%)	132
	12 mos	Skin reactions from CGM sensor	129/1724 (7%)	129
Device-related AE				
Rachmiel 2015	12 mos	Local reaction to CGM insertion	30/83 (36%)	30
	12 mos	Mild-to-severe local redness	16†/83 (19%)	16
	12 mos	Hyperpigmentation	14†/83 (17%)	14
Soupal 2016	12 mos	Sensor insertion site infection requiring assistance	0/65 (0%)	0

AE, adverse event; CGM, continuous glucose monitoring; NR, not reported; SMBG, self-monitoring blood glucose

*Authors state this event cause discontinuation but data was not reported
†n value back-calculated

Appendix Table H4. Safety Outcomes Reported in RCTs Using Libre Flash Glucose Monitoring System

RCT*	Group	Duration of device use	Outcome	n/N (%)	Events
AE or device associated symptom leading to discontinuation					
Bolinder 2016	Intervention group	6 mos	Itching at sensor insertion site	1/120 (1%)	1
			Rash	1/120 (1%)	1
			Erythema and itching	1/120 (1%)	1
			Rash, erythema, pain, itching	1/120 (1%)	1
			Redness and weeps	1/120 (1%)	1
			Not specified	1/120 (1%)	1
			Any withdrawal due to device-related adverse events or repetitive occurrences of sensor insertion-related symptoms	6/120 (5%)	6
Haak 2016	Intervention group	6 mos	NR	3/149 (2%)	3
Device-related AE, serious/severe †					
Bolinder 2016	Intervention group	6 mos	Allergic reaction at sensor site insertion	1/120 (1%)	1
			Erythema	2/120 (3%)	4
			Rash, erythema, pain, itching	1/120 (1%)	1
			Any serious device related AE	4/120 (3%)	6
Haak 2016	Intervention group	6 mos	Necrosis at sensor insertion site	1/149 (1%)	1
			Infection at sensor insertion site	1/149 (1%)	1
			Any serious device related AE	2/149 (1%)	2
Device-related AE, any †					
Bolinder 2016	Intervention group	6 mos	Allergic reaction at sensor site insertion	1/120 (1%)	1
			Sensor site reaction	1/120 (1%)	1
			Itching at sensor insertion site	1/120 (1%)	1
			Rash	1/120 (1%)	1
			Erythema	3/120 (3%)	5
			Rash, erythema, pain, itching	1/120 (1%)	1
			Oedema	1/120 (1%)	1
			Allergy (Itching, redness, pustules, weeps)	1/120 (1%)	2
			Any device related AE	10/120 (8%)	13
Haak 2016	Intervention group	6 mos	Erythema and itching at sensor site insertion	1/149 (1%)	1
			Sensor-site insertion reaction	1/149 (1%)	1
			Sensor-site allergic reaction, and necrosis at sensor insertion site	1/149 (1%)	2
			Infection at sensor insertion site	1/149 (1%)	2
			Rash at sensor site	1/149 (1%)	2
			Sensor allergy	1/149 (1%)	1

RCT*	Group	Duration of device use	Outcome	n/N (%)	Events
			Any device related AE	6/149 (4%)	9
Sensor insertion-site symptoms †					
Bolinder 2016	Intervention group	6 mos	Erythema	30/120 (25%)	79
			Itching	20/120 (17%)	42
			Rash	12/120 (10%)	29
			Pain	19/120 (16%)	29
			Bleeding	12/120 (10%)	19
			Bruising	4/120 (3%)	4
			Oedema	5/120 (4%)	8
			Induration	3/120 (3%)	5
			Total patients with ≥1 sensor insertion-site symptom	47/120 (40%)	215
Haak 2016	Intervention group	6 mos	Erythema	23/149 (15%)	54
			Itching	14/149 (9%)	22
			Rash	8/149 (5%)	16
			Pain	15/149 (10%)	24
			Bleeding	8/149 (5%)	11
			Bruising	4/149 (3%)	4
			Oedema	5/149 (3%)	8
			Induration	3/149 (2%)	4
			Total patients with ≥1 sensor insertion-site symptom	41/149 (28%)	143
Bolinder 2016	Control group	1 month (blinded)	Erythema	4/121 (3%)	5
			Itching	5/121 (4%)	6
			Rash	2/121 (2%)	2
			Pain	7/121 (6%)	8
			Bleeding	5/121 (4%)	5
			Bruising	1/121 (1%)	11
			Oedema	0/121 (0%)	0
			Induration	0/121 (0%)	0
Haak 2016	Control group	1 month (blinded)	Erythema	1/75 (1%)	1
			Itching	1/75 (1%)	1
			Rash	1/75 (1%)	1
			Pain	3/75 (4%)	3
			Bleeding	2/75 (2%)	2
			Bruising	0/75 (0%)	0
			Oedema	0/75 (0%)	0
			Induration	1/75 (1%)	1
Bolinder 2016	Pre-randomization group	2 weeks	Erythema	1/252 (0.4%)	1
			Itching	2/252 (1%)	3
			Rash	0/252 (0%)	0

RCT*	Group	Duration of device use	Outcome	n/N (%)	Events
			Pain	1/252 (0.4%)	1
			Bleeding	1/252 (0.4%)	1
			Bruising	0/252 (0%)	0
			Oedema	0/252 (0%)	0
			Induration	0/252 (0%)	0
Haak 2016	Pre-randomization group	2 weeks	Erythema	1/78 (1%)	1
			Itching	1/78 (1%)	1
			Rash	2/78 (3%)	2
			Pain	2/78 (3%)	2
			Bleeding	0/78 (0%)	0
			Bruising	0/78 (0%)	0
			Oedema	0/78 (0%)	0
			Induration	0/78 (0%)	0

AE: adverse event; RCT: randomized controlled trial
*Bolinder 2016 evaluated an adult population with type 1 dibaetes mellitus, Haak 2016 evaluated a population with type 2 diabetes mellitus
† The distinction between "device related AEs (serious or not serious)" and "sensor insertion-site symptoms" was not clearly reported by study authors. Patients may have experienced both a device related AE and a sensor insertion-site symptom, but the study did not provide enough information to tell.

Appendix Table H5. Safety outcomes reported in the Summary of Safety and Effectiveness Data documents of FDA approved CGM devices

SSED	Trial Length	Outcome	n/N (%)	Events
SERIOUS DEVICE-RELATED ADVERSE EVENT				
MiniMed 670G system run-in (SG)	14 days	Device-related serious adverse events	0/89 (0%)	0
DexCom G4 (original study, IDE #G110107/S001), P120005)	7 days	Serious Adverse Device Events (SADEs)	0/72 (0%)	0
DexCom G4 (pediatric [2-17 years], IDE #G140042), P120005/S002)	7 days	Serious Adverse Device Events (SADEs)	0/176 (0%)	0
DexCom G4 (software 505 study in pediatric [2-17 years], IDE #G140042), P120005/S031)	7 days	Serious Adverse Device Events (SADEs)	0/79 (0%)	0
MiniMed 530G (pivotal study, IDE# G100028, P120010)	NR	Serious Adverse Device Events (SADEs)	0/50 (0%)	0
MiniMed 530G (pivotal study, IDE# G110131/A001, P120010)	6 days	Serious Adverse Device Events (SADEs)	0/90 (0%)	0
Paradigm REAL time and Guardian REAL-Time (pediatric)	6 day	Serious device-related events	0/61 (0%)	0
DexCom STS (DexCom Seven) (feasibility study [PTL9001], 72 hours)	72 hrs	Serious Adverse Device or Procedure-related Events (SADEs)	0/42 (0%)	0

SSED	Trial Length	Outcome	n/N (%)	Events
MiniMed 530G (ASPIRE in home study, IDE# G110044/S002, P120010/S046)	3 mos	Serious Adverse Device or Procedure-related Events (SADEs)	0/247 (0%)	0
UNANTICIPATED DEVICE-RELATED AE				
DexCom G4 (original study, IDE #G110107/S001), P120005)	7 days	Unanticipated Adverse Device Events (IADEs)	0/72 (0%)	0
DexCom G4 (pediatric [2-17 years], IDE #G140042), P120005/S002)	7 days	Unanticipated Adverse Device Events (IADEs)	0/176 (0%)	0
DexCom G4 (software 505 study in pediatric [2-17 years], IDE #G140042), P120005/S031)	7 days	Unanticipated Adverse Device Events (IADEs)	0/79 (0%)	0
DexCom STS (DexCom Seven) (feasibility study [PTL9001], 72 hours)	72 hrs	Unanticipated Adverse Device Events (IADEs)	0/42 (0%)	0
MiniMed 530G (ASPIRE in home study, IDE# G110044/S002, P120010/S046)	3 mos	Unanticipated Adverse Device Events (IADEs)	0/247 (0%)	0
MiniMed 530G (pivotal study, IDE# G100028, P120010)	NR	Unanticipated Adverse Device Events (IADEs)	0/50 (0%)	0
MiniMed 530G (pivotal study, IDE# G110131/A001, P120010)	6 days	Unanticipated Adverse Device Events (IADEs)	0/90 (0%)	0
MiniMed 670G system study (SG)	3.5 mos	Unanticipated Adverse Device Events (IADEs)	0/123 (0%)	0
DEVICE-RELATED AE				
Any				
Freestyle Libre Flash GM	10 days	AE (any) at sensor application site	5/50 (10%)	6
Freestyle navigator (in-clinical study)	5 days	AE (any) related to sensor insertion site	34/58 (59%)	NR
Freestyle navigator (in-clinical study)	5 days	Device-related AE (any)	1/58 (2%)	NR
Paradigm REAL time and Guardian REAL-Time (pediatric)	6 days	Any device-related (probable) event	5/61 (8%)	5
MiniMed 530G (pivotal study, IDE# G100028, P120010)	NR	Any device-related AE	2/50 (4%)	2
MiniMed 530G (pivotal study, IDE# G110131/A001, P120010)	6 days	Any device-related AE	1/90 (1%)	1
DexCom G4 (original study, IDE #G110107/S001), P120005)	7 days	Any device-related AE (due to sensor insertion and adhesive area irritations, all deemed mild and resolved)	NR/72	22
DexCom G4 (pediatric [2-17 years], IDE #G140042), P120005/S002)	7 days	Any device-related AE (due to sensor insertion and adhesive area irritations, all deemed mild/moderate and resolved)	10/176 (6%)	17
DexCom G4 (software 505 study, IDE #G130238), P120005/S018)	7 days	Any device-related AE (due to sensor insertion and adhesive area irritations, all deemed mild and resolved)	12/51(24 %)	12

SSED	Trial Length	Outcome	n/N (%)	Events
Any skin-related (no further delineated)				
MiniMed 530G (ASPIRE in home study, IDE# G110044/S002, P120010/S046)	3 mos	Skin-related (skin irritation, skin infection, rash, bleeding, bruising (ecchymosis), redness, rash, abrasion, dermatitis and pruritus)	NR/247	NR
Bleeding or bruising at sensor insertion site				
DexCom STS (DexCom Seven) (feasibility study [PTL9000], 12 hour clinic day, up to 2 sensors inserted)	12 hrs	bleeding at insertion site	1/31 (3%)	1
DexCom STS (DexCom Seven) (feasibility study [PTL9001], 72 hours)	72 hrs	bleeding at insertion site	1/42 (2%)	1
Paradigm REAL time and Guardian Real-Time (pediatric)	6 day	Bleeding at insertion site	1/61 (2%)	1
MiniMed 530G (pivotal study, IDE# G100028, P120010)	NR	bleeding at sensor site	1/50 (2%)	1
DexCom STS (DexCom Seven) (feasibility study [PTL9000], 12 hour clinic day, up to 2 sensors inserted)	12 hrs	bruising	1/31 (3%)	1
MiniMed 530G (pivotal study, IDE# G100028, P120010)	NR	bruising at sensor site	1/50 (2%)	1
DexCom G4 (pediatric [2-17 years], IDE #G140042), P120005/S002)	7 days	Bruising or bleeding at sensor insertion or adhesive site	0/176 (0%)	0
DexCom G4 (software 505 study in pediatric [2-17 years], IDE #G140042), P120005/S031)	7 days	Bruising or bleeding at sensor insertion or adhesive site	0/79 (0%)	0
Freestyle Libre Flash GM	10 day	Mild bruising at sensor insertion site	3/ 50 (6%)	3
Blisters				
Freestyle navigator (in-clinical study)	5 days	Blisters under sensor mount	1/58 (2%)	NR
DexCom STS (DexCom Seven) (feasibility study [PTL9000], 12 hour clinic day, up to 2 sensors inserted)	12 hrs	blisters	NR/31	2
DexCom STS (DexCom Seven) (feasibility study [PTL9001], 72 hours)	72 hrs	blisters	1/42 (2%)	1
MiniMed 670G system run-in (SG)	14 days	Blisters from skin tac used under tape	1/89 (1%)	1
DexCom STS (DexCom Seven) (pivotal study, randomized to unblinded and blinded groups, 9 days)	9 days	blisters	NR/91	2
Edema				

SSED	Trial Length	Outcome	n/N (%)	Events
DexCom STS (DexCom Seven) (feasibility study [PTL9000], 12 hour clinic day, up to 2 sensors inserted)	12 hrs	edema	1/31 (3%)	1
DexCom STS (DexCom Seven) (feasibility study [PTL9001], 72 hours)	72 hrs	edema	1/42 (2%)	1
DexCom STS (DexCom Seven) (pivotal study, randomized to unblinded and blinded groups, 9 days)	9 days	edema	NR/91	2
DexCom G4 (software 505 study in pediatric [2-17 years], IDE #G140042), P120005/S031)	7 days	Edema	2/79 (3%)	2
DexCom G4 (original study, IDE #G110107/S001), P120005)	7 days	Edema, adhesive area (device-related)	2/72 (3%)	3
Erythema				
DexCom STS (DexCom Seven) (feasibility study [PTL9000], 12 hour clinic day, up to 2 sensors inserted)	12 hrs	erythema	NR/31	14
DexCom STS (DexCom Seven) (feasibility study [PTL9001], 72 hours)	72 hrs	erythema	NR/42	15
DexCom STS (DexCom Seven) (pivotal study, randomized to unblinded and blinded groups, 9 days)	9 days	erythema	NR/91	17
DexCom G4 (software 505 study in pediatric [2-17 years], IDE #G140042), P120005/S031)	7 days	Erythema	7/79 (9%)	7
Freestyle Libre Flash GM	10 days	Erythema at sensor insertion site	2/50 (4%)	3
DexCom G4 (original study, IDE #G110107/S001), P120005)	7 days	Erythema, adhesive area (device-related)	7/72 (10%)	12
DexCom G4 (software 505 study, IDE #G130238), P120005/S018)	7 days	Erythema, adhesive area (device-related)	9/51 (17%)	12
DexCom G4 (original study, IDE #G110107/S001), P120005)	7 days	Erythema, sensor site (device-related)	4/72 (6%)	7
DexCom G4 (software 505 study, IDE #G130238), P120005/S018)	7 days	Erythema, sensor site (device-related)	3/51 (6%)	12
Freestyle navigator (in-clinical study)	5 days	Mild erythema	16/58 (28%)	NR
DexCom G4 (pediatric [2-17 years], IDE #G140042), P120005/S002)	7 days	Redness at sensor insertion site	1/176 (1%)	1
Edema or Erythema				
DexCom G4 (pediatric [2-17 years], IDE #G140042), P120005/S002)	7 days	Erythema/edema (device-related skin irritation)	9/176 (5%)	16
DexCom G4 (pediatric [2-17 years], IDE #G140042), P120005/S002)	7 days	mild edema/erythema	1/176 (1%)	1
Infection				

SSED	Trial Length	Outcome	n/N (%)	Events
DexCom G4 (pediatric [2-17 years], IDE #G140042), P120005/S002)	7 days	Infection, sensor or adhesive area	0/176 (0%)	0
DexCom G4 (software 505 study in pediatric [2-17 years], IDE #G140042), P120005/S031)	7 days	Infection, sensor or adhesive area	0/79 (0%)	0
DexCom G4 (original study, IDE #G110107/S001), P120005)	7 days	Infection, sensor or adhesive area (device-related)	0/72 (0%)	0
DexCom G4 (software 505 study, IDE #G130238), P120005/S018)	7 days	Infection, sensor or adhesive area (device-related)	0/51 (0%)	0
Pain				
Paradigm REAL time and Guardian REAL-Time (pediatric)	6 days	Pain	1/61 (2%)	1
MiniMed 530G (pivotal study, IDE# G110131/A001, P120010)	6 days	Pain at sensor site during sensor wear (device-related)	1/90 (1%)	1
DexCom G4 (pediatric [2-17 years], IDE #G140042), P120005/S002)	7 days	Pain/discomfort (device-related; excessive per protocol)	1/176 (1%)	1
Rash, itching				
Paradigm REAL time and Guardian REAL-Time (pediatric)	6 days	Rash	1/61 (2%)	1
MiniMed 670G system run-in (SG)	14 days	Rash	1/89 (1%)	1
Freestyle navigator (in-clinical study)	5 days	Mild itching	10/58 (17%)	10
Paradigm REAL time and Guardian REAL-Time (pediatric)	6 days	Skin irritation	2/61 (3%)	2
Technical/mechanical issues				
DexCom G4 (original study, IDE #G110107/S001), P120005)	7 days	Broken sensor wires/wire detachment	0/72 (0%)	0
DexCom G4 (pediatric [2-17 years], IDE #G140042), P120005/S002)	7 days	Broken sensor wires/wire detachment	0/176 (0%)	0
DexCom G4 (software 505 study in pediatric [2-17 years], IDE #G140042), P120005/S031)	7 days	Broken sensor wires/wire detachment	0/79 (0%)	0
DexCom G4 (software 505 study, IDE #G130238), P120005/S018)	7 days	Broken sensor wires/wire detachment	0/51 (0%)	0
MiniMed 530G (ASPIRE in home study, IDE# G110044/S002, P120010/S046)	3 mos	infusion-set related, resulting in hyperglycemia	NR/247	NR
MiniMed 530G (ASPIRE in home study, IDE# G110044/S002, P120010/S046)	3 mos	pump-priming issue and hypoglycemia	NR/247	NR
Other				
MiniMed 530G (pivotal study, IDE# G100028, P120010)	NR	urine ketones due to improper infusion tubing connection	1/50 (2%)	1

SSED	Trial Length	Outcome	n/N (%)	Events
MiniMed 670G system study (SG)	3.5 mos	Device-related events leading to hyperglycemia (included infusion set issues, software of hardware issues resulting in depletion of pump's battery backup, and sensor values trigger the safe basal insulin delivery rate that was sufficient to maintain normal glucose levels)	17/123 (14)	17
PROCEDURE-RELATED AE				
Any				
MiniMed 530G (pivotal study, IDE# G100028, P120010)	NR	Any procedure-related AE	5/50 (10%)	6
MiniMed 530G (pivotal study, IDE# G110131/A001, P120010)	6 days	Any procedure-related AE	7/90 (8%)	7
DexCom G4 (software 505 study, IDE #G130238), P120005/S018)	7 days	Any procedure-related AE	1/51 (2%)	1
Freestyle Libre Flash GM	10 days	AE (any) due to study procedure (beyond sensor application site events)	8/ 50 (16%)	11
IV-related (e.g., pain, discomfort, bruising)				
MiniMed 530G (pivotal study, IDE# G110131/A001, P120010)	6 days	discomfort related to IV catheter (procedure-related)	5/90 (6%)	5
DexCom G4 (pediatric [2-17 years], IDE #G140042), P120005/S002)	7 days	brief period of syncope during IV insertion attempts during the clinic session (study-related)	1/176 (1%)	1
MiniMed 530G (ASPIRE in home study, IDE# G110044/S002, P120010/S046)	3 mos	syncope	NR/247	NR
Freestyle Libre Flash GM	10 days	IV infiltrations	1/50 (2%)	1
DexCom G4 (software 505 study in pediatric [2-17 years], IDE #G140042), P120005/S031)	7 days	IV insertion issues during clinic	1/79 (1%)	1
Freestyle Libre Flash GM	10 days	Mild bruising at IV insertion	3/50 (6%)	3
MiniMed 530G (pivotal study, IDE# G100028, P120010)	NR	pain at IV site	1/50 (2%)	2
MiniMed 670G system study (SG)	3.5 mos	pain at IV site (procedure-related)	1/123 (1%)	1
MiniMed 670G system study (SG)	3.5 mos	thrombophlebitis (procedure-related)	1/123 (1%)	1
Other skin irritation or pain/discomfort				
MiniMed 530G (pivotal study, IDE# G110131/A001, P120010)	6 days	edema due to heating pad placement (procedure-related)	1/90 (1%)	1
DexCom G4 (software 505 study, IDE #G130238), P120005/S018)	7 days	Blister on left elbow during session	1/51 (2%)	1

SSED	Trial Length	Outcome	n/N (%)	Events
MiniMed 530G (pivotal study, IDE# G100028, P120010)	NR	blisters on toes (exercising during study procedure)	1/50 (2%)	1
MiniMed 670G system study (SG)	3.5 mos	irritation/bruising (procedure-related)	1/123 (1%)	1
MiniMed 530G (pivotal study, IDE# G100028, P120010)	NR	strained muscle (exercise during study procedure)	1/50 (2%)	2
Freestyle Libre Flash GM	10 days	Mild erythema (left elbow)	1/50 (2%)	1
MiniMed 670G system study (SG)	3.5 mos	pain (procedure-related)	1/123 (1%)	1
Other				
MiniMed 530G (ASPIRE in home study, IDE# G110044/S002, P120010/S046)	3 mos	emesis (mixed meal tolerance test used to assess C-peptide)	NR/247	NR
MiniMed 530G (pivotal study, IDE# G100028, P120010)	NR	headache (large carb intake during study procedure)	1/50 (2%)	1
MiniMed 530G (pivotal study, IDE# G110131/A001, P120010)	6 days	headache at beginning of hyperglycemic challenge (procedure-related)	1/90 (1%)	1
MiniMed 530G (pivotal study, IDE# G100028, P120010)	NR	loss of dental filling (during food intake during study)	1/50 (2%)	1
DEVICE- AND/OR PROCEDURE-RELATED AE (ANY)				
DexCom STS (DexCom Seven) (feasibility study [PTL9000], 12 hour clinic day, up to 2 sensors inserted)	12 hrs	Any adverse event related to device and/or procedure	14/31 (45%)	19
DexCom STS (DexCom Seven) (feasibility study [PTL9001], 72 hours)	72 hrs	Any adverse event related to device and/or procedure	11/42 (26%)	18
DexCom STS (DexCom Seven) (pivotal study, randomized to unblinded and blinded groups, 9 days)	9 days	Any adverse event related to device and/or procedure	16/91 (18%)	21
MiniMed 530G (ASPIRE in home study, IDE# G110044/S002, P120010/S046)	3 mos	Any device or procedure-related adverse event	NR/247	NR
MiniMed 530G (pivotal study, IDE# G100028, P120010)	NR	Any procedure and device-related AE	1/50 (2%)	1
DexCom G4 (pediatric [2-17 years], IDE #G140042), P120005/S002)	7 days	"other" AE (were device, disease or study related)	4/176 (2%)	4
ANY SERIOUS AE (NOT NECESSARILY RELATED TO DEVICE, PROCEDURE OR STUDY)				
MiniMed 530G (pivotal study, IDE# G100028, P120010)	NR	Serious Adverse Events (SAEs)	0/50 (0%)	0
MiniMed 530G (pivotal study, IDE# G110131/A001, P120010)	6 days	Serious Adverse Events (SAEs)	0/90 (0%)	0
Freestyle navigator (in-clinical study)	5 days	Serious AE (any)	0/58 (0%)	NR
ANY AE (NOT NECESSARILY RELATED TO DEVICE, PROCEDURE OR STUDY)				

SSED	Trial Length	Outcome	n/N (%)	Events
DexCom G4 (original study, IDE #G110107/S001), P120005)	7 days	Any AE (not necessarily related to device, procedure or study)	NR/72	38
DexCom G4 (pediatric [2-17 years], IDE #G140042), P120005/S002)	7 days	Any AE (not necessarily related to device, procedure or study)	14/176 (8%)	21
DexCom G4 (software 505 study in pediatric [2-17 years], IDE #G140042), P120005/S031)	7 days	Any AE (not necessarily related to device, procedure or study)	10/79 (13%)	10
DexCom G4 (software 505 study, IDE #G130238), P120005/S018)	7 days	Any AE (not necessarily related to device, procedure or study)	NR/51	13
MiniMed 530G (pivotal study, IDE# G100028, P120010)	NR	Any AE (not necessarily related to device, procedure or study)	21/50 (42%)	29
MiniMed 530G (pivotal study, IDE# G110131/A001, P120010)	6 days	Any AE (not necessarily related to device, procedure or study)	NR/90	NR
MiniMed 530G (pivotal study, IDE# G100028, P120010)	NR	Any non-device or procedure-related AE	18/50 (36%)	20
MiniMed 530G (pivotal study, IDE# G110131/A001, P120010)	6 days	Any non-device or procedure-related AE	13/90 (14%)	13
DexCom G4 (original study, IDE #G110107/S001), P120005)	7 days	Any non-device-related AE	NR/72	16

AE, adverse event; NR, not reported

Appendix Table H6. Overview of device-related adverse events rates for FDA-approved CGM devices* from FDA Summaries of Safety and Effectiveness Data

Device (year of SSED)	CGM Duration/Use	Reported Adverse Events
Freestyle Libre Flash CGM system (2017) *Pivotal study* N = 50 Mean age: 41.1 ± 14.4 y % completed: 96% Study duration: 10 days	10 days	• Adverse reaction at sensor application site: 5 events, 12% (6/50) • Mild bruising: 6% (3/50) • Erythema at sensor insertion site: 4% (2/50) • Mild bruising at IV insertion site: 2% (1/50) • IV infiltration: 2% (1/50) • Mild erythema unrelated to sensor insertion: 2% (1/50)
Minimed 670G system with smartguard (Sept 2016) *Pivotal study* N = 123 Mean age: 37.8 ± 16.46 y % completed: 97% Study duration: 3.5 months	3.5 months	*Pivotal study* • Appendicitis: 1% (1/123) • Arthritis of the right wrist: 1% (1/123) • *C. difficile* diarrhea: 1% (1/123) • Worsened rheumatoid arthritis: 1% (1/123) • 4 procedure related events: thrombophlebitis, pain, irritation/bruising, pain at IV site (n=NR)
Correlational study N = 89 Mean age: 41.7 ± 19.14 y % completed: 93% Study duration: 14 days	7 days	*Correlational study* • Gastroenteritis: 1% (1/89) • Worsened benign prostatic hypertrophy: 1% (1/89) • Rash at IV site: 1% (1/89) • Upper respiratory symptoms: 1% (1/89) • Skin blister from skin tac: 1% (1/89)
Minimed 630G system with smartguard (Aug 2016) *No additional clinical trials were conducted for the Minimed 630G system with smartguard. See data from Minimed 530G for safety information*		
T:slim X2 Insulin Pump with Dexcom G5 Mobile CGM (2017) *No additional clinical studies were conducted for the T:slim X2 system. See data from Dexcom G4 and G5 Systems for all safety information*		

Device (year of SSED)	CGM Duration/Use	Reported Adverse Events
Dexcom G5 Mobile CGM system (2016) and Dexcom G4 PLATINUM system (2014) *In-clinic and at-home study* N = 51 Mean age: 46.7 ± 15.8 y % completed: 98% Study duration: 7 days	7 days	• Skin blister: 2% (1/51) • Erythema at sensor insertion site: 6% (3/51) • Erythema around adhesive areas: 17% (9/51)
Dexcom G4 PLATINUM (pediatric) system (2015) *Pivotal Study* N = 176 Adults age 2-17 Mean age: 11.5 ± 4.2 y % completed: 100% Study duration: 7 days *Software 505 Clinical study* N = 79 Adults age 2-17 Mean age: 12.2 ± 4.6 y % completed: 100% Study duration: 7 days	7 days 7 days	*Pivotal Study* • Skin irritation: 5% (9/176) • Pain and discomfort at sensor site: 1% (1/176) • Redness at sensor insertion site: 1% (1/176) • Edema/erythema and a skin cut at location of the sensor: 1% (1/176) • Symptomatic hyperglycemia: 1% (1/176) • Syncope during IV insertion: 1% (1/176) *Software 505 Clinical Study* • Erythema: 9% (7/79) • Edema: 3% (2/79) • IV insertion issues: 1% (1/79)
Paradigm REAL-Time Revel System (2015) *Pivotal Study 1* N = 90 Adults age 18-75 Mean age: 44.4 ± 13.8 y % completed: 98.8% Study duration: 6 days	6 days	• Sinusitis 1% (1/90) • Pain at sensor insertion site during sensor wear: 1% (1/90) • Pain and discomfort related to IV catheter: 6% (5/90) • Headache: 1% (1/90) • Edema in left hand: 1% (1/90) • Chest Pain 1% (1/90) • Hypoglycemia: 1% (1/90)
Minimed 530G (September 2013) *Prospective correlational study* N = 90 Mean age: 44.4 ± 16.9 y % completed: 99% Study duration: NR *In-clinic study* N = 50 Mean age: 28.33 ± 11.71 y † % completed: 100% Study duration: NR	NR NR	*Prospective correlational study* • Sinusitis: 1% (1/90) • Pain at sensor site: 1% (1/90) • Pain and discomfort with IV catheter: 6% (5/90) • Headache: 1% (1/90) • Edema from heating pad: 1% (1/90) *In-clinic study* • Blisters from exercise during study procedure: 1% (1/90) • Strained muscle due to exercise: 1% (1/90)

Device (year of SSED)	CGM Duration/Use	Reported Adverse Events
In-home study N = 414 run-in phase, 247 randomized Mean age: 43.3 ± 13.41 y‡ % completed: 64% run-in phase 97% randomized phase Study duration: 4-5 months	3 months	• Headache from increased carbohydrate intake: 1% (1/90) • Lost dental filling during food intake: 1% (1/90) • Pain at IV site: 2% (2/90) • Bruising at sensor site: 1% (1/90) • Urine ketones: 1% (1/90) • Bleeding at sensor site: 1% (1/90) *In-home study*§ • Skin-related adverse events: 6% (20/320),** 3% (4/121) vs 10% (12/126) • Syncope: <1% (1/320), 0% vs 0% • Emesis from mixed meal tolerance test: <1% (1/320), 0% vs 0%
Devices No Longer Commercially Available or Being Phased Out		
OneTouch Vibe Plus System (2016) *No additional clinical studies were conducted for the OneTouch Vibe Plus System. See data from Dexcom G4 and G5 Systems for all safety information The OneTouch Vibe Plus Pump is no longer commercially available.*		
Animas Vibe System (2015) *No additional clinical studies were conducted for the Animas Vibe System. See Data from Dexcom G4 and G5 Systems for safety information. The Animas Vibe pump is no longer commercially available.*		
t:slim G4 Insulin Pump/"t-slim G4 System" (2015) *No additional clinical studies were conducted for the t:slim G4 System. See Data from Dexcom G4 and G5 Systems for safety information. The t:slim G4 insulin pump is no longer commercially available.*		
Paradigm REAL-Time System and Guardian REAL-Time System (Pediatric Versions) (2007) N = 61 age 7-12 n =30	6 days	• Bleeding at insertion site: 2% (1/61) • Rash: 2% (1/61) • Pain: 2% (1/61) • Skin irritation: 3% (2/61)

Device (year of SSED)	CGM Duration/Use	Reported Adverse Events
age 13-17 n = 31 % completed: 93% Study duration: 6 days		
DexCom SEVEN PLUS (2006)		
Pilot study N = 31 Mean Age: 42 ± 13 y % completed: 100% Study duration: 12-24 h	12 hours: N = 16 24 hours: N = 15	*Pilot study* • Bleeding at insertion site: 3% (1/31) • Bruising: 3% (1/31) • Blisters: 6% (2/31) • Edema: 3% (1/31) • Redness: 45% (14/31)
72-hour study N = 42 Mean Age: 43 ± 12 y % completed: 100% Study duration: 72 h	72 hours	*72-hour study* • Bleeding at insertion site: 2% (1/42) • Blisters: 2% (1/42) • Edema: 2% (1/42) • Redness: 36% (15/42)
Pivotal study N = 91 Mean Age: 44 ± 13 y % completed: 100% Study duration: 9 days	9 days	*9-day study* • Blisters: 2% (2/91) • Edema: 2% (2/91) • Redness: 19% (17/91)
FreeStyle Navigator (2008) *In-clinic study* N = 58 Mean Age 40.5 ± 11.2 y % completed: 98% Study duration: 5 days	5 days	*5-day study* • Blisters: 2% (1/58) • Redness: 28% (16/58) • Itching (17%) (10/58)

Appendix Table H7. Overview of device-related true and false alarm rates for FDA-approved CGM devices* from FDA Summaries of Safety and Effectiveness Data

	Low Alerts				High Alerts			
	True Alert †		False Alert Rate (False positive)		True Alert †		False Alert Rate (False positive)	
	Threshold (mg/dL)	Rate, %	Threshold (mg/dL)	Rate, %	Threshold (mg/dL)	Rate, %	Threshold (mg/dL)	Rate, %
Paradigm REAL-Time Revel System (Adults)	Threshold Only (12 hr calibration)							
	60	40.7	60	51.7	180	90.4	180	10.4
	70	61.8	70	28.1	220	87.7	220	11.3
	80	76.5	80	18.4	250	83.3	250	12.4
	90	85.1	90	14	300	77.8	300	21.7
	100	88.4	100	12.8				
	Predictive Alerts Only (12 hr calibration)							
	60	64.4	60	65.5	180	91.5	180	15.2
	70	75.9	70	44.8	220	90	220	18.1
	80	85.1	80	33	250	87.8	250	19.7
	90	88.6	90	27	300	84.3	300	30.4
	100	91	100	24.3				
	Threshold and Predictive (12 hr calibration)							
	60	66.1	60	68.2	180	95.5	180	18.7
	70	78.2	70	47.4	220	93	220	22.5
	80	86.7	80	35.1	250	92.9	250	22
	90	90.7	90	28.6	300	84.6	300	37.7
	100	92.6	100	25.7				
Dexcom G5 CGM system (2016) and Dexcom G4 PLATINUM system (2014) ‡	Original study§, adult							
	55	50	55	50	120	95	120	5
	60	64	60	36	140	94	140	6
	70	79	70	21	180	92	180	8
	80	87	80	13	200	92	200	8
	90	90	90	10	220	91	220	9
					240	91	240	9
					300	82	300	18
	Software 505 study**, adult							
	55	71	55	29	120	98	120	2

	Low Alerts				High Alerts			
	True Alert †		False Alert Rate (False positive)		True Alert †		False Alert Rate (False positive)	
	Threshold (mg/dL)	Rate, %	Threshold (mg/dL)	Rate, %	Threshold (mg/dL)	Rate, %	Threshold (mg/dL)	Rate, %
	60	85	60	15	140	97	140	3
	70	92	70	8	180	97	180	3
	80	95	80	5	200	96	200	4
	90	96	90	4	220	94	220	6
					240	93	240	7
					300	86	300	14
Original study§, pediatric ages 6-17								
	55	0	55	100	120	91	120	9
	60	11	60	89	140	87	140	13
	70	47	70	53	180	75	180	25
	80	55	80	45	200	71	200	29
	90	69	90	31	220	67	220	33
	100	75	100	25	240	62	240	28
					300	43	300	57
Software 505 study**, pediatric ages 6-17								
	55	22	55	78	120	98	120	2
	60	42	60	58	140	97	140	3
	70	68	70	32	180	94	180	6
	80	86	80	14	200	94	200	6
	90	90	90	10	220	93	220	7
	100	91	100	9	240	88	240	12
					300	69	300	31
Original study§, pediatric ages 2-5								
	55	3	55	97	120	92	120	8
	60	11	60	89	140	90	140	10
	70	29	70	71	180	87	180	13
	80	35	80	65	200	85	200	15
	90	51	90	49	220	81	220	19
	100	64	100	36	240	80	240	20
					300	71	300	29
Software 505 study**, pediatric ages 2-5								

	Low Alerts				High Alerts			
	True Alert †		False Alert Rate (False positive)		True Alert †		False Alert Rate (False positive)	
	Threshold (mg/dL)	Rate, %	Threshold (mg/dL)	Rate, %	Threshold (mg/dL)	Rate, %	Threshold (mg/dL)	Rate, %
	55	25	55	75	120	97	120	3
	60	20	60	80	140	98	140	2
	70	20	70	80	180	99	180	1
	80	61	80	39	200	98	200	2
	90	78	90	22	220	100	220	0
	100	82	100	18	240	99	240	1
					300	95	300	5
MiniMed 670G system with SmartGuard	Threshold††							
	50	25 (30), 25 (15)	50	75 (30), 75 (15)	180	94 (30), 93 (15)	180	6 (30), 7 (15)
	60	54 (30), 52 (15)	60	47 (30), 48 (15)	220	92 (30), 92 (15)	220	8 (30), 8 (15)
	70	67 (30), 67 (15)	70	33 (30), 33 (15)	250	90 (30), 90 (15)	250	10 (30), 10 (15)
	80	69 (30), 69 (15)	80	31 (30), 31 (15)	300	81 (30) 81 (15)	300	19 (30), 19 (15)
	90	75 (30), 74 (15)	90	25 (30), 26 (15)				
	Predictive††							
	50	15 (30), 12 (15)	50	85 (30), 88 (15)	180	71 (30), 67 (15)	180	30 (30), 33 (15)
	60	41 (30), 37 (15)	60	59 (30), 63 (15)	220	69 (30) 66 (15)	220	31 (30), 34 (15)
	70	53 (30), 48 (15)	70	47 (30), 52 (15)	250	64 (30), 60 (15)	250	36 (30), 40 (15)
	80	58 (30), 51 (15)	80	42 (30), 49 (15)	300	58 (30), 54 (15)	300	42 (30), 46 (15)
	90	64 (30), 59 (15)	90	36 (30), 42 (15)				
	Threshold and predictive††							
	50	18 (30), 16 (15)	50	82 (30), 84 (15)	180	78 (30), 75 (15)	180	22 (30), 25 (15)
	60	46 (30), 43 (15)	60		220		220	23 (30), 25 (15)

	Low Alerts				High Alerts			
	True Alert †		False Alert Rate (False positive)		True Alert †		False Alert Rate (False positive)	
	Threshold (mg/dL)	Rate, %	Threshold (mg/dL)	Rate, %	Threshold (mg/dL)	Rate, %	Threshold (mg/dL)	Rate, %
	70 80 90	58 (30), 55 (15) 62 (30), 58 (15) 68 (30), 64 (15)	70 80 90	54 (30), 57 (15) 42 (30), 45 (15) 38 (30), 42 (15) 32 (30), 36 (15)	250 300	77 (30), 75 (15) 73 (30), 70 (15) 65 (30), 63 (15)	250 300	28 (30), 30 (15) 35 (30), 37 (15)
MiniMed 630G system with SmartGuard	Threshold							
	60 70 80 90 100	67.5 (30), 59.6 (15) 81.9 (30), 76.4 (15) 85.4 (30), 81.9 (15) 89.3 (30), 85.1 (15) 91.6 (30), 87.8 (15)	60 70 80 90 100	32.5 (30), 40.4 (15) 18.1 (30), 23.6 (15) 14.6 (30), 18.1 (15) 10.7 (30), 14.9 (15) 8.4 (30), 12.2 (15)	180 220 250 300	94.9 (30), 91.8 (15) 91.5 (30), 88.6 (15) 93.2 (30), 89.9 (15) 87.5 (30), 80.3 (15)	180 220 250 300	5.1 (30), 8.2 (15) 8.5 (30), 11.4 (15) 6.8 (30), 10.1 (15) 12.5 (30), 19.7 (15)
	Threshold and predictive							
	60 70 80	50.3 (30), 26.9 (15) 67.0 (30),	60 70	49.7 (30), 73.1 (15)	180 220 250	88.3 (30), 83.1 (15) 84.5 (30) 79.6 (15)	180 220 250	11.7 (30), 16.9 (15) 25.5 (30), 20.4 (15) 14.5 (30),

	Low Alerts				High Alerts			
	True Alert †		False Alert Rate (False positive)		True Alert †		False Alert Rate (False positive)	
	Threshold (mg/dL)	Rate, %	Threshold (mg/dL)	Rate, %	Threshold (mg/dL)	Rate, %	Threshold (mg/dL)	Rate, %
	90 100	48.5 (15) 73.5 (30), 60.4 (15) 78.7 (30), 66.5 (15) 82.5 (30) 70.3 (15)	80 90 100	33.0 (30), 51.5 (15) 26.5 (30), 39.6 (15) 21.3 (30), 33.5 (15) 17.5 (30), 29.7 (15)	300	85.5 (30), 79.0 (15) 73.5 (30), 63.2 (15)	300	21.0 (15) 26.5 (30), 36.8 (15)
MiniMed 530G system	Threshold (12 hr calibration)							
	60 70 80 90 100	70.2 83.1 89.8 94.9 95.4	60 70 80 90 100	48.6 25.5 16.5 12.4 12.2	180 220 250 300	91.1 90.1 87.9 82.0	180 220 250 300	5.4 7.2 7.7 15.3
	Threshold and predictive (12 hr calibration)							
	60 70 80 90 100	86.3 92.5 96.5 97.3 98.1	60 70 80 90 100	60.3 38.2 27.8 23.1 21.2	180 220 250 300	94.6 94.3 94.5 89.1	180 220 250 300	11.4 14.8 15.5 26.8
Devices Being Phased Out or No Longer Commercially Available								
Paradigm REAL-Time and Guardian	70 75 80 85	24.2 41.0 51.6 61.1	70 75 80 85	47.8 44.1 45.7 49.3	180 185 190 195	95.4 94.8 93.7 92.7	180 185 190 195	43.8 41.8 39.9 37.9

	Low Alerts				High Alerts			
	True Alert †		False Alert Rate (False positive)		True Alert †		False Alert Rate (False positive)	
	Threshold (mg/dL)	Rate, %	Threshold (mg/dL)	Rate, %	Threshold (mg/dL)	Rate, %	Threshold (mg/dL)	Rate, %
REAL-Time Systems (Pediatric Version)	90	69.7	90	52.0	200	90.8	200	35.5
	95	77.9	95	54.6	205	89.9	205	32.7
	100	85.3	100	57.3	210	87.8	210	29.7
					215	86.1	215	26.6
					225	81.3	225	21.4
					250	63.9	250	13.1
DexCom SEVEN PLUS	60	54	60	36	140	99	140	21
	70	57	70	24	180	98	180	24
	80	62	80	13	200	98	200	31
	90	68	90	9	240	96	240	43
					300	97	300	67
FreeStyle Navigator	Day							
	65	46	65	19	180	89	180	11
	70	56	70	16	240	78	240	12
	75	59	75	9	270	70	270	12
	85	61	85	7	300	61	300	12
	Night							
	65	80	65	41	180	69	180	7
	70	79	70	40	240	41	240	25
	75	72	75	37	270	21	270	36
	85	65	85	33	300	12	300	33
Animas Vibe System	*No additional clinical studies were conducted for the Animas Vibe System. See Data from Dexcom G4 and G5 Systems for safety information. The Animas Vibe pump is no longer commercially available.*							
OneTouch Vibe Plus System	*No additional clinical studies were conducted for the OneTouch Vibe Plus System. See data from Dexcom G4 and G5 Systems for all safety information The OneTouch Vibe Plus Pump is no longer commercially available.*							
t:slim G4 Insulin Pump/"t-slim G4 System"	*No additional clinical studies were conducted for the t:slim G4 System. See Data from Dexcom G4 and G5 Systems for safety information. The t:slim G4 insulin pump is no longer commercially available.*							

Appendix Table H8. Overview of device-related detection rates and false notification rates for the Freestyle Libre Flash CGM system

Type of Notification	Parameter	Rate (%)
Notification of Hypoglycemic Events (Low Glucose message, <70 mg/dL)	Detection Rate	85.4
	Missed Detection Rate	14.6
	False Notification Rate	39.9
Notification of Hyperglycemic Events (High Glucose message)	Detection Rate	95.1
	Missed Detection Rate	4.9
	False Notification Rate	22.1
Impending Notification of Hypoglycemic Events (Glucose Going Low message, <70mg/dL)	Detection Rate	95.0
	Missed Detection Rate	5.0
	False Notification Rate	46.8
Impending Notification of Hyperglycemic Events (Glucose Going High message)	Detection Rate	97.2
	Missed Detection Rate	2.8
	False Notification Rate	28.4

Appendix Table H9. Definitions of Severe Hypoglycemia in Included Parallel RCTs and Cross-over Trials

Study	Reported	Definition
Battelino 2011	Yes	NR
Battelino 2012 (SWITCH trial) index publication/ Hommel 2014	Yes	An episode requiring assistance from another person or neurological recovery in response to restoration of plasma glucose to normal.
Beck 2017 (DIAMOND)/ Polonsky 2017	Yes	An event that required assistance from another person to administer carbohydrate, glucagon, or other resuscitative actions.
Beck 2017b	Yes	An event that required assistance from another person to administer carbohydrates or other resuscitative action.
Bergenstal 2010, Rubin 2012, Slover 2012	Yes	Severe hypoglycemia was defined as an episode requiring assistance and was confirmed by documentation of a blood glucose value of less than 50 mg per deciliter (2.8 mmol per liter) or recovery with restoration of plasma glucose.
Bolinder 2016	Yes	Requiring third-party assistance
Deiss 2006	Yes	NR
Ehrhardt 2011/ Vigersky 2012	No	NR
Feig 2017	Yes	An episode requiring third-party assistance.
Haak 2016	Yes	Requiring third-party assistance.

Study	Reported	Definition
Hermanides 2011	Yes	Clinical episode of hypoglycemia ≤ 2.8 mmol ⁄ l, resulting in seizure or coma, intravenous glucose or glucagon, or any third-party assistance
Hirsch 2008	Yes	A clinical episode of hypoglycemia, resulting in seizure or coma, requiring hospitalization or intravenous glucose or glucagon, or any hypoglycemia that required assistance from another person.
JDRF Trial 2008/ Lawrence 2010	Yes	An event that required assistance from another person to administer carbohydrate, glucagon, or other resuscitative actions.
JDRF 2009a	Yes	Defined as an event that required assistance from another individual to administer carbohydrate, glucagon, or other resuscitative actions
Kordonouri 2010	Yes	NR
Langeland 2012	Yes	Defined as need of help from others.
Lind 2017 (GOLD trial)	Yes	Defined as unconsciousness from hypoglycemia or requiring assistance from another person.
Mauras 2012	Yes	An event requiring assistance of another person, as a result of altered consciousness, to administer carbohydrate, glucagon, or other resuscitative actions.
New 2015 (GLADIS)	No	NR
O'Connell 2009	Yes	An episode of hypoglycaemia resulting in seizure or coma or requiring third-party assistance or the use of glucagon or intravenous glucose for recovery
Raccah 2009	Yes	Episode of hypoglycemia with lost consciousness.
Peyrot 2009	Yes	NR
Secher 2013	Yes	Self-reported events with symptoms of hypoglycemia requiring help from another person to actively administer oral carbohydrate or injection of glucose or glucagon in order to restore normal blood glucose level .
Tildesley 2013, Tang 2014	Yes	NR
Tumminia 2015	Yes	Plasma glucose <50 mg/dL requiring the support of another person.
van Beers 2016 (IN CONTROL trial)	Yes	Hypoglycemic events requiring third party assistance
Wei 2016	No	NR
Yoo 2008	No	NR

NR, not reported

Appendix Table H10. Definitions of Severe Hypoglycemia in Included Observational Studies

Study	Reported Severe Hypoglycemia Outcomes	Specific Definition
Anderson 2011	Yes	NR
Battelino 2015	No	NR
Chase 2010	Yes	An event that required assistance from another person to administer carbohydrate, glucagon, or other resuscitative actions.
Cordua 2013	Yes	Severe neonatal hypoglycemia was defined as 2-h plasma glucose < 2.5 mmol/l requiring intravenous glucose infusion, based on clinical evaluation by the pediatric team.
Fresa 2013	No	NR
JDRF 2009b	No	NR
JDRF/Bode 2009c	Yes	An event that required assistance from another person to administer resuscitative actions
JDRF 2010	Yes	Defined as an event that required assistance from another person to administer carbohydrate, glucagon, or other resuscitative actions.
Kordonouri 2012	Yes	NR
Ludwig-Seibold 2012	Yes	Defined after ISPAD consensus guidelines grade 3: "Severe hypoglycemia is defined as an event with severe cognitive impairment (including coma and convulsions) requiring external assistance of another person to actively administer carbohydrates, glucagon, or take other corrective actions. Severe hypoglycemic coma is defined as a subgroup of severe hypoglycemia, as an event associated with a seizure or loss of consciousness"
Rachmiel 2015	Yes	Defined as glucose level <50 mg/dl and inability to self-treat, requiring treatment by another person.
Scaramuzza 2011	Yes	Severe hypoglycemia was defined as a blood glucose value of <70 mg/dL (3.9mmol/L) with a loss of consciousness or the patient's need for assistance.
Secher 2014	Yes	Hypoglycemia requiring assistance from another person to administer oral carbohydrate or injection of glucagon/glucose to restore the blood glucose level.
Wong 2014	Yes	Occurrences of SH (severe hypoglycemia) with seizure or loss of consciousness and DKA resulting in overnight hospitalization in the prior 3 months

NR, not reported;

APPENDIX I. Quality of Life or Treatment Satisfaction Abstraction Tables

Appendix Table I1. Summary of results for health-related quality of life or treatment satisfaction from RCTs Evaluating CGM vs. SMBG in children

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
			Intervention	Control		
JDRF 2008‡ Beck/Lawrence 2010 Study Period: 26 weeks	*QoL*					
	HFS Worry (Participants <18 years)	Baseline	25.7±16.6 (n=107)	25.9±14.9 (n=111)	NR	NR
		6 mos.	20.8±13.1 (n=103)	22.6±14.4 (n=106)	NR	0.270
	HFS Worry (Participants <18 years with CGM use ≥6 days/week)	Baseline	24.9±15.2 (n=43)	NA	NA	NA
		6 mos.	18.8±11.8 (n=43)	NA	NA	NA
		Δ from baseline	-6.1±12.0	NA	NA	NA
	HFS Worry (Participants <18 years with CGM use <6 days/week)	Baseline	26.3±17.8 (n=60)	NA	NA	NA
		6 mos.	22.3±13.9 (n=60)	NA	NA	NA
		Δ from baseline	−4.0±12.6 (n=60)	NA	NA	NA
	PedsQL Generic (Participants <18 years)	Baseline	78.5±12.5 (n=107)	79.7±11.7 (n=111)	NR	NR
		6 mos.	80.5±12.4 (n=103)	81.4±12.0 (n=106)	NR	0.960
	PedsQL Generic (Participants <18 years with CGM use ≥6 days/week)	Baseline	80.8±11.5 (n=43)	NA	NA	NA
		6 mos.	83.9±11.0 (n=43)	NA	NA	NA
		Δ from baseline	3.2±11.5 (n=43)	NA	NA	NA
	PedsQL Generic (Participants <18 years with CGM use <6 days/week)	Baseline	76.9 ± 13.1 (n=59)	NA	NA	NA
		6 mos.	78.1±12.8 (n=59)	NA	NA	NA
		Δ from baseline	+0.9±9.0 (n=59)	NA	NA	NA
	PedsQL Diabetes-Specific (Participants <18 years)	Baseline	82.2±12.2 (n=107)	81.6±12.9 (n=111)	NR	NR
		6 mos.	81.7±12.9 (n=103)	82.6±13.2 (n=106)	NR	0.280

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
			Intervention	Control		
	PedsQL Diabetes-Specific (Participants <18 years with CGM use ≥6 days/week)	Baseline	84.3 ± 11.6 (n=43)	NA	NA	NA
		6 mos.	85.1±10.4 (n=43)	NA	NA	NA
		Δ from baseline	+0.9±8.3 (n=43)	NA	NA	NA
	PedsQL Diabetes-Specific (Participants <18 years with CGM use <6 days/week)	Baseline	80.6 ± 12.5 (n=59)	NA	NA	NA
		6 mos.	79.1 ± 14.0 (n=59)	NA	NA	NA
		Δ from baseline	−1.8 ± 10.8 (n=59)	NA	NA	NA
	HFS Worry (parents of participants <18 years)	Baseline	41.5±16.0 (n=110)	42.2±19.8 (n=113)	NR	NR
		6 mos.	37.0±14.6 (n=107)	38.0±17.2 (n=107)	NR	0.880
	HFS Worry (parents of participants <18 years with CGM use ≥6 days/week)	Baseline	42.1 ± 13.9 (n=45)	NA	NA	NA
		6 mos.	37.0 ± 13.9 (n=45)	NA	NA	NA
		Δ from baseline	−5.2 ± 13.3 (n=45)	NA	NA	NA
	HFS Worry (parents of participants <18 years with CGM use <6 days/week)	Baseline	40.8 ± 17.5 (n=62)	NA	NA	NA
		6 mos.	37.0 ± 15.2 (n=62)	NA	NA	NA
		Δ from baseline	−3.5 ± 13.2 (n=62)	NA	NA	NA
	PAID-P (parents of participants <18 years)	Baseline	46.3±14.0 (n=110)	43.8±15.9 (n=113)	NR	NR
		6 mos.	47.1±12.7 (n=107)	43.8±17.0 (n=107)	NR	0.250
	PAID-P (parents of participants <18 years with CGM use ≥6 days/week)	Baseline	48.6 ± 12.3 (n=45)	NA	NA	NA
		6 mos.	47.0 ± 13.2 (n=45)	NA	NA	NA
		Δ from baseline	−1.6 ± 13.2 (n=45)	NA	NA	NA
	PAID-P (parents of participants <18 years with CGM use <6 days/week)	Baseline	45.1 ± 14.8 (n=62)	NA	NA	NA
		6 mos.	47.3 ± 12.4 (n=62)	NA	NA	NA
		Δ from baseline	+2.6 ± 13.2 (n=62)	NA	NA	NA
	PedsQL Generic (parents of participants <18 years)	Baseline	76.7±11.8 (n=110)	77.2±13.7 (n=113)	NR	NR
		6 mos.	76.7±12.6 (n=107)	77.5±13.5 (n=107)	NR	0.700

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
			Intervention	Control		
	PedsQL Generic (parents of participants <18 years with CGM use ≥6 days/week)	Baseline	74.9 ± 11.1 (n=45)	NA	NA	NA
		6 mos.	77.3 ± 13.4 (n=45)	NA	NA	NA
		Δ from baseline	+2.4 ± 11.1 (n=45)	NA	NA	NA
	PedsQL Generic (parents of participants <18 years with CGM use <6 days/week)	Baseline	77.9 ± 12.2 (n=62)	NA	NA	NA
		6 mos.	76.4 ± 12.1 (n=62)	NA	NA	NA
		Δ from baseline	−1.6 ± 10.9 (n=62)	NA	NA	NA
	PedsQL Diabetes-Specific (parents of participants <18 years)	Baseline	76.0±12.1 (n=110)	75.7±14.2 (n=113)	NR	NR
		6 mos.	76.5±11.6 (n=107)	74.6±13.3 (n=107)	NR	0.280
	PedsQL Diabetes-Specific (parents of participants <18 years with CGM use ≥6 days/week)	Baseline	75.3 ± 11.0 (n=45)	NA	NA	NA
		6 mos.	77.9 ± 11.2 (n=45)	NA	NA	NA
		Δ from baseline	+2.6 ± 11.6 (n=45)	NA	NA	NA
	PedsQL Diabetes-Specific (parents of participants <18 years with CGM use <6 days/week)	Baseline	76.3 ± 12.9 (n=62)	NA	NA	NA
		6 mos.	75.4 ± 11.9 (n=62)	NA	NA	NA
		Δ from baseline	−1.4 ± 12.3 (n=62)	NA	NA	NA
Kordonouri 2010 (ONSET) 52 weeks	*QoL*					
	Mother's wellbeing (WHO-5)	Baseline	49.3±23.9	44.7±21.6	NR	0.217
		6 mos.	60.2±22.6	60.7±22.6	NR	0.892
		12 mos.	62.7±18.9	60.8±19.3	NR	0.528
	KIDSCREEN-27: Physical wellbeing Proxy/Parent Reported	Baseline	40.4±9.7 (n=76)	38.7±9.2 (n=78)	NR	0.418
		6 mos.	49.4 ±9.0 (n=76)	46.8±8.8 (n=78)	2.6 (-0.23 to 5.43) p=0.072*	0.114
		12 mos.	50.0±8.1 (n=76)	50.3±9.7 (n=78)	-0.3 (-3.15 to 2.55); p=0.836*	0.879
	KIDSCREEN-27: Physical wellbeing Children Self-Reported	Baseline	43.7±9.4 (n=76)	39.8±8.2 (n=78)	NA	0.058
		6 mos.	49.1±8.5 (n=76)	49.6±9.0 (n=78)	-0.5 (-3.3 to 2.3); p=0.724*	0.685

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
			Intervention	Control		
		12 mos.	51.2±8.8 (n=76)	49.9±8.2 (n=78)	1.3 (-1.4 to 4.0); p=0.344*	0.359
	KIDSCREEN-27: Psychological wellbeing Proxy/Parent Reported	Baseline	40.3±10.5 (n=76)	40.4±10.9 (n=78)	NR	0.890
		6 mos.	48.4±10.4 (n=76)	48.3±10.2 (n=78)	0.1 (-3.18 to 3.38) p=0.952*	0.934
		12 mos.	47.8±9.3 (n=76)	48.6±10.3 (n=78)	-0.8 (-3.93 to 2.33) p=0.614*	0.826
	KIDSCREEN-27: Psychological wellbeing Children Self-Reported	Baseline	45.0±10.6 (n=76)	44.4±11.0 (n=78)	NR	0.847
		6 mos.	49.1±12.7 (n=76)	52.3±10.1 (n=78)	-3.2 (-6.8 to 0.4); p=0.085*	0.153
		12 mos.	50.4±9.2 (n=76)	50.3±10.8 (n=78)	0.1 (-3.1 to 3.3); p-0.951*	0.905
	KIDSCREEN-27: Autonomy and parents Proxy/Parent Reported	Baseline	50.3±10.4 (n=76)	49.5±8.6 (n=78)	NR	0.594
		6 mos.	51.4±11.2 (n=76)	50.4±8.9 (n=78)	1.0 (-2.22 to 4.22) p=0.540*	0.570
		12 mos.	52.6±11.2 (n=76)	50.9±10.1 (n=78)	1.7 (-1.69 to 5.09) p=0.324*	0.206
	KIDSCREEN-27: Autonomy and parents Children Self-Reported	Baseline	51.1±8.5 (n=76)	48.8±9.6 (n=78)	NR	0.313
		6 mos.	50.7±10.6 (n=76)	51.4±11.01 (n=78)	-0.7 (-4.14 to 2.74) p=0.688*	0.648
		12 mos.	52.5±10.0 (n=76)	50.2±9.9(n=78)	2.3 (-0.87 to 5.47); p=0.154*	0.158
	KIDSCREEN-27: Social support and peers Proxy/Parent Reported	Baseline	44.5±14.9 (n=76)	44.7±13.3 (n=78)	NR	0.998
		6 mos.	50.3±9.9 (n=76)	50.7±10.4 (n=78)	-0.4 (-3.63 to 2.83) p=0.807*	0.826
		12 mos.	51.1±10.2 (n=76)	51.3±8.9 (n=78)	-0.2 (-3.25 to 2.85) p=0.897*	0.860
	KIDSCREEN-27: Social support and peers Children Self-Reported	Baseline	47.1±11.0 (n=76)	44.2±10.7(n=78)	NR	0.370
		6 mos.	53.3±9.2 (n=76)	50.9±9.6 (n=78)	2.4 (-0.60 to 5.40) p=0.115*	0.262

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
			Intervention	Control		
		12 mos.	52.4±9.6 (n=76)	50.8±9.0 (n=78)	1.6 (-1.36 to 4.56) p=0.288*	0.377
	KIDSCREEN-27: School environment Proxy/Parent Reported	Baseline	45.8±14.0 (n=76)	47.1±11.6 (n=78)	NR	0.511
		6 mos.	50.9±12.1 (n=76)	50.6±9.0 (n=78)	0.3 (-3.09 to 3.69) p=0.861*	0.854
		12 mos.	51.4±10.1 (n=76)	50.9±9.2 (n=78)	0.5 (-2.57 to 3.57) p=0.748*	0.792
	KIDSCREEN-27: School environment Children Self-Reported	Baseline	47.4±11.7 (n=76)	45.4±10.1 (n=78)	NR	0.612
		6 mos.	49.7±11.7 (n=76)	51.3±10.1 (n=78)	-1.6 (-5.08 to 1.88) p=0.365*	0.493
		12 mos.	52.8±9.8 (n=76)	51.3±10.2 (n=78)	1.5 (-1.69 to 4.69) p=0.354*	0.436
Mauras 2012 Study Period: 6 mos.	*QoL*					
	PAID	Baseline	52±15 (n=74)	55±16 (n=72)	NR	NR
		6 mos.	44±17 (n=69)	49±16 (n=68)	NR	0.420
	Hypoglycemia Fear Survey	Baseline	45±17 (n=74)	47±19 (n=72)	NR	NR
		6 mos.	38±17 (n=69)	42±19 (n=68)	NR	0.380
Rubin 2012 Follow-up trial of Bergenstal 2010 *also reports data on adults 6 mos.	*QoL*					
	Δ from baseline, Peds QL Psychosocial Health Summary Score (Participants <18 years)	Baseline	78.38±14.59 (n=77)	78.76±10.27 (n=70)	NR	NR
		Δ 12 mos.	3.39 (n=77)	3.64 (n=70)	Diff. -0.25 (NR)	NR
	Δ from baseline, Peds QL Physical Health Summary Score (Participants <18 years)	Baseline	86.99±12.93 (n=77)	88.37±11.16 (n=70)	NR	NR
		Δ 12 mos.	2.53 (n=77)	1.41 (n=70)	Diff. 1.12 (NR)	NR
	Δ from baseline, HFS Worry subscale (Participants <18 years)	Baseline	28.88±9.74 (n=77)	26.97±8.06 (n=70)	NR	NR
		Δ 12 mos.	-3.62 (n=77)	-2.43 (n=70)	Diff. 1.19 (NR)	NR
		Baseline	30.60±5.43 (n=77)	29.70±6.04 (n=70)	NR	NR

Author	Outcome	F/U post-tx	Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
			Intervention	Control		
	Δ from baseline, HFS Avoidant subscale (Participants <18 years)	Δ 12 mos.	-4.01 (n=77)	-2.25 (n=70)	Diff. 1.76 (NR)	NR
	Δ from baseline, Peds QL Psychosocial Health Summary Score (Parents of participants <18 years)	Baseline	78.61±12.87 (n=77)	73.27±13.36 (n=70)	NR	NR
		Δ 12 mos.	4.06 (n=77)	3.06 (n=70)	Diff. 1.00 (NR)	NR
	Δ from baseline, Peds QL Physical Health Summary Score (Parents of participants <18 years)	Baseline	87.92±10.58 (n=77)	85.53±13.06 (n=70)	NR	NR
		Δ 12 mos.	0.94(n=77)	0.01 (n=70)	Diff. 0.93 (NR)	NR
	Δ from baseline, HFS Worry subscale (Parents of participants <18 years)	Baseline	42.49±10.11 (n=77)	43.21±12.28 (n=70)	NR	NR
		Δ 12 mos.	-3.64 (n=77)	-1.56 (n=70)	Diff. 2.08	NR
	Δ from baseline, HFS Avoidant subscale (Parents of participants <18 years)	Baseline	31.65±6.56 (n=77)	30.94±5.63 (n=70)	NR	NR
		Δ 12 mos.	-4.16 (n=77)	-1.07 (n=70)	3.09	p<0.01

HFS, Hypoglycemia Fear Survey; NR, not reported; PedsQL, Pediatric Quality of Life;
* Calculated by AAI
† Includes data on an adult population – abstraction can be found in corresponding adult section.

Appendix Table I2. Summary of results for health-related quality of life or treatment satisfaction from RCTs of CGM vs. SMBG in adults

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**		
Beck 2017 (DIAMOND) Polonsky 2017	*QoL measures**					
	World Health Organization (five) Well-Being Index (WHO-5), mean (SD)	Baseline	71.3±14.7 (n=102)	69.1±14.9 (n=53)	NR	NR
		6 mos.	70.5 ±16.7 (n=102)	67.3±16.9 (n=53)	Model 1: MD -1.3 (-5.4 to 2.9) Model 2: MD -1.6 (-5.9 to 2.6)	Model 1: 0.62 Model 2 : 0.50
	EQ-5D-5L, mean (SD)	Baseline	0.90±0.11 (n=102)	0.89±0.11 (n=53)	NR	NR
		6 mos.	0.89±0.10 (n=102)	0.88±0.10 (n=53)	Model 1: MD 0.00 (-0.03 to 0.03) Model 2: MD 0.00 (-0.03 to 0.03)	Model 1: 0.86 Model 2: 0.92
	Diabetes Distress Scale (DDS) Total, mean (SD)	Baseline	1.8±0.7 (n=102)	1.7±0.6 (n=53)	NR	NR
		6 mos.	1.6±0.5 (n=102)	1.8±0.7 (n=53)	Model 1: MD 0.22 (0.08 to 0.4) Model 2: MD 0.23 (0.09 to 0.4)	Model 1: 0.009 Model 2: 0.03
	DDS Regimen subscale, mean (SD)	Baseline	2.1±0.9 (n=102)	2.1±1.0 (n=53)	NR	NR

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	Outcome	F/U post-tx	Intervention	Control		
		6 mos.	1.8±0.7 (n=102)	2.1±0.9 (n=53)	Model 1: MD 0.25 (0.05 to 0.46) Model 2: MD 0.26 (0.05 to 0.47)	Model 1: 0.04 Model 2: 0.04
	DDS Emotional Burden subscale, mean (SD)	Baseline	2.1±0.9 (n=102)	1.9±0.8 (n=53)	NR	NR
		6 mos.	1.9±0.8 (n=102)	2.0±1.0 (n=53)	Model 1: MD 0.21 (0.01 to 0.41) Model 1: MD 0.21 (0.00 to 0.41)	Model 1: 0.08 Model 2: 0.09
	DDS Interpersonal subscale, mean (SD)	Baseline	1.5±0.8 (n=102)	1.5±0.7 (n=53)	NR	NR
		6 mos.	1.4±0.6 (n=102)	2.0±1.0 (n=53)	Model 1: MD 0.37 (0.16 to 0.56) Model 2: MD 0.37 (0.16 to 0.58)	Model 1: 0.009 Model 2: 0.01
	DDS Physician subscale, mean (SD)	Baseline	1.2±0.6 (n=102)	1.1±0.3 (n=53)	NR	NR
		6 mos.	1.1±0.3 (n=102)	1.2±0.7 (n=53)	Model 1: MD 0.10 (-0.04 to 0.25) Model 2: MD 0.12 (-0.03 to 0.27)	Model 1: 0.12 Model 2: 0.18

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**		
	Hypoglycemic Confidence Scale (HCS), mean (SD)	Baseline	3.3±0.6 (n=102)	3.2±0.6 (n=53)	NR	NR
		6 mos.	3.5±0.6 (n=102)	3.2±0.6 (n=53)	Model 1: MD 0.2 (0.06 to 0.4) Model 2: MD 0.2 (0.05 to 0.4)	Model 1: 0.03 Model 2: 0.03
	Hypoglycemic Fear Survey (HFS-II), mean (SD)	Baseline	15.8±12.3 (n=102)	17.3±13.2 (n=53)	NR	NR
		6 mos.	13.5±10.6 (n=102)	17.7±14.9 (n=53)	Model 1: MD 3.2 (0.2 to 6.1) Model 2: MD 2.5 (-0.6 to 5.5)	JDRF 2009Model 1: 0.07 Model 2: 0.15
	Clarke Hypoglycemia Unawareness Questionnaire, mean (SD)	Baseline	2.1±1.8 (n=102)	2.7 ±2.1 (n=53)	NR	NR
		6 mos.	2.0±1.8 (n=102)	2.5 ±2.1 (n=53)	NR	NR
Bergenstal 2010† Rubin 2012	*QoL measures*					
	Δ from baseline, SF-36 PCS (Participants ≥18 years)	Baseline	49.86±9.64 (n=166)	49.50±9.09 (n=168)	NR	NR
		Δ 12 mos.	0.05 (n=166)	-1.26 (n=168)	Diff. -1.31 (NR)	NR
	Δ from baseline, SF-36 MCS (Participants ≥18 years)	Baseline	50.61±7.12 (n=166)	50.97±7.86 (n=168)	NR	NR
		Δ 12 mos.	1.22 (n=166)	0.26 (n=168)	Diff. -0.96 (NR)	NR

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**		
	Δ from baseline, HFS Worry subscale (Participants ≥18 years)	Baseline	21.96±14.34 (n=166)	21.52±13.37 (n=168)	NR	NR
		Δ 12 mos.	-6.36 (n=166)	-1.87 (n=168)	Diff. 4.49 (NR)	<0.001
	Δ from baseline, HFS Avoidant subscale (Participants ≥18 years)	Baseline	16.38±8.24 (n=166)	16.70±8.00 (n=168)	NR	NR
		Δ 12 mos.	-2.30 (n=166)	-0.52 (n=168)	Diff. 1.78 (NR)	<0.01
Bolinder 2016	*QoL measures*					
	DTSQ total treatment satisfaction, mean (95% CI) PP population	6 mos	13.9 (12.2 to 14.6)	6.8 (5.4 to 8.1)	NR	<0.0001
	DTSQ perceived frequency of hyperglycemia, mean (95% CI) PP population	6 mos	-0.52 (-0.20 to -0.82)	0.46 (0.16 to 0.81)	NR	<0.0001
	DTSQ perceived frequency of hypoglycemia, mean (95% CI) PP population	6 mos	-0.26 (-0.61 to 0.02)	0.13 (-0.22 to 0.45)	NR	0.0629
	DTSQ total treatment satisfaction, mean (95% CI) full analysis population	6 mos	13.3 (12.0 to 14.4)	7.3 (5.6 to 8.5)	Adj MD 6.1 (0.84)	<0.0001
	DTSQ perceived frequency of hyperglycemia, mean (95% CI) full analysis population	6 mos	-0.60 (-0.24 to -0.86)	0.40 (0.08 to 0.76)	Adj MD-1.0 (0.22)	<0.0001
	DTSQ perceived frequency of hypoglycemia, mean (95% CI) full analysis population	6 mos	-0.32 (0.0 to -0.64)	0.08 (-0.28 to 0.42)	NR	0.0713
	DQoL total scale, mean (95% CI), PP population	6 mos	1.96 (1.90 to 2.02)	2.04 (1.98 to 2.10)	NR	0.0466
	DQoL satisfaction with treatment subscale, mean (95% CI), PP population	6 mos	1.87 (1.80 to 1.95)	2.11 (2.02 to 2.20)	NR	<0.0001

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	Outcome	F/U post-tx	Intervention	Control		
	DQoL social worry subscale, mean (95% CI), PP population	6 mos	1.78 (1.67 to 1.89)	1.75 (1.63 to 1.87)	NR	0.7661
	DQoL diabetes worry subscale, mean (95% CI), PP population	6 mos	1.96 (1.86 to 2.10)	2.07 (1.94 to 2.20)	NR	0.2504
	DQoL impact of treatment subscale, mean (95% CI), PP population	6 mos	2.11 (2.05 to 2.18)	2.12 (2.07 to 2.19)	NR	0.5041
	DQoL total scale, mean (95% CI), full analysis population	6 mos	1.95 (189 to 2.01)	2.03 (1.97 to 2.09)	Adj MD -0.08 (0.039)	0.0524
	DQoL satisfaction with treatment subscale, mean (95% CI), full analysis population	6 mos	1.83 (1.77 to 1.90)	2.08 (2.01 to 2.17)	NR	<0.0001
	DQoL social worry subscale, mean (95% CI), full analysis population	6 mos	1.77 (1.68 to 1.96)	1.71 (1.60 to 1.82)	NR	0.3794
	DQoL diabetes worry subscale, mean (95% CI), full analysis population	6 mos	1.97 (1.86 to 2.08)	2.04 (1.92 to 2.16)	NR	0.4055
	DQoL impact of treatment subscale, mean (95% CI), full analysis population	6 mos	2.10 (2.04 to 2.16)	2.13 (2.08 to 2.19)	NR	0.4057
	HFS behavior subscale, mean (95% CI), PP population	6 mos	13.7 (12.6 to 14.8)	13.4 (12.3 to 14.6)	NR	0.8203
	HFS worry subscale, mean (95% CI), PP population	6 mos	14.7 (12.3 to 17.0)	15.9 (13.6 to 18.2)	NR	0.4294
	HFS behavior subscale, mean (95% CI), full analysis population	6 mos	13.8 (12.8 to 14.9)	13.8 (12.7 to 15.0)	Adj MD 0.0 (0.72)	0.9834
	HFS worry subscale, mean (95% CI), full analysis population	6 mos	14.9 (12.7 to 17.1)	16.0 (13.8 to 18.3)	Adj MD -1.2 (1.48)	0.4154
	DDS total score, mean (95% CI), PP population	6 mos	1.81 (1.67 to 1.96)	1.84 (1.70 to 1.89)	NR	0.7233

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**		
	DDS emotional burden subscale, mean (95% CI), PP population	6 mos	1.92 (1.75 to 2.09)	1.98 (1.81 to 2.15)	NR	0.5621
	DDS physician distress, mean (95% CI), PP population	6 mos	1.68 (1.48 to 1.88)	1.62 (1.41 to 1.83)	NR	0.6765
	DDS regimen distress, mean (95% CI), PP population	6 mos	1.90 (1.75 to 2.06)	1.97 (1.80 to 2.11)	NR	0.5378
	DDS interpersonal distress, mean (95% CI), PP population	6 mos	1.63 (1.48 to 1.78)	1.67 (1.51 to 1.82)	NR	0.6900
	DDS total score, mean (95% CI), full analysis population	6 mos	1.80 (1.76 to 1.94)	1.82 (1.68 to 1.97)	Adj MD -0.03 (0.089)	0.7634
	DDS emotional burden subscale, mean (95% CI), full analysis population	6 mos	1.91 (1.76 to 2.07)	1.95 (1.80 to 2.10)	NR	0.6727
	DDS physician distress, mean (95% CI), full analysis population	6 mos	1.64 (1.45 to 1.93)	1.60 (1.40 to 1.80)	NR	0.7130
	DDS regimen distress, mean (95% CI), full analysis population	6 mos	1.89 (1.73 to 2.04)	1.95 (1.80 to 2.10)	NR	0.4777
	DDS interpersonal distress, mean (95% CI), full analysis population	6 mos	1.63 (1.49 to 1.77)	1.64 (1.50 to 1.79)	NR	0.8698
Hermanides 2011	*QoL measures*					
	Hypoglycemia Fear Survey, mean (SD)	Baseline	29.8±19.2 (n=30)	21.0±17.7 (n=24)	NR	NR
		6 mos.	24.1±20.2 (n=30)	20.3±16.9 (n=24)	3.9 (-5.7 to 13.4)	0.42
	SF-36 Physical Functioning	Baseline	89.4±14.5 (n=42)	90.5±14.3 (n=33)	NR	NR
		6 mos.	92.7±11.2 (n=42)	91.4±12.7 (n=33)	1.4 (-4.1 to 6.9)	0.620

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	Outcome	F/U post-tx	Intervention	Control		
	SF-36 Role-Physical	Baseline	76.8±23.8 (n=42)	84.4±19.3 (n=33)	NR	NR
		6 mos.	85.7±20.7 (n=42)	87.3±20.4 (n=33)	1.6 (-11.2 to 8.0)	0.740
	SF-36 Bodily Pain	Baseline	78.9±25.4 (n=42)	78.7±23.0 (n=33)	NR	NR
		6 mos.	79.9±24.4 (n=42)	78.7±22.6 (n=33)	1.3 (-9.7 to 12.2)	0.820
	SF-36 General Health	Baseline	55.5±20.3 (n=42)	59.8±22.3 (n=33)	NR	NR
		6 mos.	67.7±21.6 (n=42)	63.1±19.1 (n=33)	4.5 (-5.0 to 14.1)	0.350
	SF-36 Vitality	Baseline	53.9±20.0 (n=42)	61.0±23.7 (n=33)	NR	NR
		6 mos.	66.7±20.2 (n=42)	65.2±19.3 (n=33)	1.5 (-7.7 to 10.7)	0.740
	SF-36 Social Functioning	Baseline	81.5±20.3 (n=42)	86.4±21.0 (n=33)	NR	NR
		6 mos.	89.3±16.0 (n=42)	82.2±25.2 (n=33)	7.1 (-3.0 to 17.2)	0.170
	SF-36 Role-emotional	Baseline	84.9±20.4 (n=42)	89.6±16.7 (n=33)	NR	NR
		6 mos.	87.1±19.6 (n=42)	88.0±16.0 (n=33)	0.9 (-7.6 to 9.4)	0.830
	SF-36 Mental Health	Baseline	72.6±14.8 (n=42)	77.9±20.2 (n=33)	NR	NR
		6 mos.	79.2±12.5 (n=42)	76.8±16.5 (n=33)	2.3 (-4.3 to 9.0)	0.49

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**		
JDRF 2008‡ Beck/Lawrence 2010**	*QoL measures***					
	SF-12 PCS (Participants ≥18 years), mean (SD)	Baseline	54.1 (5.9) (n=122)	54.1 (7.2) (n=106)	NR	NR
		6 mos.	55.5 (4.9) (n=120)	54.1 (6.9) (n=106)	NR	0.030
	SF-12 MCS (Participants ≥18 years), mean (SD)	Baseline	49.5 (8.4) (n=122)	48.2 (10.0) (n=106)	NR	NR
		6 mos.	48.4 (10.1) (n=122)	48.7 (9.6) (n=106)	NR	0.350
	PAID (Participants ≥18 years), mean (SD)	Baseline	22.7 (15.3) (n=122)	21.7 (18.0) (n=106)	NR	NR
		6 mos.	18.1 (14.1) (n=120)	18.2 (14.6) (n=106)	NR	0.500
	HFS Total (Participants ≥18 years), mean (SD)	Baseline	37.4 (12.8) (n=122)	37.8 (14.3) (n=106)	NR	NR
		6 mos.	33.3 (11.5) (n=120)	36.0 (13.6) (n=106)	NR	0.040
	HFS Worry (Participants ≥18 years), mean (SD)	Baseline	30.1 (18.3) (n=122)	30.6 (18.3) (n=106)	NR	NR
		6 mos.	25.3 (15.8) (n=120)	27.7 (17.3) (n=106)	NR	0.120
	HFS Behavior (Participants ≥18 years), mean (SD)	Baseline	46.9 (11.0) (n=122)	47.3 (13.1) (n=106)	NR	NR
		6 mos.	43.8 (11.2) (n=120)	46.8 (13.3) (n=106)	NR	0.030
	Usage					
	Hours per week of CGM glucose readings§, mean	1-4 wks	132 hrs/week	NA	NA	NA

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	**Outcome**	**F/U post-tx**	**Intervention**	**Control**		
		5-8 wks	123 hrs/week	NA	NA	NA
		9-13 wks	126 hrs/week	NA	NA	NA
		14-17 wks	122 hrs/week	NA	NA	NA
		18-21 wks	120 hrs/week	NA	NA	NA
		22-26 wks	118 hrs/week	NA	NA	NA
New 2015 (GLADIS)	*Quality of life measures*					
	Diabetes Distress Scale (DDS)	14.3 wks	NR	NR	NR	NS
	SF-8 mental component score CGM no alarms vs SMBG, mean (SD)	Baseline	49.1 ± 9.4 (n=44)	49.0 ± 10.4 (n=39)	NR	NR
		14.3 wks	50.9 ± 9.4 (n=44)	49.3 ± 10.7 (n=39)	MD NR (-2.2 to 5.2)	0.440
	SF-8 mental component score CGM w/alarms vs SMBG, mean (SD)	Baseline	47.6 ± 11.2 (n=43)	49.0 ± 10.4 (n=39)	NR	NR
		14.3 wks	48.9 ± 11.4(n=43)	49.3 ± 10.7 (n=39)	MD NR (-3.5 to 4.0)	0.890
	SF-8 physical component score CGM no alarms vs SMBG, mean (SD)	Baseline	48.6 ± 9.7 (n=44)	49.1± 7.9 (n=39)	NR	NR
		14.3 wks	49.0 ± 9.8 (n=44)	47.5 ± 8.5 (n=39)	MD NR (-1.3, 4.9)	0.260
	SF-8 physical component score CGM no alarms vs SMBG, mean (SD)	Baseline	46.7 ± 8.8 (n=43)	49.1 ± 7.9 (n=39)	NR	NR

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
Author	Outcome	F/U post-tx	Intervention	Control		
		14.3 wks	49.4 ± 9.6 (n=43)	47.5 ± 8.5 (n=39)	MD NR (-0.5 to 6.7)	0.025

HFS, Hypoglycemia Fear Survey; hrs, hours; NA, not applicable; Wks, weeks;
* Model 1 values are adjusted for baseline values of each outcome. Model 2 values are adjusted for the demographic factors of age, sex, and number of years since diagnosis
† Includes data for a pediatric population—abstraction can be found in corresponding pediatric sections
‡ Includes data for a pediatric population and a mixed ages population—abstraction can be found in corresponding pediatric and mixed ages sections
§ Values estimated from graph
** Quality of Life values are derived from Lawrence 2010, a follow-up study of JDRF 2008.

Appendix Table I3. Summary of results for health-related quality of life or treatment satisfaction from cross-over trials of CGM vs. SMBG in adults

Author year (ROB)	Outcome	Timing	CGM Mean ± SD	SMBG Mean ± SD	MD (95% CI) Effect Size (SE)	p-value
Cross-over trials	**Outcome**	**Timing**	**CGM Periods Mean ± SD or 95% CI**	**SMBG Periods Mean ± SD 95% CI**	**MD (95% CI) Effect Size (SE)**	**p-value**
Hypoglycemic Fear						
GOLD trial Lind 2017 Treatment periods: 26 weeks; Washout 17 weeks *Moderately high ROB* N = 161	Hypoglycemic Fear Survey Behavior/Avoidance (0-4, higher score=greater fear)	Baseline	1.99 (0.58)	1.85 (0.58)	NR	NR
		Across both treatment periods*	1.93 (1.83 to 2.03)	1.91 (1.81 to 2.00)	0.03 (-0.05 to 0.10)	0.45
DTSQ						
GOLD trial Lind 2017	DTSQ (0-36, higher score=better satisfaction)	Baseline	25.8 (6.1), n=69	24.6 (5.8), n=73		

Author year (ROB)	Outcome	Timing	CGM Mean ± SD	SMBG Mean ± SD	MD (95% CI) Effect Size (SE)	p-value
Treatment periods: 26 weeks; Washout 17 weeks *Moderately high ROB* N = 161		Across both treatment periods*	30.21 (29.47 to 30.96)	26.62 (25.61 to 27.64)	3.43 (2.31 to 4.54)	<0.001
SWITCH **Hommel 2014** Treatment periods: 6 months Washout phase: 4 months *Moderately low ROB* N = 79	DTSQs (0-48, higher score=better satisfaction)	Across both treatment periods†	NR	NR	Change versus baseline 1.16	0.010
WHO-5 Well-Being Index						
GOLD trial **Lind 2017** Treatment periods: 26 weeks; Washout 17 weeks *Moderately high ROB* N = 161	WHO-5 Well-Being Index (0-100, higher score=better well-being)	Baseline	63.8 (16.6)	57.3 (18.0)	NR	NR
		Across both treatment periods*	66.13 (62.94 to 69.32)	62.74 (60.18 to 65.31)	3.54 (0.61 to 6.48)	0.02

CGM: Continuous Glucose Monitoring; CI: confidence interval; F/U: follow-up; HbA1C: hemoglobin A1C; SMBG: self-monitoring of blood glucose; SD: standard deviation; CI: confidence interval; NR: not reported; AUC: area under the curve; DTSQ: Diabetes Treatment Satisfaction Questionnaire; HFS: Hypoglycemic Fear Survey; WHO-5: World Health Organization-5 Well Being Index

*Regression model. Least-square means (95% CIs) and P value were calculated with sequence, patient (sequence), treatment period, and treatment as class variables (calculated only for normally distributed variables). For other variables in which nonparametric tests were performed, values are reported as mean (95% CI).

† Treatment satisfaction in adults was analyzed by linear mixed models. DTSQs perceived frequency of hyperglycaemia and perceived frequency of hypoglycaemia were treated individually in these analyses, as per DTSQs user instructions.

Appendix Table I4. Summary of results for health-related quality of life or treatment satisfaction from RCT of CGM vs. SMBG in mixed adults and children

Author	Outcome
Parallel Trials	
Battelino 2011	NR
JDRF 2008	NR
JDRF 2009a	NR
O'Connell 2009	NR
Raccah 2009	NR

Appendix Table I5. Summary of results for health-related quality of life or treatment satisfaction from RCT Evaluating CGM vs. SMBG in Adults with Type 1 or Type 2 Diabetes Mellitus

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
	Outcome	F/U post-tx	Intervention	Control		
Beck 2017b (DIAMOND)	EQ-5D-5L	Baseline	0.82 ± 0.15 (n=79)	0.82 ± 0.14 (n=79)	NR	NR
		6 mos.	0.82 ± 0.14 (n=77)	0.82 ± 0.16 (n=73)	NR	NR
	World Health Organization (five) Well-Being Index (WHO-5)	Baseline	16 ± 4 (n=79)	17 ± 4 (n=79)	NR	NR
		6 mos.	16 ± 5 (n=77)	17 ± 4 (n=73)	NR	NR
	Diabetes Distress Scale (DDS) Total,	Baseline	1.9 ± 0.8 (n=79)	2.0 ± 0.8 (n=79)	NR	NR
		6 mos.	1.8 ± 0.9 (n=77)	1.8 ± 0.6 (n=73)	NR	NR
	DDS Regimen subscale	Baseline	2.2 ± 0.9 (n=79)	2.4 ± 1.0 (n=79)	NR	NR
		6 mos.	2.0 ± 0.9 (n=77)	2.1 ± 0.9 (n=73)	NR	NR
	DDS Emotional Burden subscale	Baseline	2.3 ± 1.2 (n=79)	2.3 ± 1.1 (n=79)	NR	NR
		6 mos.	2.2 ± 1.2 (n=77)	2.1 ± 1.0 (n=73)	NR	NR
	DDS Interpersonal subscale	Baseline	1.8 ± 1.0 (n=79)	2.0 ± 1.2 (n=79)	NR	NR
		6 mos.	1.7 ± 1.1 (n=77)	1.7 ± 0.8 (n=73)	NR	NR
	DDS Physician subscale	Baseline	1.3 ± 0.6 (n=79)	1.3 ± 0.8 (n=79)	NR	NR

			Results (mean±SD or %(n/N))		Effect Estimate (95% CI)	p-value
	Outcome	**F/U post-tx**	**Intervention**	**Control**		
		6 mos.	1.3 ± 0.9 (n=77)	1.1 ± 0.3 (n=73)	NR	NR
	Hypoglycemia Fear Survey, worry subscale,	Baseline	0.8 ± 0.7 (n=79)	0.8 ± 0.6 (n=79)	NR	NR
		6 mos.	0.8 ± 0.6 (n=77)	0.7 ± 0.5 (n=73)	NR	NR
	Hypoglycemia Confidence Scale, worry subscale,	Baseline	3.2 ± 0.7 (n=79)	3.4 ± 0.6 (n=79)	NR	NR
		6 mos.	3.3 ± 0.6 (n=77)	3.4 ±0.6 (n=73)	NR	NR
Ehrhardt 2011, Vigersky 2012	Problem Areas in Diabetes (PAID) questionnaire, mean (SD)	Baseline	23.9 (22.3) (n=50)	25.7 (20.8) (n=50)	NA	NR
		12 wks	17.1 (18.0) (n=50)	19.9 (17.1) (n=50)	NR	NR
		52 wks	18.4 (20.5) (n=50)	19.6 (20.5) (n=50)	NR	NR
Tildesley 2013, Tang 2014	Diabetes Treatment Satisfaction Questionnaire, mean (SD)	24 wks PP	24.80 (7.10) (n=25)	33.41 (2.65) (n=25)	NR	<0.001

APPENDIX J. FDA Approved Devices

Appendix Table J1. List of FDA Approved Devices

Device name Applicant	PMA#, Approval Date	DM Population	Description/Indication	Commercial availability
Stand-alone CGM devices included in 2011 HTA				
Freestyle Navigator CGM System Abbott Diabetes Care, Inc., CA, USA	P050020 March 12, 2008	• Adults (age ≥18 years)	• Stand-alone CGM • Provides real-time readings, graphs, trends and glucose alarms directly to the user for the purpose of improving DM management • Provides a built-in blood glucose meter to confirm the continuous glucose result. • Intended for both in-home use and use in clinical settings	Not commercially available. Freestyle Navigator II commercially available in some European countries
Guardian REAL-Time System Medtronic MiniMed, CA, USA	P980022/S015/ S011 March 8, 2007 (Pediatric version, approved for use in persons age 7-17) June 14, 2006 (original approval, for use in persons age 18 and older)	• Children and adults (ages ≥7 years)	• Stand-alone CGM • Provides real-time readings, graphs, trends and glucose alarms directly to the user for the purpose of improving DM management • Continuous or periodic monitoring of interstitial glucose levels	Unclear whether or not commercially available
DexCom STS Continuous Glucose Monitoring System DexCom, Inc. CA, USA	P050012 March 24, 2006	• Adults (age ≥18 years)	• Stand-alone CGM • Provides real-time readings, graphs, trends and glucose alarms directly to the user for the purpose of improving DM management	Not commercially available
CGM + Insulin Pump systems included in 2011 HTA				
Paradigm REAL-Time System Medtronic MiniMed, CA, USA	P980022/S015/ S013 March 8, 2007	• Children and adults (ages ≥7 years)	• CGM + Insulin Pump • Continuous or periodic monitoring of interstitial glucose levels (in real-time) for the purpose of improving DM management and/or continuous	Getting phased out Second generation system is the Paradigm REAL-Time Revel system,

Device name Applicant	PMA#, Approval Date	DM Population	Description/Indication	Commercial availability
	(Pediatric version, approved for use in persons age 7-17) April 7, 2006 (original approval, for use in persons age 18 and older)		delivery of insulin (at set and variable rates) via infusion pump	which is commercially available.
New stand-alone CGM devices				
Freestyle Libre Flash Glucose Monitoring System Abbott Diabetes Care, Inc., CA, USA	P160030 September 27, 2017	• Adults (age ≥18 years)	• Stand-alone CGM • Provides real-time readings and trends of glucose levels directly to the user for the purpose of replacing blood glucose testing for diabetes treatment decisions • **Approved and designed to replace fingerstick blood glucose testing for diabetes treatment decisions** • **The only device that is factory calibrated and does not require calibration from blood glucose measurements**	Commercially available
Dexcom G5 Mobile CGM System Dexcom, Inc. CA, USA	P120005/S041 December 20, 2016 (replace fingerstick blood glucose testing) P120005/S033 August 19, 2015 (mobile application) P120005/S002 February 3, 2014 (expanded age range to ≥2 years) P120005	• Children and adults (age ≥2 years)	• Stand-alone CGM • Provides real-time readings, graphs, trends and glucose alarms directly to the user for the purpose of improving DM management • Mobile application allows data and alerts to be sent directly to users smart device (Apple/iOS only, though Android compatibility is in the works); Dexcom Share service allows data to be shared in real-time with up to five selected individuals • **Approved for and designed to replace fingerstick blood glucose testing for diabetes treatment decisions**	Commercially available

Device name Applicant	PMA#, Approval Date	DM Population	Description/Indication	Commercial availability
	October 5, 2012 (original PMA; persons age ≥18 years)			
Dexcom G4 PLATINUM CGM System Dexcom, Inc. CA, USA	P120005/S031 May 22, 2015 (approval expanded to include children age 2-17) P120005 October 5, 2012 (original PMA, use in persons ≥18 years)	• Children and adults (age ≥2 years)	• Stand-alone CGM • Provides real-time readings, graphs, trends and glucose alarms directly to the user for the purpose of improving DM management • Works with the Dexcom Share app, which sends real-time glucose values to the cloud, allowing up to five caregivers using Dexcom's Follow app to view real-time glucose readings on Apple or select Android devices • Compatible with the Animas Vibe and Tandem t:slim G4 pumps	Commercially available
New CGM + Insulin Pump systems				
T:slim X2 Insulin Pump with Dexcom G5 Mobile CGM Tandem Diabetes Care, Inc., CA, USA	P140015/S020 August 25, 2017	• Children and adults (age ≥6 years)	• CGM + Insulin Pump • Continuous delivery of basal and bolus insulin at set and variable rates • Updated technology from the t:slim G4 Insulin pump—t:slim X2 pump has been modified to include the functionality of the Dexcom G5 receiver and Dexcom G5 has Bluetooth capabilities that the Dexcom G4 does not • **Only approved CGM and pump system approved to replace fingerstick blood testing for diabetes treatment decisions**	Commercially available
MiniMed 670G System with SmartGuard Medtronic MiniMed, CA, USA	P160017 September 28, 2016	• Adolescents and adults (age ≥14 years)	• CGM + Insulin pump (**closed loop)** • Continuous delivery of basal insulin (at user selectable rates) and administration of insulin boluses (in user selectable amounts) • SmartGuard technology can be programmed to automatically adjust delivery of basal insulin based on CGM sensor glucose values and can suspend delivery of insulin when the sensor glucose value	Commercially available

Device name Applicant	PMA#, Approval Date	DM Population	Description/Indication	Commercial availability
			falls below (or is predicted to fall below) a predefined threshold. • Not intended to be used directly for making therapy adjustments	
OneTouch Vibe Plus System Animas Corporation, PA, USA	P130007/S016 December 16, 2016	• Children and adults (age ≥2 years)	• CGM + Insulin Pump • Consists of Animas Vibe Insulin Pump paired with Dexcom G5 Sensor and Transmitter • Provides continuous subcutaneous insulin infusion and continuous measurements of glucose for up to seven days • Provides glucose trends, alerts, and a low glucose alarm	Not commercially available October 5, 2017, Animas released a statement saying it was discontinuing the sale of its pumps in the US and Canada. Medtronic was selected as the partner for the transition, with all current Animas patients offered the option to transfer to a Medtronic pump.
MiniMed 630G System with SmartGuard Medtronic MiniMed, CA, USA	P150001 August 10, 2016	• Adolescents and adults (age ≥16 years)	• CGM + Insulin Pump • Continuous delivery of basal insulin (at user selectable rates) and administration of insulin boluses (in user selectable amounts) and/or for the continuous, real-time monitoring of interstitial glucose levels for the purpose of improving DM management • SmartGuard technology automatically stops insulin delivery for up to 2 hours when glucose values reach a user-selected low threshold and there is no response to the alarm. • Works with CareLink Professional and Personal Therapy Management Software for Diabetes (CareLink Pro, CareLink Personal)	Commercially available

Device name Applicant	PMA#, Approval Date	DM Population	Description/Indication	Commercial availability
Animas Vibe System Animas Corporation, PA, USA	P130007/S004 December 24, 2015 (expanded to include age ≥2 years) P130007 November 25, 2014 (original PMA, age ≥18 years)	• Children and adults (age ≥2 years)	• CGM + Insulin Pump • Can be used solely for continuous insulin delivery and to receive and display continuous, real-time glucose measurements (from the Dexcom G4 Platinum CGM System) for the purpose of improving DM management	Not commercially available October 5, 2017, Animas released a statement saying it was discontinuing the sale of its pumps in the US and Canada. Medtronic was selected as the partner for the transition, with all current Animas patients offered the option to transfer to a Medtronic pump.
Paradigm REAL-Time Revel System Medtronic MiniMed, CA, USA	P150019 December 7, 2015	• Adults (age ≥18 years)	• CGM + Insulin Pump • Continuous or periodic monitoring of interstitial glucose levels in real-time for the purpose of improving DM management and/or continuous delivery of insulin (at set and variable rates) via infusion pump	Commercially available
t:slim G4 Insulin Pump/"t-slim G4 System" Tandem Diabetes Care, Inc., CA, USA	P140015 September 8, 2015	• Adolescents and adults (age ≥12 years)	• CGM + Insulin Pump • Can be used solely for continuous insulin delivery and as part of the t:slim G4 System and to receive and display continuous, real-time glucose measurements (from the Dexcom G4 Platinum CGM System) for the purpose of improving DM management	Not commercially available T:slim X2 upgrade program ran through September 2017, upgraded all t:slim G4 systems to t:slim X2 systems.
MiniMed 530G System Medtronic MiniMed, CA, USA	P120010 September 26, 2013	• Adolescents and adults (age ≥16 years)	• CGM + Insulin Pump • Continuous delivery of basal insulin (at user selectable rates) and administration of insulin boluses (in user selectable amounts) and/or for the	Commercially available

Device name Applicant	PMA#, Approval Date	DM Population	Description/Indication	Commercial availability
			continuous, real-time monitoring of interstitial glucose levels for the purpose of improving DM management • SmartGuard technology automatically stops insulin delivery for up to 2 hours when glucose values reach a user-selected low threshold and there is no response to the alarm. • Works with CareLink Professional and Personal Therapy Management Software for Diabetes (CareLink Pro, CareLink Personal)	
EXCLUDED				
Freestyle Libre Pro Flash Glucose Monitoring System Abbott Diabetes Care, Inc., CA, USA	September 23, 2016 P150021	• Adults (age ≥18 years)	Professional CGM device only. The System is intended for use by health care professionals to aid in the review, analysis, and evaluation of a patient's glucose readings in support of an effective diabetes management program; Readings from the FreeStyle Libre Pro sensor are only made available to patients through consultation with a health care professional.	NA
iPro2 CGM System Medtronic, Inc. Diabetes, CA, USA	June 17, 2016 P150029 (for use with the Enlite sensor) P980022/S071 (approved in 2011 for use with the Sof-Sensor)	• Unclear	Does not allow data to be made available directly to patients in real time; Provides data that will be available for review by physicians after the recording interval (up to 144 hours); Is intended for occasional rather than everyday use	NA

APPENDIX K. CGM Device and Sensor Wear Data

Appendix Table K1. Devices and wear time reported in studies of traditional CGM in children with type 1 diabetes mellitus

Study	Device, year of device FDA approval	MARD	Wear time
RCTs			
Bergenstal 2010 Slover 2012, Rubin 2012	MiniMed Paradigm REAL-Time System, 2006	19.7%	Median sensor compliance, children (7-12 years) vs adolescents (13-18 years): · 0-3 months: 62% vs 63% · 3-12 months: 63% vs 55%
JDRF 2008 Lawrence 2010	1. Dexcom SEVEN, 2007 2. MiniMed Paradigm REAL-Time System, 2006 3. Abbott Freestyle Navigator, 2008	1. 17.0% 2. 19.7% 3. 12.8%	% of patients with ≥6.0 days/week of sensor use: · 8-14 years old: 50%
Kordonouri 2010	MiniMed Paradigm REAL-Time System, 2006	19.7%	Sensor uses* per week, mean ± SD: · 6 weeks: 2.1 ± 0.9 · 26 weeks: 1.4 ± 1.0 · 52 weeks: 1.1 ± 0.7
Mauras 2012	1. Abbott Freestyle Navigator, 2008 2. MiniMed Paradigm REAL-Time system, 2006	1. 12.8% 2. 19.7%	Mean sensor use, hours per week†: · 1-4 weeks: 99 hours/week · 5-8 weeks: 90 hours/week · 9-13 weeks: 88 hours/week · 14-17 weeks: 85 hours/week · 18-21 weeks: 83 hours/week · 22-26 weeks: 80 hours/week
Battelino 2012 Hommel 2014	MiniMed Paradigm REAL-Time System, 2006	19.7%	Sensor use % of required time‡, mean (median): · 6-18 years old: 73% (78%) Mean sensor use % of required time over final month: · 6-18 years old: 74%
Raccah 2009	MiniMed Paradigm REAL-Time System, 2006	19.7%	Sensor use % of required time: · 5-14 years old: 68.4%
Observational studies			
Chase 2010 (JDRF subanalysis)	1. Dexcom SEVEN, 2007	1. 17.0% 2. 19.7%	Median use, days/week (n patients using CGM): · 6 months: 5.5 days/week (n=76)

Study	Device, year of device FDA approval	MARD	Wear time
	2. MiniMed Paradigm REAL-Time System, 2006 3. Abbott Freestyle Navigator, 2008	3. 12.8%	· 12 months: 4.0 days/week (n=67)
JDRF 2009b (JDRF subanalysis)	1. Dexcom SEVEN, 2007 2. MiniMed Paradigm REAL-Time System, 2006 3. Abbott Freestyle Navigator, 2008	1. 17.0% 2. 19.7% 3. 12.8%	% of patients with ≥6.0 days/week of sensor use in month 6: · 8-14 years old: 46%
JDRF 2010 (JDRF subanalysis)	1. Dexcom SEVEN, 2007 2. MiniMed Paradigm REAL-Time System, 2006 3. Abbott Freestyle Navigator, 2008	1. 17.0% 2. 19.7% 3. 12.8%	% of patients with 0 days/week of sensor use, n/N (%): · 8-14 years old: 11/47 (23%) % of patients with >0-4 days/week of sensor use, n/N (%): · 8-14 years old: 15/47 (32%) % of patients with 4-<6 days/week of sensor use, n/N (%): · 8-14 years old: 10/47 (21%) % of patients with ≥6 days/week of sensor use, n/N (%): · 8-14 years old: 11/47 (23%)
Kordonouri 2012 (Kordonouri 2010 subanalysis)	MiniMed Paradigm REAL-Time System, 2006	19.7%	≥1 sensor per week, n/N (%): 33/65 (51%)
Rachmiel 2015	NR§	NR	% of patients using CGM ≥75% of study days at 12 months, n/N (%): 32/83 (38%)
Scaramuzza 2011	NR	NR	Median sensor use per month: 13.4 days/month
Wong 2014	NR	NR	% of patients with sensor use ≥6 days/week: · 13-<18 years old: 45% · <13 years old: 55%

CGM: continuous glucose monitoring; FDA: Food and Drug Administration; MARD: mean absolute relative difference; NR: not reported
*Not further defined
†Values estimated from figure
‡Required time was calculated as the number of days in the Sensor On arm (6 months) multiplied by 288 (the maximum number of sensor readings per day)
§Available systems included MiniMed Paradigm REAL-Time System and Freestyle Navigator. Unclear if other devices or systems were used.

Appendix Table K2. Devices and wear time reported in studies of traditional CGM in adults with type 1 diabetes mellitus

Study	Device, year of device FDA approval	MARD	Wear time
RCTs			
Bergenstal 2010 Rubin 2012	MiniMed Paradigm REAL-Time System, 2006	19.7%	NR
JDRF 2008 Lawrence 2010	1. Dexcom Seven, 2007 2. MiniMed Paradigm REAL-Time System, 2006 3. Abbott Freestyle Navigator, 2008	1. 17.0% 2. 19.7% 3. 12.8%	% of patients with ≥6.0 days/week of sensor use: • ≥25 years old: 83%
Beck 2017 Polonsky 2017	Dexcom G4 Platinum CGM System with software 505, 2015	9.0%	Median CGM use in month 6: 7 days/week
Hermanides 2011	MiniMed Paradigm REAL-Time System, 2006	19.7%	Mean sensor use throughout trial: 4.5 ± 1.0 days/week % of patients using sensor >60% of the time: 79%
Langeland 2012	MiniMed Guardian REAL-Time device, 2006	19.7%	Mean days of sensor use: 19 days (out of 4 weeks)
Lind 2017	Dexcom G4 Platinum CGM System, 2015	9.0%	Mean % of time of CGM use during CGM periods: 87.8%
New 2015	Abbott Freestyle Navigator, 2008	12.8%	Mean % of time of CGM use: • CGM w/o alarms: 83% • CGM w/alarms: 90%
Peyrot 2009	MiniMed Paradigm REAL-Time System, 2006	19.7%	NR
Tumminia 2015	MiniMed Guardian REAL-Time device, 2006	19.7%	Mean % sensor use: 44% % of patients sensor ≥40% of the time: 70%
Van Beers 2016	MiniMed Paradigm Veo System, NR*	10.5%	Median % of sensor use during CGM period: 89.4% (IQR 80.8%-95.5%)
Battelino 2012 Hommel 2014	MiniMed Paradigm REAL-Time System, 2006	19.7%	Sensor use % of required time†, mean (median): • 19-70 years old: 86% (89%) Mean sensor use % of required time over final month: • 19-70 years old: 87%

Study	Device, year of device FDA approval	MARD	Wear time
Raccah 2009	MiniMed Paradigm REAL-Time System, 2006	19.7%	Sensor use % of required time: • ≥25 years old: 74.9%
Observational studies			
JDRF 2009b (JDRF subanalysis)	1. Dexcom SEVEN, 2007 2. MiniMed Paradigm REAL-Time System, 2006 3. Abbott Freestyle Navigator, 2008	1. 17.0% 2. 19.7% 3. 12.8%	% of patients with ≥6.0 days/week of sensor use in month 6: • ≥25 years old: 79%
JDRF 2010 (JDRF subanalysis)	1. Dexcom SEVEN, 2007 2. MiniMed Paradigm REAL-Time System, 2006 3. Abbott Freestyle Navigator, 2008	1. 17.0% 2. 19.7% 3. 12.8%	% of patients with 0 days/week of sensor use, n/N (%): • ≥25 years old: 4/51 (8%) % of patients with >0-4 days/week of sensor use, n/N (%): • ≥25 years old: 4/51 (8%) % of patients with 4-<6 days/week of sensor use, n/N (%): • ≥25 years old: 6/51 (12%) % of patients with ≥6 days/week of sensor use, n/N (%): • ≥25 years old: 37/51 (73%)
Ludwig-Seibold 2012 Pediatric and adult population	NR	NR	Sensor use <30 days: 67.7% Sensor use 30-60 days: 13.0% Sensor use >60 days: 19.3%
Wong 2014	NR	NR	% of patients with sensor use ≥6 days/week: • ≥26 years old: 60% • 18-<26 years old: 37%
Anderson 2011	NR	NR	Average CGM use for long-term users‡, mean: 1.1 years Average CGM use for short-term users§, mean: 33 days
JDRF 2009c (JDRF subanalysis)	1. Dexcom SEVEN, 2007 2. MiniMed Paradigm REAL-Time System, 2006 3. Abbott Freestyle Navigator, 2008	1. 17.0% 2. 19.7% 3. 12.8%	CGM use, median (IQR): • 6 months: 7.0 days/week (6.3 to 7.0) • 12 months: 6.8 days/week (5.8 to 7.0)

CGM: continuous glucose monitoring; FDA: Food and Drug Administration; MARD: mean absolute relative difference; NR: not reported
*MiniMed Paradigm Veo system is currently only marketed outside the U.S. but the calibration algorithm and threshold suspend software is identical to that of the MiniMed 530. The MiniMed 530G received FDA approval in 2013.
†Required time was calculated as the number of days in the Sensor On arm (6 months) multiplied by 288 (the maximum number of sensor readings per day)
‡Patients using CGM for ≥3 months
§Patients using CGM for <3 months

Appendix Table K3. Devices and wear time reported in studies of flash glucose monitoring in adults with type 1 diabetes mellitus

Study	Device, year of device FDA approval	MARD	Wear time
RCTs			
Bolinder 2016	Freestyle Libre Flash CGM System, 2017	9.7%	Device use*, mean ± SD: 92.8 ± 9.2% Average number of scans per day, mean ± SD: 15.1 ± 6.9

CGM: continuous glucose monitoring; FDA: Food and Drug Administration; MARD: mean absolute relative difference; SD: standard deviation
*Defined as the percentage of data collected assuming continuous device wear for 6 months

Appendix Table K4. Device and Sensor Wear Data for trials of Mixed Children and Adults with Type 1 Diabetes Mellitus

Study	Device, year of device FDA approval	MARD	Wear time
RCTs			
Deiss 2006	MiniMed Guardian REAL-Time device, 2006	19.7%	NR
Hirsch 2008 Pediatric and adult population	MiniMed Paradigm REAL-Time System, 2006	19.7%	Sensor compliance*, n/N (%): • <60% compliance: 4/66 (6%) • 60-80% compliance: 12/66 (18%) • 80-100%: 32/66 (48%) • >100%: 18/66 (27%)
JDRF 2008 Lawrence 2010	1. Dexcom SEVEN, 2007 2. MiniMed Paradigm REAL-Time System, 2006 3. Abbott Freestyle Navigator, 2008	1. 17.0% 2. 19.7% 3. 12.8%	% of patients with ≥6.0 days/week of sensor use: • 15-24 years old: 30%
JDRF 2009	Dexcom SEVEN, 2007	17.0%	% of patients with ≥6.0 days/week of sensor use: • 0 to 3 months: 78% • 5 to 6 months: 67% • 15-24 years old (over whole study duration): 53% % of patients with <4.0 days/week of sensor use from 5 to 6 months: 13% Median sensor use over 6 month study duration: • 15-24 years old: 6.2 days/week

Study	Device, year of device FDA approval	MARD	Wear time
Battelino 2011	Abbott Freestyle Navigator, 2008	12.8%	Total number of days of sensor wear, mean ± SD: 136 ± 52 days Days/week of sensor wear, mean ± SD: 5.6 ± 1.4 days/week
Battelino 2012 Hommel 2014	MiniMed Paradigm REAL-Time System, 2006	19.7%	Sensor use % of required time†, mean (median): • Total population: 80% (84%) Mean sensor use % of required time over final month: • Total population: 81% % of patients with sensor use ≥70% of required time: 72% % of patients with sensor use ≥90% of required time: 24%
O'Connell 2009	MiniMed Paradigm REAL-Time System, 2006	19.7%	Time spent using sensor of total 90 day period, median (IQR): 62.5% (17.7% to 93.8%) Patients adhering to sensor use ≥70%, n/N (%): 11/25 (44%)
Raccah 2009	MiniMed Paradigm REAL-Time System, 2006	19.7%	Patients adhering to sensor use ≥70%, n/N (%): 23/55 (42%) Sensor use % of required time: • 15-24 years old: 52.4%
Observational studies			
JDRF 2009b (JDRF subanalysis)	1. Dexcom SEVEN, 2007 2. MiniMed Paradigm REAL-Time System, 2006 3. Abbott Freestyle Navigator, 2008	1. 17.0% 2. 19.7% 3. 12.8%	% of patients with ≥6.0 days/week of sensor use in month 6: • 15-24 years old: 29%
JDRF 2010 (JDRF subanalysis)	1. Dexcom SEVEN, 2007 2. MiniMed Paradigm REAL-Time System, 2006 3. Abbott Freestyle Navigator, 2008	1. 17.0% 2. 19.7% 3. 12.8%	% of patients with 0 days/week of sensor use, n/N (%): • 15-24 years old: 11/56 (20%) % of patients with >0-4 days/week of sensor use, n/N (%):

Study	Device, year of device FDA approval	MARD	Wear time
			• 15-24 years old: 26/56 (46%) % of patients with 4-<6 days/week of sensor use, n/N (%): • 15-24 years old: 7/56 (13%) % of patients with ≥6 days/week of sensor use, n/N (%): • 15-24 years old: 12/56 (21%)
Ludwig-Seibold 2012 Pediatric and adult population	NR	NR	Sensor use <30 days: 67.7% Sensor use 30-60 days: 13.0% Sensor use >60 days: 19.3%

CGM: continuous glucose monitoring; FDA: Food and Drug Administration; MARD: mean absolute relative difference; NR: not reported
*Defined as sensor use 6 days per week
†Required time was calculated as the number of days in the Sensor On arm (6 months) multiplied by 288 (the maximum number of sensor readings per day)

Appendix Table K5. Devices and wear time reported in studies of traditional CGM in adults with type 2 diabetes mellitus

Study	Device, year of device FDA approval	MARD	Wear time
RCTs			
Ehrhardt 2011 Vigersky 2012	Dexcom SEVEN, 2007	17.0%	Sensor use <48 days*, n/N (%): 16/50 (32%) Sensor use ≥48 days, n/N (%): 34/50 (68%)
Tildesley 2013 Tang 2014	MiniMed Guardian REAL-Time System, 2006	19.7%	NR
Yoo 2008	MiniMed Guardian REAL-Time System, 2006	19.7%	NR

FDA: Food and Drug Administration; MARD: mean absolute relative difference; NR: not reported
*Sensor use was measured out of 8 weeks

Appendix Table K6. Devices and wear time reported in studies of flash glucose monitoring in adults with type 2 diabetes mellitus

Study	Device, year of device FDA approval	MARD	Wear time
RCTs			
Haak 2016	Freestyle Libre Flash CGM System, 2017	9.7%	Device use*, mean ± SD: • 6 months randomized phase: 88.7 ± 9.2% • 12 months open-label phase: 83.6 ± 13.8% Average number of scans per day, mean ± SD: • 6 months randomized phase: 8.4 ± 4.6 12 months open-label phase: 7.1 ± 3.5

CGM: continuous glucose monitoring; FDA: Food and Drug Administration; MARD: mean absolute relative difference; SD: standard deviation
*Defined as the percentage of data collected assuming continuous device wear for 6 months

Appendix Table K7. Devices and wear time reported in studies of traditional CGM in pregnant women with type 1 diabetes mellitus

Study	Device, year of device FDA approval	MARD	Wear time
RCTs			
Secher 2013 Type 1 and Type 2 patients	MiniMed Guardian REAL-Time System, 2006	19.7%	Sensor use ≥60% of the time, n/N (%): 5/76 (7%) Per-protocol sensor use*, n/N (%): 49/76 (64%)
Observational			
Cordua 2012 (Secher 2013 subanalysis)	MiniMed Guardian REAL-Time System, 2006	19.7%	Minutes of disrupted readings, median (IQR): 31 (11-111)
Fresa 2013	1. MiniMed Paradigm REAL-Time CGM System (or Paradigm Veo CGM System) (n=15), 2006 2. MiniMed Guardian REAL-Time CGM System (n=3), 2006	1. 19.7% 2. 19.7%	NR
Secher 2014	MiniMed Guardian REAL-Time System, 2006	19.7%	Weeks of device use, median (range): 10 (7-13) weeks

FDA: Food and Drug Administration; IQR: interquartile range; MARD: mean absolute relative difference; NR: not reported
*Not otherwise defined

Appendix Table K8. Devices and wear time reported in studies of traditional CGM in pregnant women with type 2 diabetes mellitus

Study	Device, year of device FDA approval	MARD	Wear time
RCTs			
Secher 2013 Type 1 and Type 2 patients	MiniMed Guardian REAL-Time System, 2006	19.7%	Sensor use ≥60% of the time, n/N (%): 5/76 (7%) Per-protocol sensor use*, n/N (%): 49/76 (64%)
Feig 2017			Days/week of sensor use, median (IQR): • Pregnant population: 6.1 days/week (4.0 to 6.8) • Planning pregnancy population: 6.2 days/week (5.2 to 6.9) Percent of population using sensor >75% of the time: • Pregnant population: 70% • Planning pregnancy population: 77%

FDA: Food and Drug Administration; MARD: mean absolute relative difference; NR: not reported
*Not otherwise defined

Appendix Table K9. Devices and wear time reported in studies of traditional CGM in pregnant women with gestational diabetes

Study	Device, year of device FDA approval	MARD	Wear time
RCTs			
Wei 2016	MiniMed Gold CGMS, 2011	NR	NR

FDA: Food and Drug Administration; MARD: mean absolute relative difference; NR: not reported

APPENDIX L. Summary of Time Spent in Target Glycemic Range

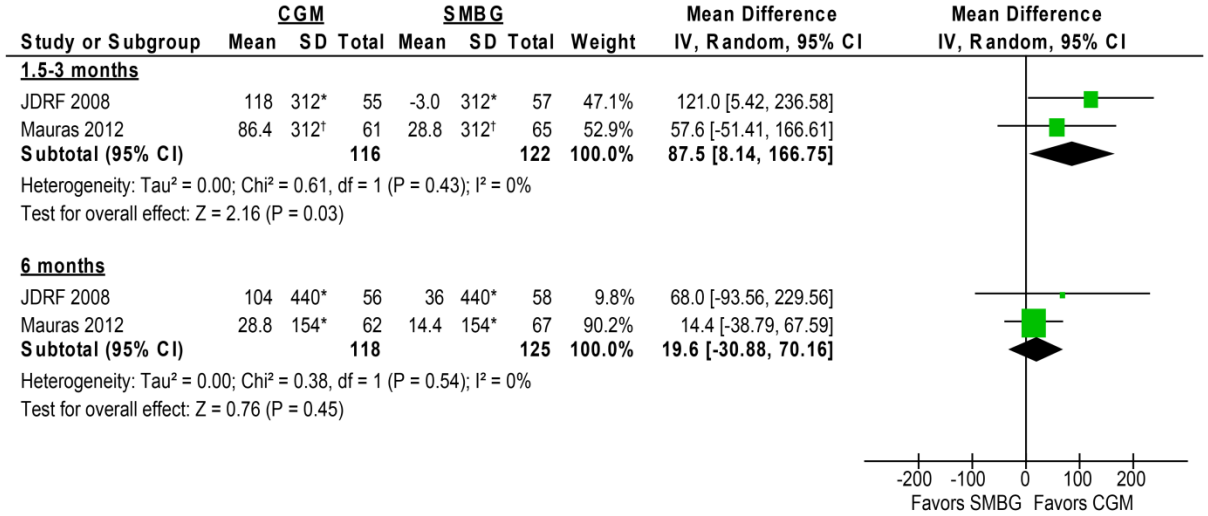
Note: This outcome was variably reported across trials and generally did not include data on estimate variation (e.g. standard deviations) or effect sizes. Calculations to compensate for these deficiencies are described below based on methods used for Cochrane Reviews as described in the Cochrane Handbook. The following analyses should be interpreted with caution. These findings are not considered to be a formal part of the report evidence summary.

Appendix Table L1. Outcomes measuring time spent target glycemic range in a pediatric population with T1DM from parallel trials of CGM vs SMBG

Author year *ROB*	Outcome	Timing	CGM Mean ± SD (n) or Median (IQR) (n)	SMBG Mean ± SD (n) or Median (IQR) (n)	MD (95% CI)	p-value
JDRF 2008 *Moderately Low*	Minutes/day in target glycemic range (71-180 mg/dl)	Baseline	646 ± NR (n=56)	710 ± NR (n=58)	NR	NR
		3 months	764 ± NR (n=55)	707 ± NR (n=57)	NR	0.04
		6 months	750 ± NR (n=56)	746 ± NR (n=58)	NR	0.53
Mauras 2012 *Moderately Low*	Minutes/day in target glycemic range (71-180 mg/dl)*	Baseline	662.4 (NR) (n=62)	691.2 (NR) (67)	NR	NR
		3 months	748.8 (NR) (n=61)	720.0 (NR) (n=65)	NR	NR
		6 months	691.2 (NR) (n=62)	705.6 (NR) (n=67)	NR	0.60

CGM: continuous glucose monitoring; CI: confidence interval; IQR: interquartile range; MD: mean difference; NR: not reported; ROB: risk of bias; SD: standard deviation; SMBG: self-monitoring blood glucose; T1DM: type 1 diabetes mellitus;

*AAI converted "% of day in glycemic range 71-180 mg/dl" into "minutes per day in glycemic range 71-180 mg/dl"



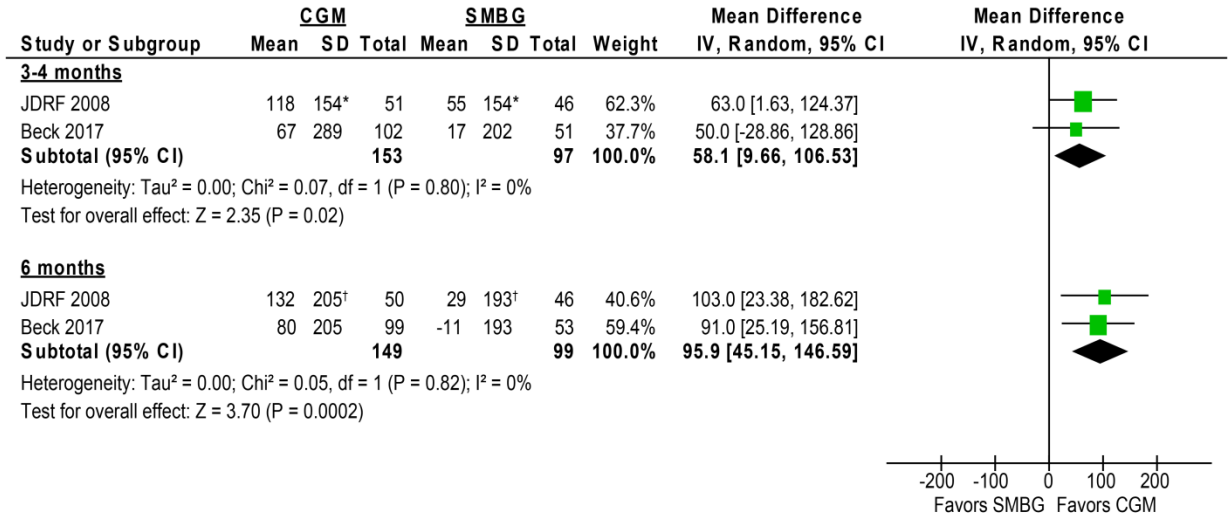
*Final SD back-calculated from p-value and then assumed constant from baseline to follow-up
†SD imputed from studies in same timeframe and treatment group

Appendix Table L2. Outcomes measuring time spent target glycemic range in an adult population with T1DM from parallel trials of CGM vs SMBG

Author year *ROB*	Outcome	Timing	CGM Mean ± SD (n)	SMBG Mean ± SD (n)	MD (95% CI)	p-value
JDRF 2008 *Moderately Low*	Minutes/day in target glycemic range (71-180 mg/dl)	Baseline	854 ± NR (n=52)	811 ± NR (n=46)	NR	NR
		3 months	972 ± NR (n=51)	866 ± NR (n=46)	NR	0.02
		6 months	986 ± NR (n=50)	840 ± NR (n=46)	NR	<0.001
Beck 2017 *Moderately Low*	Minutes/day in target glycemic range (70-180 mg/dl)	Baseline	660 ± 179 (n=105)	650 ± 170 (n=53)	NR	NR
		3 months	727 ± 222 (n=102)	667 ± 224 (n=51)	NR	NR*
		6 months	740 ± 223 (n=99)	639 ± 210 (n=53)	NR	NR*

CGM: continuous glucose monitoring; CI: confidence interval; MD: mean difference; NR: not reported; ROB: risk of bias; SD: standard deviation; SMBG: self-monitoring blood glucose

*p-value for 3 and 6 month data combined was 0.005



*Final SD back-calculated from p-value and then assumed constant from baseline to follow-up
†SD imputed from studies in same timeframe and treatment group

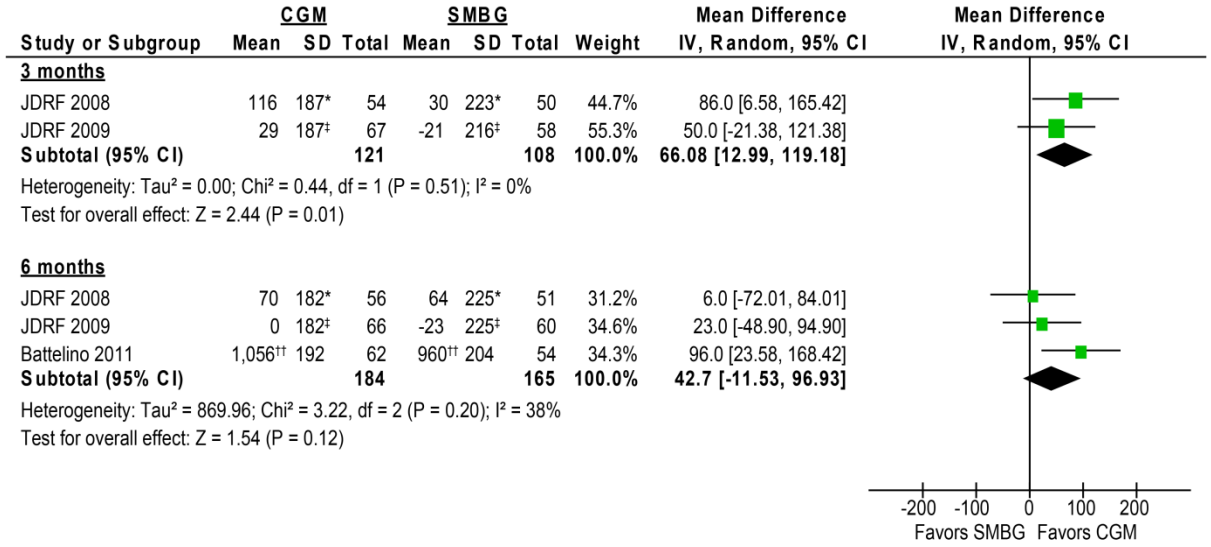
Appendix Table L3. Outcomes measuring time spent target glycemic range in a mixed adult and pediatric population with T1DM from parallel trials of CGM vs SMBG

Author year *ROB*	Outcome	Timing	CGM Mean ± SD (n)	SMBG Mean ± SD (n)	Ratio of means (95% CI) or MD (95% CI)	p-value
JDRF 2008 *Moderately Low*	Minutes/day in target glycemic range (71-180 mg/dl)	Baseline	691 ± NR (n=57)	697 ± NR (n=53)	NR	NR
		3 months	807 ± NR (n=54)	727 ± NR (n=50)	NR	0.02
		6 months	761 ± NR (n=56)	761 ± NR (n=51)	NR	0.79
JDRF 2009 *Moderately Low*	Minutes/day in target glycemic range (71-180 mg/dl)	Baseline	1063 (921-1174) (n=67)	972 (809-1089) (n=62)	NR	NR
		3 months	1092 (947-1200) (n=67)	951 (778-1079) (n=58)	NR	NR*
		6 months	1063 (948-1185) (n=66)	949 (784-1106) (n=60)	NR	0.003/0.002/ 0.004*,†
Battelino 2011		Baseline	NR	NR	NR	NR

Author year *ROB*	Outcome	Timing	CGM Mean ± SD (n)	SMBG Mean ± SD (n)	Ratio of means (95% CI) or MD (95% CI)	p-value
Moderately Low	Minutes/day in target glycemic range (70-180 mg/dl)‡	6 months	1056 ± 192 (n=62)	960 ± 204 (n=54)	Ratio of means 1.10 (1.02-1.18)	0.009
O'Connell 2009 *Moderately Low*	Proportion of time (%) spent in target glycemic range (72-180 mg/dl§)	Baseline	62.1 ± 12.5 (n=31)	58.0 ± 9.4 (n=31)	NR	NR
		3 months	57.2 ± 11.3 (n=26)	53.9 ± 15.0 (n=29)	Adj MD 1.72 (-5.37-8.81)	0.63

CGM: continuous glucose monitoring; CI: confidence interval; MD: mean difference; NR: not reported; ROB: risk of bias; SMBG: self-monitoring blood glucose; T1DM: type 1 diabetes mellitus

*P values for 3 and 6 month combined data were <0.001/<0.001/0.001. See footnote below for a description of the methods used for the three different values
†P values were obtained from three methods. The first value was found using an ANCOVA model based on van der Waerden scores, the second value was found using an ANCOVA model with truncation of outliers, and the third value was found using an ANCOVA model with a square root transformation
‡ AAI converted "hours per day in glycemic range 70-180-mg/dl" into "minutes per day in glycemic range 70-180-mg/dl"
§Values converted from mmol/l to mg/dl



*Final SD back-calculated from p-value and then assumed constant from baseline to follow-up
‡SD estimate obtained through IQR using the following formula: (3rd Quartile – 1st Quartile) / 1.35. While the mean was taken to be the median.
††Final scores used rather than change scoresA

APPENDIX M. Clinical Expert Peer Review

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