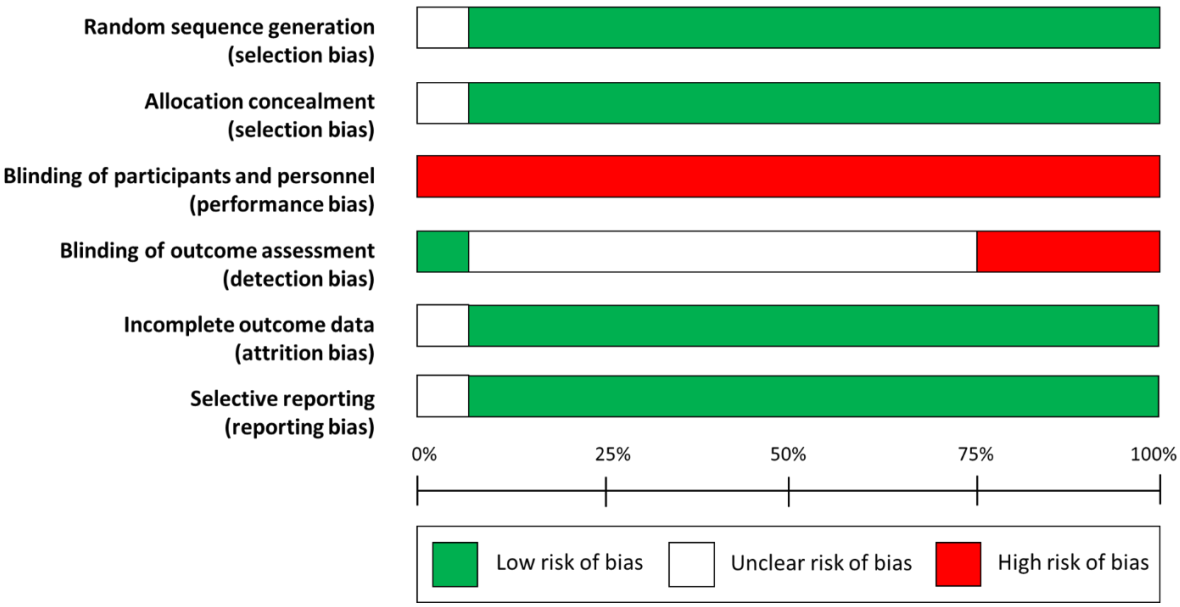
SUPPLEMENTARY DATA

Effects of continuous glucose monitoring on metrics of glycemic control in diabetes: a systematic review with meta-analysis of randomized controlled trials

Supplemental Material

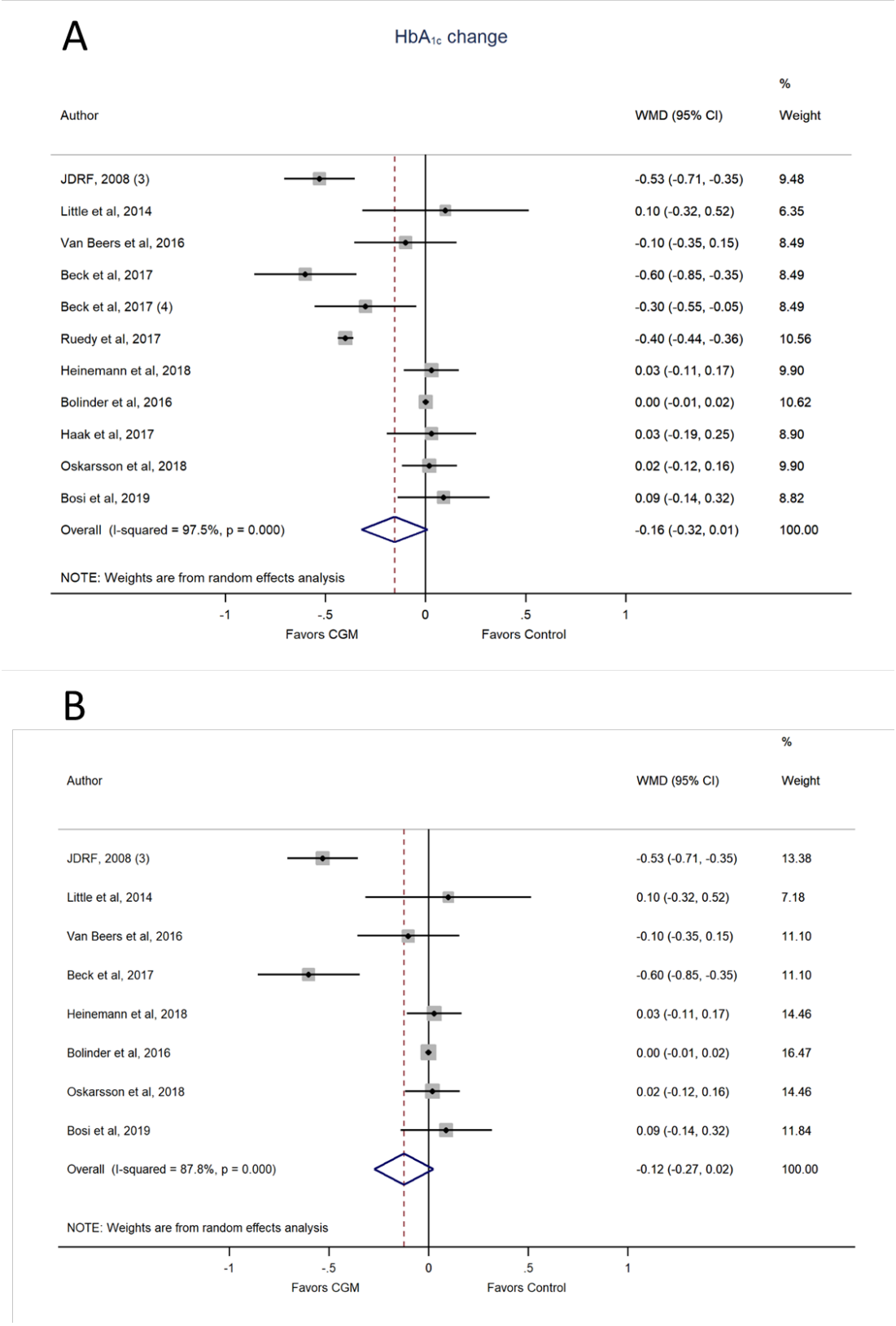
SUPPLEMENTARY DATA

Supplementary Figure S1. Cochrane risk of bias (graph) for the 15 studies



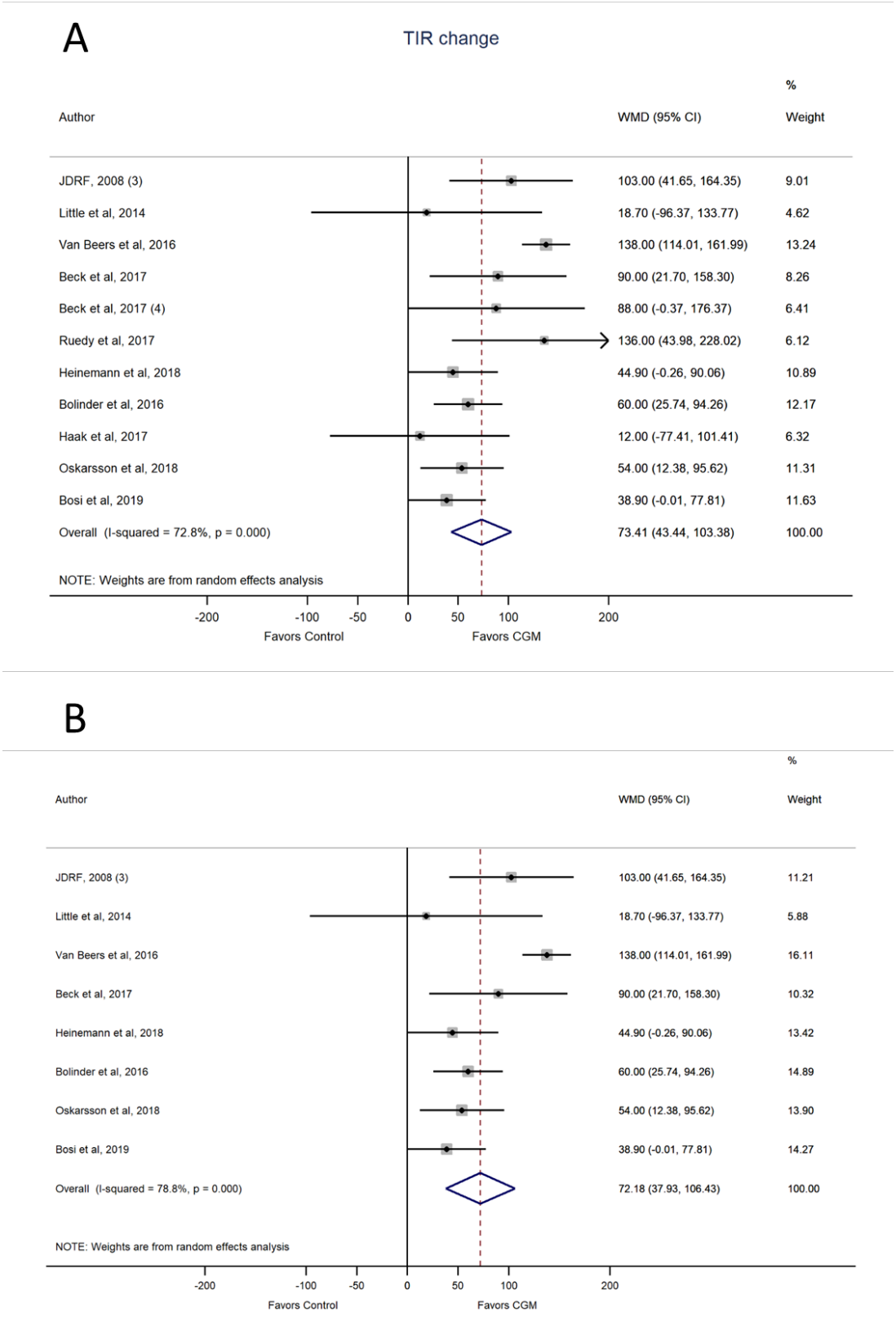
SUPPLEMENTARY DATA

Supplementary Figure S2. Forest plot of meta-analysis for HbA1c change excluding pediatric patients and pregnant or planning pregnant women (P = 0.066) (A), and also patients with type 2 diabetes (P = 0.103) (B).



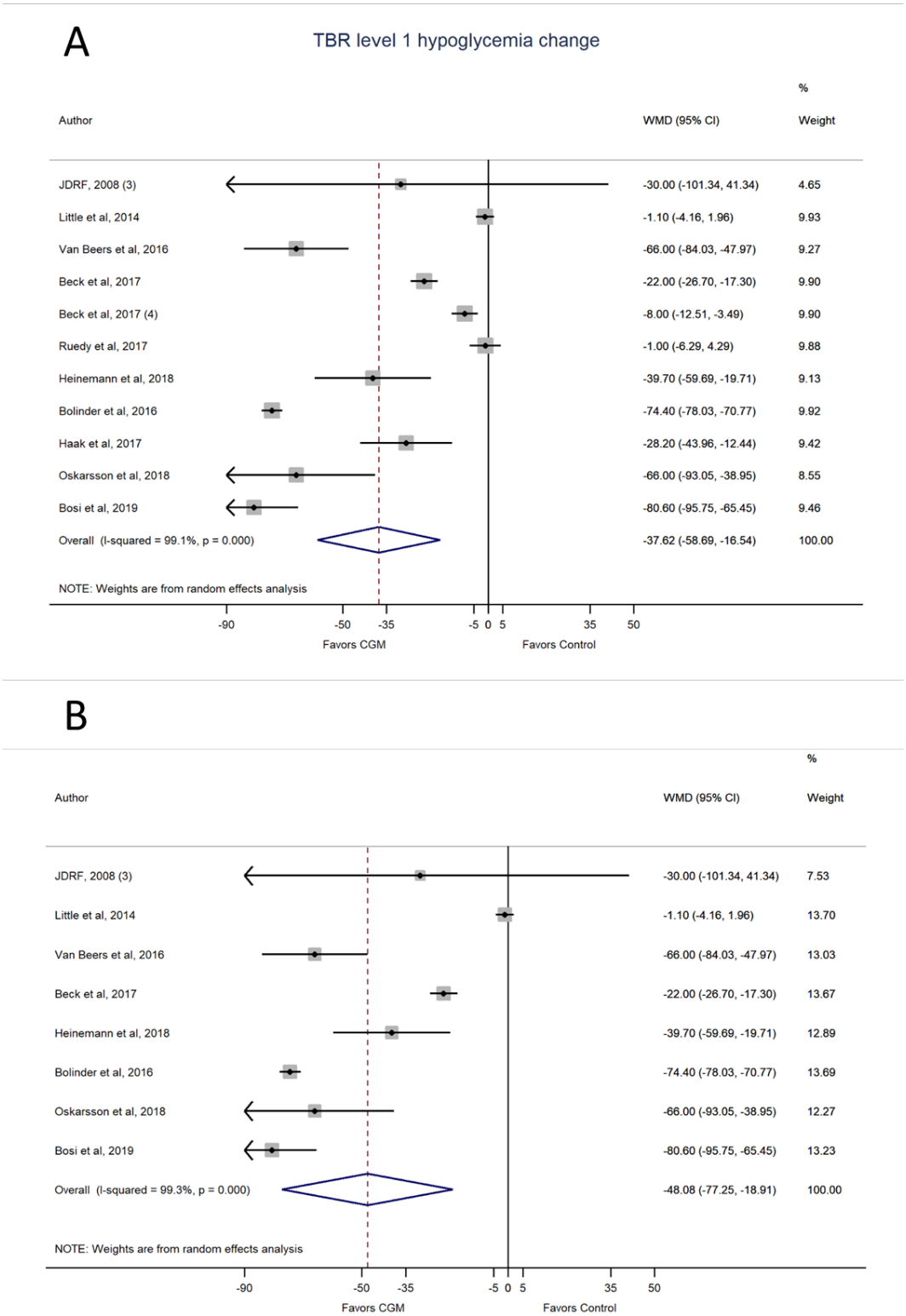
SUPPLEMENTARY DATA

Supplementary Figure S3. Forest plot of meta-analysis for TIR change excluding pediatric patients and pregnant or planning pregnant women (P <0.001) (A) and also patients with type 2 diabetes (P <0.001) (B).



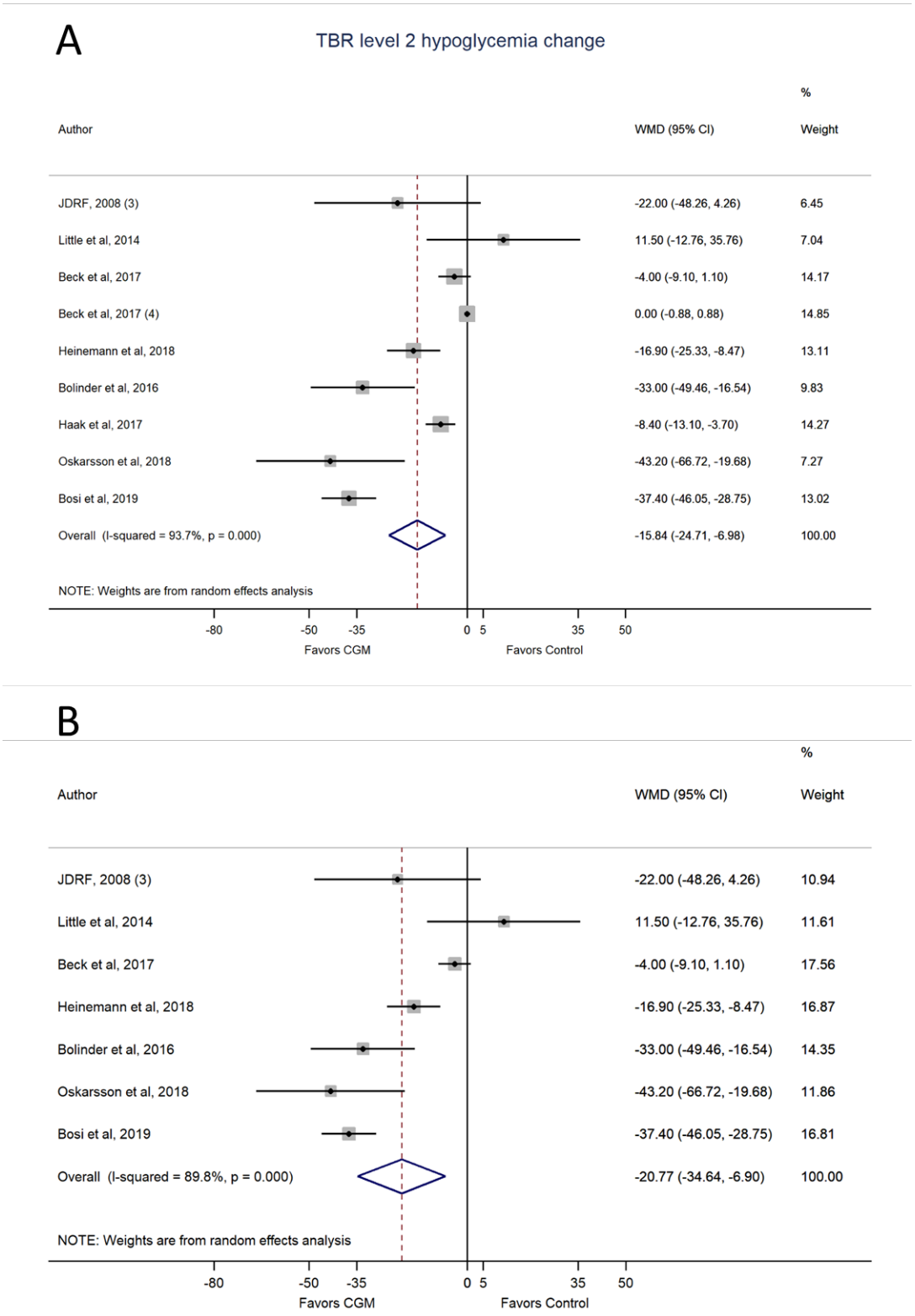
SUPPLEMENTARY DATA

Supplementary Figure S4. Forest plot of meta-analysis for TBR change level 1 hypoglycemia excluding pediatric patients and pregnant or planning pregnant women (P <0.001) (A), and also patients with type 2 diabetes (P <0.001) (B).



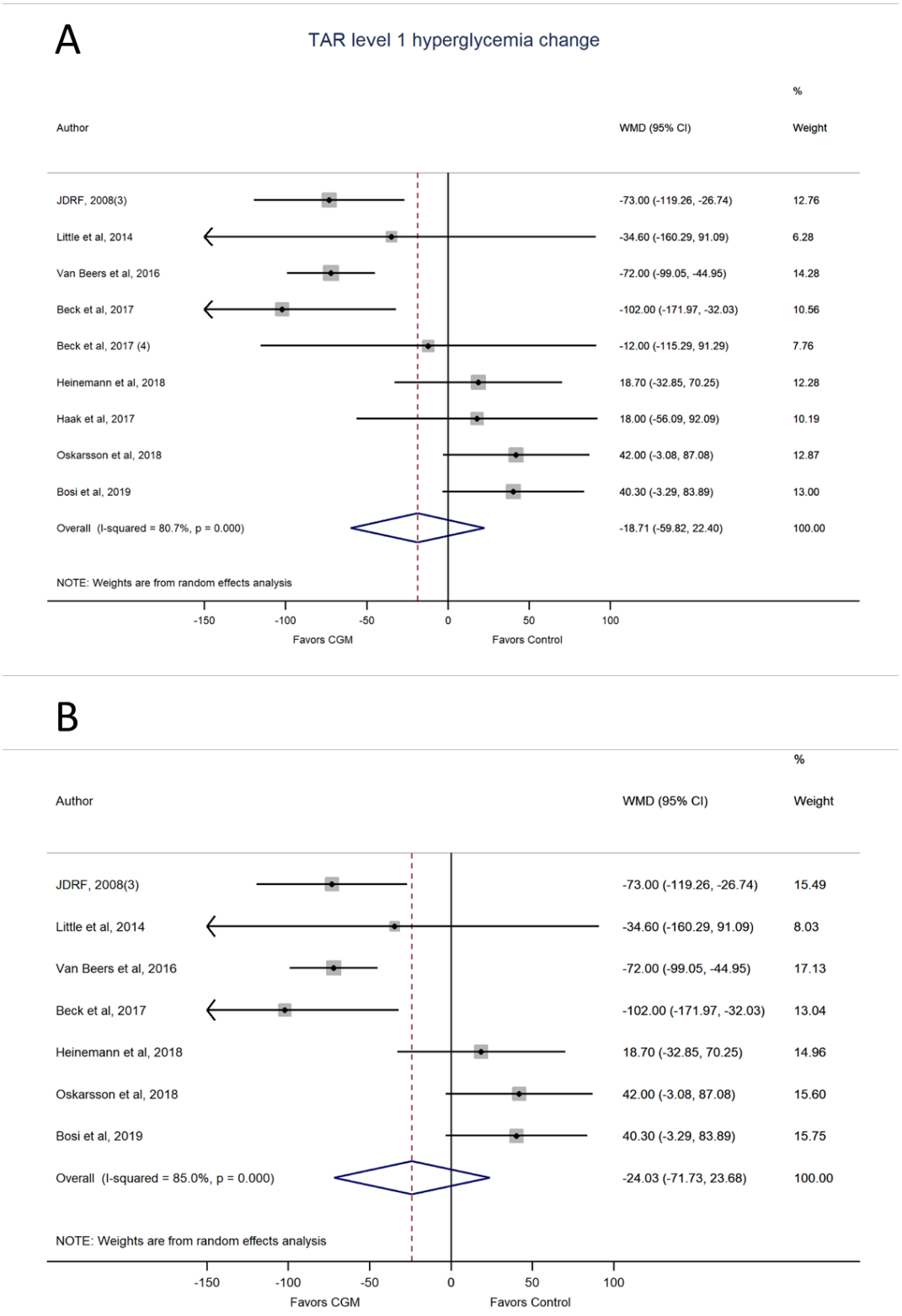
SUPPLEMENTARY DATA

Supplementary Figure S5. Forest plot of meta-analysis for TBR change level 2 hypoglycemia excluding pediatric patients and pregnant or planning pregnant women (P <0.001) (A), and also patients with type 2 diabetes (P = 0.003) (B).



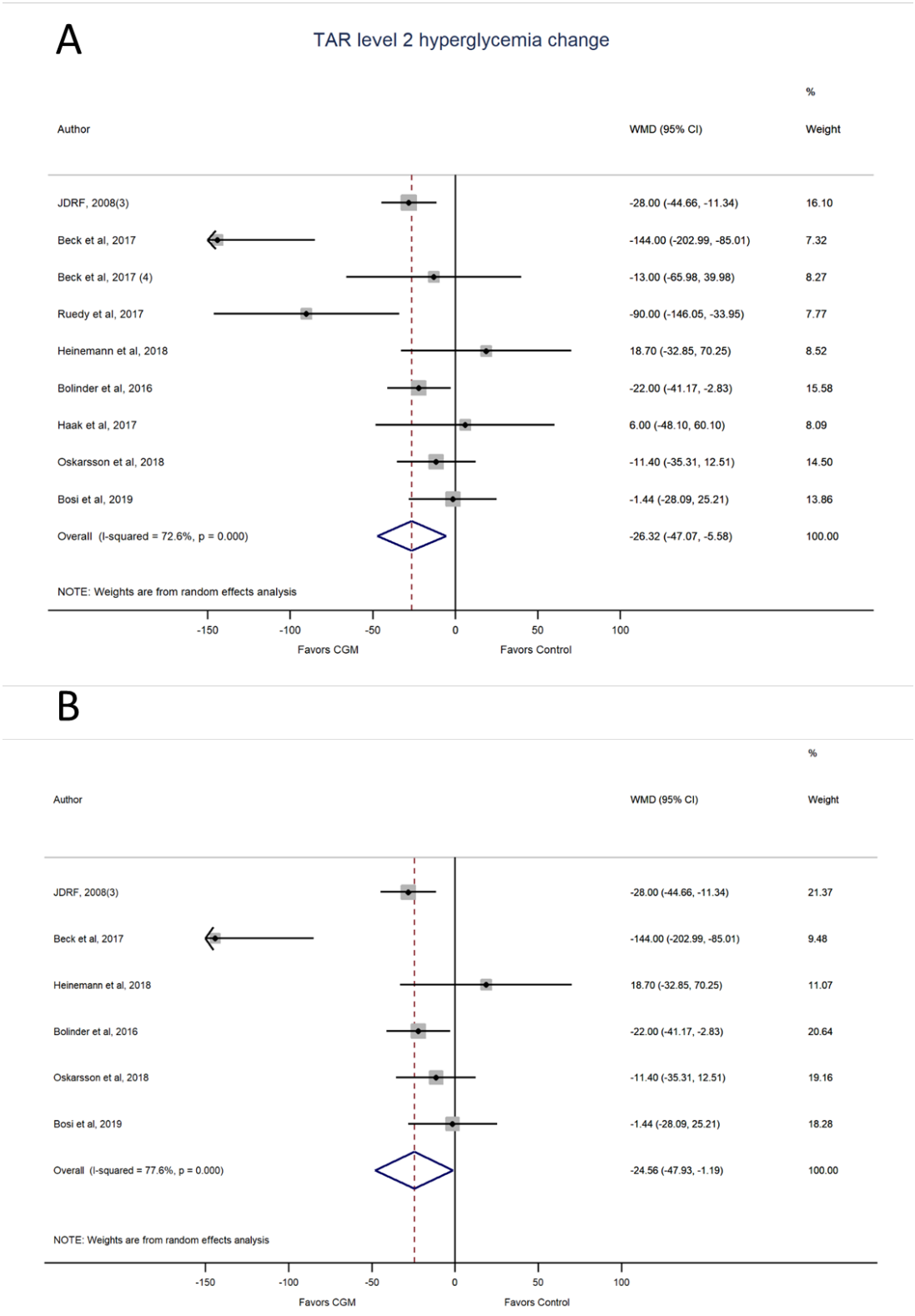
SUPPLEMENTARY DATA

Supplementary Figure S6. Forest plot of meta-analysis for TAR change level 1 hypoglycemia excluding pediatric patients and pregnant or planning pregnant women (P = 0.372) (A), and also patients with type 2 diabetes (P = 0.324) (B).



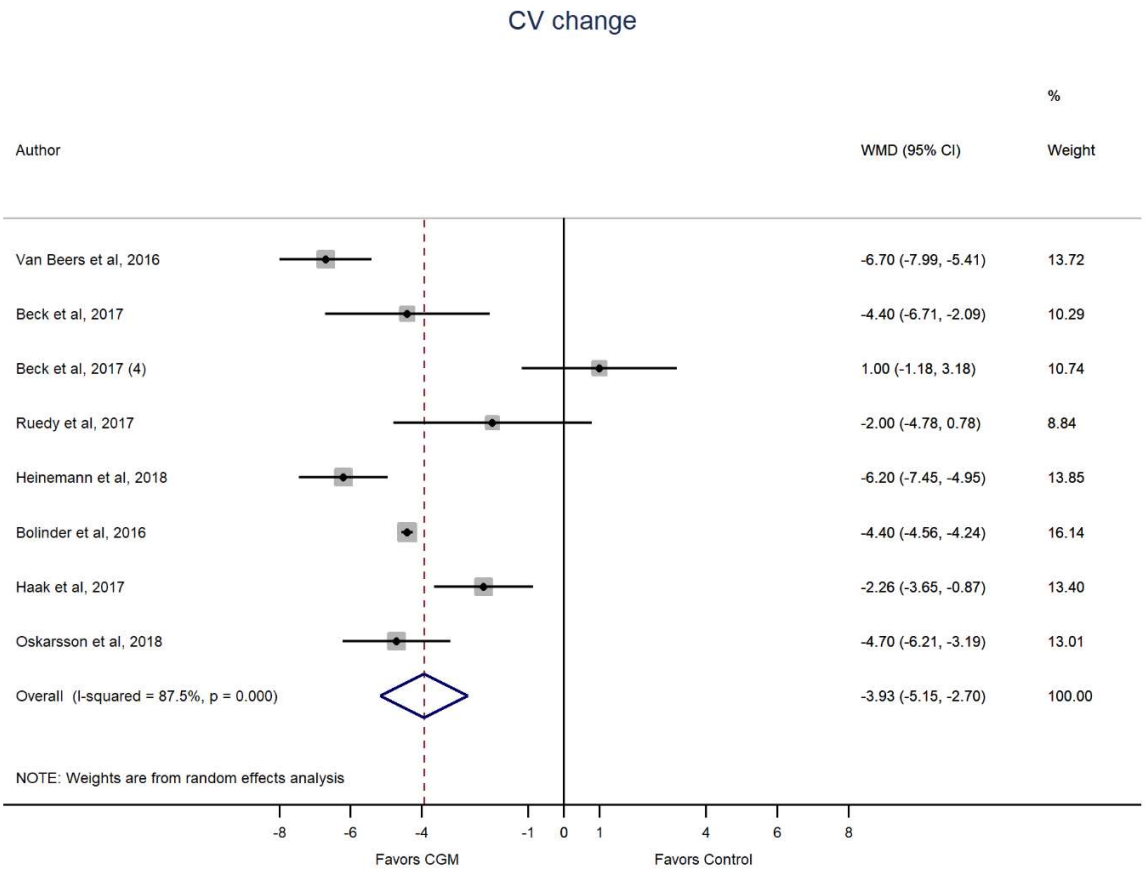
SUPPLEMENTARY DATA

Supplementary Figure S7. Forest plot of meta-analysis for TAR change level 2 hypoglycemia excluding pediatric patients and pregnant or planning pregnant women (P = 0.013) (A), and also patients with type 2 diabetes (P = 0.039) (B).



SUPPLEMENTARY DATA

Supplementary Figure S8. Forest plot for CV change relative to sensitivity analysis performed excluding pediatric patients and pregnant or planning pregnant women.



SUPPLEMENTARY DATA

Supplementary Table S1. Trials excluded from meta-analysis

Deiss D, Bolinder J, Riveline JP et al. Improved glycemic control in poorly controlled patients with type 1 diabetes using real-time continuous glucose monitoring. Diabetes Care 2006;29:2730-2.	**Lack of interest data (TIR, TAR, TBR)**
Deiss D, Hartmann R, Schmidt J et al. Results of a randomised controlled cross-over trial on the effect of continuous subcutaneous glucose monitoring (CGMS) on glycaemic control in children and adolescents with type 1 diabetes. Exp Clin Endocrinol Diabetes 2006;114:63-7.	**Lack of interest data (TIR)**
Lagarde WH, Barrows FP, Davenport ML, et al. Continuous subcutaneous glucose monitoring in children with type 1 diabetes mellitus: a single-blind, randomized, controlled trial. Pediatr Diabetes 2006;7:159-64.	**Lack of interest data (data expressed as AUC)**
Lee SW, Sweeney T, Clausen D, et al. Combined insulin pump therapy with real-time continuous glucose monitoring significantly improves glycemic control compared to multiple daily injection therapy in pump naïve patients with type 1 diabetes; single center pilot study experience. J Diabetes Sci Technol 2007;1:400-4.	**Lack of interest data (TIR, TAR,TBR)**
Hirsch IB, Abelseth J, Bode BW et al. Sensor-augmented insulin pump therapy: results of the first randomized treat-to-target study. Diabetes Technol Ther 2008;10:377-83.	**Lack of interest data (data expressed as AUC)**
Peyrot M, Rubin RR. Patient-reported outcomes for an integrated real-time continuous glucose monitoring/insulin pump system.Diabetes Technol Ther 2009;11:57-62.	**Lack of interest data (TIR, TAR, TBR)**
Raccah D, Sulmont V, Reznik Y,et al.Incremental value of continuous glucose monitoring when starting pump therapy in patients with poorly controlled type 1 diabetes: the RealTrend study. Diabetes Care 2009;32:2245-50.	**Lack of interest data (TIR)**
Bergenstal RM, Tamborlane WV, Ahmann A, STAR 3 Study Group. Effectiveness of sensor-augmented insulin-pump therapy in type 1 diabetes. N Engl J Med 2010;363:311-20.	**Lack of interest data (data expressed as AUC)**
Ehrhardt NM, Chellappa M, Walker MS et al. The effect of real-time continuous glucose monitoring on glycemic control in patients with type 2 diabetes mellitus. J Diabetes Sci Technol 2011;5:668-75.	**Lack of interest data (not comparable with the control group)**
Kordonouri O, Pankowska E, Rami B, et al.Sensor-augmented pump therapy from the diagnosis of childhood type 1 diabetes: results of the Paediatric Onset Study (ONSET) after 12 months of treatment. Diabetologia 2010;53:2487-95.	**Lack of interest data (TIR, TAR,TBR)**
Hermanides J, Nørgaard K, Bruttomesso D, et al. Sensor-augmented pump therapy lowers HbA(1c) in suboptimally controlled Type 1 diabetes; a randomized controlled trial. Diabet Med 2011;28:1158-67.	**Lack of interest data (TIR)**
Slover RH, Welsh JB, Criego A,et al. Effectiveness of sensor-augmented pump therapy in children and adolescents with type 1 diabetes in the STAR 3 study. Pediatr Diabetes 2012;13:6-11.	**Lack of interest data (TIR, data expressed in AUC)**
Ly TT, Nicholas JA, Retterath A, et al.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. 2013;310:1240-7.	**Lack of interest data (TIR, TAR)**
New JP, Ajjan R, Pfeiffer AF, et al. Continuous glucose monitoring in people with diabetes: the randomized controlled Glucose Level Awareness in Diabetes Study (GLADIS). Diabet Med 2015;32:609-17.	**Lack of interest data(TIR)**
Rosenlund S, Hansen TW, Rossing P et al. Effect of Sensor-Augmented Pump Treatment Versus Multiple Daily Injections on Albuminuria: A 1-Year Randomized Study. J Clin Endocrinol Metab 2015;100:4181-8	**Lack of interest data (TIR, TAR, TBR)**
Tumminia A, Crimi S, Sciacca L, et al. Efficacy of real-time continuous glucose monitoring on glycaemic control and glucose variability in type 1 diabetic patients treated with either insulin pumps or multiple insulin injection therapy: a randomized controlled crossover trial. Diabetes Metab Res Rev 2015;31:61-8.	**Lack of interest data(TIR, data expressed in AUC)**
El-Laboudi AH, Godsland IF, Johnston DG,et al. Measures of Glycemic Variability in Type 1 Diabetes and the Effect of Real-Time Continuous Glucose Monitoring. Diabetes Technol Ther 2016;18:806-812.	**Lack of interest data (TIR, TAR, TBR)**
Ish-Shalom M, Wainstein J, Raz I, et al. Improvement in Glucose Control in Difficult-to-Control Patients With Diabetes Using a Novel Flash Glucose Monitoring Device. J Diabetes Sci Technol 2016;10:1412-1413.	**Lack of interest data (TIR, TAR, TBR)**

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Dover AR, Stimson RH, Zammitt NN et al. Flash Glucose Monitoring Improves Outcomes in a Type 1 Diabetes Clinic. J Diabetes Sci Technol 2017;11:442-443.	**Lack of interest data (TIR, TAR, TBR)**
Gu W, Liu Y, Chen Y,et al. Multicentre randomized controlled trial with sensor-augmented pump vs multiple daily injections in hospitalized patients with type 2 diabetes in China: Time to reach target glucose. Diabetes Metab 2017;43:359-363.	**Lack of interest data (HbA1c)**
Lind M, Polonsky W, Hirsch IB,et al. Continuous Glucose Monitoring vs Conventional Therapy for Glycemic Control in Adults With Type 1 Diabetes Treated With Multiple Daily Insulin Injections: The GOLD Randomized Clinical Trial. JAMA 2017;317:379-387	**Lack of interest data(TIR,TBR, TAR)**
Polonsky WH, Hessler D, Ruedy KJ,et al. The Impact of Continuous Glucose Monitoring on Markers of Quality of Life in Adults With Type 1 Diabetes: Further Findings From the DIAMOND Randomized Clinical Trial. Diabetes Care 2017;40:736-741.	**Lack of interest data (TIR, TAR, TBR)**
Abraham MB, Nicholas JA, Smith GJ et al.Reduction in Hypoglycemia With the Predictive Low-Glucose Management System: A Long-term Randomized Controlled Trial in Adolescents With Type 1 Diabetes. Diabetes Care 2018;41:303-310.	**Lack of interest data (TIR,TAR)**
Ólafsdóttir AF, Polonsky W, Bolinder J et al. A Randomized Clinical Trial of the Effect of Continuous Glucose Monitoring on Nocturnal Hypoglycemia, Daytime Hypoglycemia, Glycemic Variability, and Hypoglycemia Confidence in Persons with Type 1 Diabetes Treated with Multiple Daily Insulin Injections (GOLD-3). Diabetes Technol Ther 2018;20:274-284.	**Lack of interest data (HbA_{1c}, TAR)**
Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group, Bode B, Beck RW et al. Sustained benefit of continuous glucose monitoring on A1C, glucose profiles, and hypoglycemia in adults with type 1 diabetes. Diabetes Care 2009;32:2047-9.	**Extension Study**
Chase HP, Beck RW, Xing D et al. Continuous glucose monitoring in youth with type 1 diabetes: 12-month follow-up of the Juvenile Diabetes Research Foundation continuous glucose monitoring randomized trial. Diabetes Technol Ther 2010;12:507-15.	**Extension Study**
Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group, Weinzimer S, Miller K, et al. Effectiveness of continuous glucose monitoring in a clinical care environment: evidence from the Juvenile Diabetes Research Foundation continuous glucose monitoring (JDRF-CGM) trial. Diabetes Care 2010;33:17-22.	**Extension Study**
Bergenstal RM, Tamborlane WV, Ahmann A, et al. Sensor-augmented pump therapy for A1C reduction (STAR 3) study: results from the 6-month continuation phase. Diabetes Care 2011;34:2403-5.	**Extension Study**
Kordonouri O, Hartmann R, Pankowska E, et al. Sensor augmented pump therapy from onset of type 1 diabetes: late follow-up results of the Pediatric Onset Study. Pediatr Diabetes. 2012;13:515-8	**Extension Study**
Tansey M, Weinzimer S, Beck R, Ruedy K, Diabetes Research in Children Network (DirecNet) Study Group. Extended 6-month follow-up of a randomized clinical trial to assess the efficacy and safety of real-time continuous glucose monitoring in the management of type 1 diabetes in young children aged 4 to <10 years. Diabetes Care 2013;36:e63.	**Extension Study**
Cooke D, Hurel SJ, Casbard A, et al. Randomized controlled trial to assess the impact of continuous glucose monitoring on HbA(1c) in insulin-treated diabetes (MITRE Study). Diabet Med 2009;26:540-7.	**Compares two modalities of CGM**
Moreno-Fernandez J, Gómez FJ, Gálvez Moreno MÁ, et al. Clinical Efficacy of Two Different Methods to Initiate Sensor-Augmented Insulin Pumps: A Randomized Controlled Trial. J Diabetes Res. 2016;2016:4171789.	**Compares two modalities of CGM**
Aleppo G, Ruedy KJ, Riddlesworth TD, et al. REPLACE-BG Study Group. REPLACE-BG: A Randomized Trial Comparing Continuous Glucose Monitoring With and Without Routine Blood Glucose Monitoring in Adults With Well-Controlled Type 1 Diabetes. Diabetes Care 2017;40:538-545.	**Compares two modalities of CGM**
Reddy M, Jugnee N, El Laboudi A, et al. A randomized controlled pilot study of continuous glucose monitoring and flash glucose monitoring in people with Type 1 diabetes and impaired awareness of hypoglycaemia. Diabet Med 2018; 35:483-490.	**Compares two modalities of CGM**
Cosson E, Hamo-Tchatchouang E, Dufaitre-Patouraux L et al. 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 Metab 2009;35:312-8.	**Not real time CGM**

SUPPLEMENTARY DATA

Yoo HJ, An HG, Park SY, et al. Use of a real time continuous glucose monitoring system as a motivational device for poorly controlled type 2 diabetes.Diabetes Res Clin Pract 2008;82:73-9.	**Not real time CGM**
Anderson D, Phelan H, Jones K et al. Evaluation of a novel continuous glucose monitoring guided system for adjustment of insulin dosing - PumpTune: a randomized controlled trial. Pediatr Diabetes 2016;17:478-482.	**Not real time CGM**
Paramasivam SS, Chinna K, Singh AKK et al. Continuous glucose monitoring results in lower HbA1c in Malaysian women with insulin-treated gestational diabetes: a randomized controlled trial. Diabet Med 2018;35:1118-1129.	**Not real time CGM**
Conget I, Battelino T, Giménez M, et al. The SWITCH study (sensing with insulin pump therapy to control HbA(1c): design and methods of a randomized controlled crossover trial on sensor-augmented insulin pump efficacy in type 1 diabetes suboptimally controlled with pump therapy. Diabetes Technol Ther 2011;13:49-54.	**Study protocol**
van Beers CA, Kleijer SJ, Serné EH et al. Design and rationale of the IN CONTROL trial: the effects of real-time continuous glucose monitoring on glycemia and quality of life in patients with type 1 diabetes mellitus and impaired awareness of hypoglycemia. BMC Endocr Disord 2015;15:42.	**Study protocol**
Feig DS, Asztalos E, Corcoy R, et al.CONCEPTT: Continuous Glucose Monitoring in Women with Type 1 Diabetes in Pregnancy Trial: A multi-center, multi-national, randomized controlled trial - Study protocol. BMC Pregnancy Childbirth 2016;16:167.	**Study protocol**
Battelino T, Nimri R, Dovc K, et al. Prevention of Hypoglycemia With Predictive Low Glucose Insulin Suspension in Children With Type 1 Diabetes: A Randomized Controlled Trial. Diabetes Care 2017;40:764-770.	**Short duration of the study**
Forlenza GP, Li Z, Buckingham BA ,et al.Predictive Low-Glucose Suspend Reduces Hypoglycemia in Adults, Adolescents, and Children With Type 1 Diabetes in an At-Home Randomized Crossover Study: Results of the PROLOG Trial. Diabetes Care 2018 ;41:2155-2161.	**Short duration of the study**

SUPPLEMENTARY DATA

Supplementary Table S2. Summary of risk of bias assessment

Study ID	Random sequence generation*	Allocation concealment*	Blinding of participants and personnel°	Blinding of outcome assessment°	Incomplete outcome data°	Selective reporting°
JDRF, 2008	U	U	H	U	L	L
Battelino, 2011	L	L	H	U	L	L
Battelino, 2012	L	L	H	H	L	L
Little, 2014	L	L	H	U	L	L
van Beers, 2016	L	L	H	H	L	L
Beck, 2017	L	L	H	U	L	L
Beck, 2017 bis	L	L	H	U	L	L
Feig, 2017	L	L	H	U	L	L
Ruedy, 2017	L	L	H	U	U	U
Heinemann, 2018	L	L	H	H	L	L
Bolinder, 2016	L	L	H	U	L	L
Haak, 2017	L	L	H	H	L	L
Oskarsson, 2018	L	L	H	U	L	L
O' Connel, 2009	L	L	H	U	L	L
Bosi, 2019	L	L	H	L	L	L

L= low risk of bias; U= unclear risk of bias; H= high risk of bias

*Risk of bias assessment for random sequence generation and allocation concealment is performed at the study level.

°Risk of bias assessment for blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, and selective reporting are for the primary outcome (change in HbA1c and TIR).

SUPPLEMENTARY DATA

Supplementary Table S3. Pre-planned subgroup analysis relative to HbA_{1c} outcome. CGM, continuous glucose monitoring; CSII, continuous subcutaneous insulin infusion; MDI, multiple daily injections of insulin.

	Studies	Intervention	Control	Mean change (95%CI)	P	I^2	Heterogeneity test
	(N)	(n)	(n)				P
Diabetes type							
Type 1	15	1017	946	-0.16 (-0.25;-0.06)	0.001	88.9%	<0.001
Type 2	3	291	207	-0.24 (-0.50;0.03)	0.083	86.0%	0.001
Background therapy							
CSII	3	184	184	-0.26 (-0.60;0.09)	0.146	87.5%	<0.001
MDI	7	672	535	-0.17 (-0.37;0.04)	0.110	98.4%	<0.001
Both	8	452	434	-0.16 (-0.30;-0.01)	0.035	77.8%	<0.001
Reason for using CGM							
Hypoglycemia awareness	4	219	218	0.03 (-0.08;0.13)	0.635	0.0%	0.714
Improvement of glycemic control	2	665	512	-0.31 (-0.43;-0.19)	<0.001	79.9%	<0.001
Pregnancy or planning pregnancy	2	161	164	-0.07 (-0.12;-0.01)	0.019	0.0%	0.325
Reducing hypoglycemia	3	263	259	-0.05 (-0.18 ;0.07)	0.409	72.9%	0.025

SUPPLEMENTARY DATA

Supplementary Table S4. Pre-planned subgroup analysis relative to TIR outcome.CGM, continuous glucose monitoring; CSII, continuous subcutaneous insulin infusion; MDI, multiple daily injections of insulin.

	Studies	Intervention	Control	Mean change (95%CI)	P	I^2	Heterogeneity test
	(N)	(n)	(n)				P
Diabetes type							
Type 1	15	1017	946	69.64 (43.51;95.78)	<0.001	70.1%	<0.001
Type 2	3	291	207	78.11 (7.80;148.42)	0.029	45.5%	0.160
Background therapy							
CSII	3	184	184	58.15 (11.11;105.19)	0.015	0.0%	0.178
MDI	7	672	535	60.85 (40.87;80.83)	<0.001	42.0%	0.499
Both	8	452	434	78.80 (31.85;125.76)	0.001	76.3%	<0.001
Reason for using CGM							
Hypoglycemia awareness	4	219	218	66.67 (1.43;131.91)	0.045	88.8%	<0.001
Improvement of glycemic control	9	665	512	69.18 (34.01;104,36)	<0.001	46.3%	0.061
Pregnancy or planning pregnancy	2	161	164	88.94 (31.52;146.35)	0.002	0.0%	0.509
Reducing hypoglycemia	3	263	259	62.28 (37.5;87.06)	<0.001	0.0%	0.595

SUPPLEMENTARY DATA

Supplementary Table S5. Pre-planned subgroup analysis relative to TBR level 1 hypoglycemia outcome. CGM, continuous glucose monitoring; CSII, continuous subcutaneous insulin infusion; MDI, multiple daily injections of insulin.

	Studies	Intervention	Control	Mean change (95%CI)	P	I^2	Heterogeneity test
	(N)	(n)	(n)				P
Type 1	15	1017	946	-30.58 (-48.60; -12.55)	0.001	99.0%	<0.001
Type 2	3	291	207	-9.35 (-18.96; 0.27)	0.057	83.1%	0.003
Background therapy							
CSII	3	184	184	-31.68 (-87.55; 24.20)	0.266	96.7%	<0.001
MDI	7	672	535	-33.59 (-60.48; -6.70)	0.014	99.2%	<0.001
Both	8	452	434	-17.14 (-33.25; -1.02)	0.037	97.7%	<0.001
Reason for using CGM							
Hypoglycemia awareness	4	219	218	-46.52 (-92.41; -0.63)	0.047	98.1%	<0.001
Improvement of glycemic control	9	665	512	-9.94 (-17.27; -2.61)	0.008	86.5%	<0.001
Pregnancy or planning pregnancy	2	161	164	-8.46 (-63.69; 46.77)	0.764	78.9%	0.029
Reducing hypoglycemia	3	263	259	-60.12 (-87.10; -33.14)	<0.001	98.1%	<0.001

SUPPLEMENTARY DATA

Supplementary Table S6. Pre-planned subgroup analysis relative to TBR level 2 hypoglycemia outcome. CGM, continuous glucose monitoring; CSII, continuous subcutaneous insulin infusion; MDI, multiple daily injections of insulin.

	Studies	Intervention	Control	Mean change (95%CI)	P	I^2	Heterogeneity test
	(N)	(n)	(n)				P
Diabetes type							
Type 1	10	722	649	-16.93 (-26.89; -6.98)	0.001	87.5%	<0.001
Type 2	2	228	154	-3.87 (-12.08; 4.34)	0.355	91.5%	0.001
Background therapy							
CSII	1	76	77	-37.40 (-46.05; -28.75)	< 0.001	-	-
MDI	6	609	482	-12.34 (-20.00; -4.69)	0.002	91.0%	<0.001
Both	5	265	244	-5.73 (-13.84; 2.39)	0.167	37.6%	0.171
Reason for using CGM							
Hypoglycemia awareness	3	193	192	-17.13 (-38.19; 3.94)	0.111	90.1%	<0.001
Improvement of glycemic control	6	494	352	-3.76 (-7.97; 0.45)	0.080	70.0%	0.005
Reducing hypoglycemia	3	263	259	-27.15 (-47.01; -7.29)	0.007	79.4%	0.008

SUPPLEMENTARY DATA

Supplementary Table S7. Pre-planned subgroup analysis relative to TAR level 1 hyperglycemia outcome. CGM, continuous glucose monitoring; CSII, continuous subcutaneous insulin infusion; MDI, multiple daily injections of insulin.

	Studies	Intervention	Control	Mean change (95%CI)	P	I^2	Heterogeneity test
	(N)	(n)	(n)				P
Diabetes type							
Type 1	14	898	826	-34.54 (-64.69; -4.38)	0.025	70.2%	<0.001
Type 2	2	228	154	7.81 (-52.39; 68.01)	0.799	0.0%	0.644
Background therapy							
CSII	3	184	184	-20.94 (-108.34; 66.45)	0.639	80.1%	0.007
MDI	5	490	362	-3.21 (-53.36; 46.94)	0.900	66.8%	0.017
Both	8	452	434	-64.05 (-83.20; -44.90)	<0.001	0.0%	0.937
Reason for using CGM							
Hypoglycemia awareness	4	219	218	-10.65 (-78.53; 57.22)	0.758	86.8%	<0.001
Improvement of glycemic control	8	602	459	-52.55 (-83.20; -21.90)	0.001	17.5%	0.291
Pregnancy or planning pregnancy	2	161	164	-54.20 (-99.07; -9.32)	0.018	0.0%	0.789
Reducing hypoglycemia	2	144	139	-1.95 (-95.69; 91.79)	0.967	80.1%	0.025

SUPPLEMENTARY DATA

Supplementary Table S8. Pre-planned subgroup analysis relative to TAR level 2 hyperglycemia outcome. CGM, continuous glucose monitoring; CSII, continuous subcutaneous insulin infusion; MDI, multiple daily injections of insulin.

	Studies	Intervention	Control	Mean change (95%CI)	P	I^2	Heterogeneity test
	(N)	(n)	(n)				P
Diabetes type							
Type 1	9	680	608	-26.48 (-45.57; -7.40)	0.007	66.3%	0.003
Type 2	3	291	207	-31.83 (-88.39; 24.74)	0.270	69.2%	0.039
Background therapy							
CSII	1	76	77	-1.4 (-28.09; 25.210)	0.916	-	-
MDI	7	672	535	-32.751 (-63.71; -1.79)	0.038	77.2%	<0.001
Both	4	223	203	-29.56 (-44.03; -15.09)	<0.001	0.0%	0.841
Reason for using CGM							
Hypoglycemia awareness	2	151	151	2.80 (-20.87; 26.48)	0.816	0.0%	0.496
Improvement of glycemic control	7	557	405	-50.95 (-88.24; -13.65)	0.007	71.4%	0.002
Reducing hypoglycemia	3	263	259	-20.23 (-33.79; -6.67)	0.003	0.0%	0.605

SUPPLEMENTARY DATA

Supplementary Table S9. Study characteristics and significant results of excluded RCTs using SAP with PLGS

First author, year	Number of intervention/ control	Study design		Follow-up (weeks)	HbA1c	Time in range	Time in hypoglycemia
		Intervention	Control				
Abraham, 2018	80/74	PLGM MiniMed 640G pump with Suspend before low, Medtronic	SAP (same devices but without suspend on low and suspend before low)	24	No difference at the end of the study [mean difference, (95% CI), 0.09%, (-0.10 to 0.27%), P= 0.35]	Not investigated	**< 54 mg/dl (3.0 mmol/L)**Significant difference favoring PLGM [mean difference, (95% CI) -0.44%, (-0.64 to -0.24%), P <0.0001)[1]
Battelino, 2017	47/49	PLGM ON MiniMed 640G pump with Suspend before low, Medtronic	PLGM OFF MiniMed 640G pump with Suspend before low, Medtronic	2	No difference at the end of the study (data not reported)	No difference at the end of the study (data not reported)	**< 65 mg/dL (3.6 mmol/L)** Significant difference favoring PLGM ON (Mean ± SD PLGM ON vs PLGM OFF) 26.7 ± 28.6 min/day vs 44.7 ± 46.0 min/day, P =0.010 **50 mg/dL (3.6 mmol/L)** Significant difference favoring PLGM ON, 6.2 ± 10.0 min/day vs 9.5 ± 13.3 min/day, P = 0.008

Forlenza, 2018	102/102	PLGS (the Tandem Diabetes Care t:slim X2 with Basal-IQ Technology, an insulin pump with an embedded PLGS algorithm integrated with a Dexcom G5 sensor)	SAP	6	Not investigated	Not investigated	<**70 mg/dL (3.9 mmol/L)** Significant difference favoring PLGS [Median group difference (95% CI)] -0.8 (-1.1, -0.5)%, P < 0.001[1] **< 50 mg/dL (2.8 mmol/L)** Significant difference favoring PLGS [Median group difference (95% CI)] 0.0 (-0.1, 0.0)%, P= 0.002[1]

[1] Data are expressed as percentage of time in 24 hours. PLGM, predicitive low glucose management; PLGS, predicitive low glucose suspend; RCTs, randomized controlled trials; SAP, sensor augmented pump.

SUPPLEMENTARY DATA

PRISMA checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2-3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4-5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5(File S1)
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5-6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6-7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	6
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6-7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7-8
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7-8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8-9
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	8-9
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	8-9

Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	8-9
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9-10; Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	10-11, Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	11, Figure S1, Table S2
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	11-15, Figure 2
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	11-15, Table 2, Tables S3-S8
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	11
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	11-15,Figures S2-S8
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	15
Limitations	25	Discuss limitations at study and outcomelevel (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	18-19
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	15-19
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	20

SUPPLEMENTARY DATA

Protocol for the systematic literature search about the effect of continuous glucose monitoring (CGM) on glycemic control in diabetic patients

- Broad question 1: what is the effect of CGM, as compared with usual care, on both HbA1c and time in the target range (≥ 70-180 mg/dL)?
- Broad question 2:what is the effect of CGM, as compared with usual care, on:
  1) time spent in level 1 hypoglycemia (<70 mg/dL)
  2) time spent in level 2 hypoglycemia (<54 mg/dL)
  3) time spent in level 1 hyperglycemia (>180 mg/dL)
  4) time spent in level 2 hyperglycemia (>250 mg/dL)
  5) glucose variability measured as coefficient of variation (CV)
- Specific question 1: what is the effect of real time CGM, intermittently scanned glucose monitoring (iCGM), and sensor augmented pump (SAP) on glycemic control, as compared to usual care, in diabetic patients?

  The answer to these points was sought by evaluating randomized controlled trials (RCTs) that compared CGM, eitherrtCGM, iCGM or SAP, free or fixed-ratio, with usual care in both children and adults affected by diabetes. Change from baseline of both HbA1c and time in the target range was the co-primary endpoint of the comparison. Secondary endpoints were the time spent in hypoglycemia, the time spent in hyperglycemia, and the CV.

The review followed the outlines of PICO (study characteristics):

1. Population: the population to be included in the review consisted of children or adults withboth type 1 type 2 diabetes at baseline.
2. Exposure: CGM as either rtCGM, iCGM or SAP,compared with usual care (mainly self blood glucose monitoring).
3. Comparisons: age-matched subjects with type 1 or type 2 diabetes.
4. Outcomes: Change in HbA1c and time in the target range from baseline, time spent in hypoglycemia, the time spent in hyperglycemia, and the CV.

Published articles were considered eligible for this review if they were: RCTs with a comparator group, evaluated children or adults with type 1 or type 2 diabetes, compared the CGM with usual care, reported HbA1c change and time in the targetrange at the end of treatment (primary outcome of this meta-analysis) together with time spent in hypoglycemia, or time spent in hyperglycemia, or CV, were published up to June 2019, and without language restriction.