Appendices

Appendix 1

Protocol

The effectiveness and safety of long-term use of closed-loop insulin system in patients with type 1 diabetes: a systematic review and meta-analysis

Population

Patients with type 1 diabetes mellitus (T1DM) under free living conditions, excluded who were pregnant women or had sever diseases or were prescribed additional medications were excluded.

Intervention

Any closed-loop delivery system, which is a smart device that automatically delivers insulin based on glucose readings

Comparators

Any type of conventional insulin pump, including multiple daily injections (MDI), insulin pump therapy, sensor-augmented insulin pump therapy.

Outcomes

Primary outcome:

The proportion (%) of time in target range (TIR) (3.9-10.0mmol/L)

Secondary outcomes:

The proportion (%) of time above target range (TAR) (>10 mmol/L)

The proportion (%) of time below target range (TBR) (<3.9 mmol/L)

Glycated hemoglobin changes (HbA1c %)

Low blood glucose index (LBGI)

High blood glucose index (HBGI)

Coefficient of variation of glucose (CV)

Mean glucose (MG)

Total daily insulin dose

Study design

All randomized clinical trials (RCTs), with parallel group or cross-over design, with a minimum follow-up cycle of at least 2 months after initial treatment.

Information sources

Search strategy

Determine keywords through the PICOS principle, search for a single keyword separately, check whether there are words with the same meaning but different expressions from the summary or other meta-analysis containing the keyword, and add these words to the search query to expand Search scope, and finally, combine the keyword search formulas to limit the research type. We will search the following databases and resources (via relevant interfaces):

- MEDLINE (PubMed)
- EMBASE (OvidSP)

Jiao X, *et al. BMJ Open Diab Res Care* 2022; 10:e002633. doi: 10.1136/bmjdrc-2021-002633

- Cochrane Database of Systematic Reviews (CDSR) (Wiley Online Library)
- Cochrane Central Register of Controlled Trials (CENTRAL) (Wiley Online Library)

Study selection & data collection

Two independent reviewers screened the titles and abstracts of the obtained articles, and reviewed the full text. In addition, two independent reviewers extracted the following data in a standardized form: demographic parameters, methodological characteristics, primary and secondary outcome indicators, and serious adverse events. Any discrepancies can be resolved through discussion or negotiation with senior examiners.

Study quality assessment

The methodological quality of each clinical trial was evaluated by the Cochrane risk of bias tool[9]. Two researchers (J, C) have independently evaluated the studies based on selection bias (random sequence generation), detection bias (blinding of outcome assessment), performance bias (blinding of participants and personnel), attrition bias (incomplete outcome data) and reporting bias (selective reporting), as well as overall assessment of the risk of bias (other bias). Any disagreements were resolved by consensus or following discussion with another senior reviewer.

Data synthesis

Methods of analysis

Meta-analysis was conducted only if the data of at least two studies were available. We will calculate mean differences with 95% confidence intervals and and p value for the overall effect, using an inverse-variance weighted random effects model, performed with RevMan 5.3.5 software.

Subgroup analyses

Depending on accrued evidence, for the primary outcome we plan to conduct subgroup analyses based on mode of intervention (overnight or 24h use of closed-loop delivery system), mobile or embedded setting, with or without remote monitoring.

Sensitivity analyses

We will do sensitivity analysis for the primary outcome excluding trials at unclear or high risk of bias.

Investigation of heterogeneity

We will assess presence of statistical heterogeneity by the magnitude of heterogeneity by means of the I2 statistic, with P values < 0.10 and I2 > 50% respectively representing high heterogeneity. All analyses will be undertaken in Revman.

Appendix 2: PRISMA statement

	#	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
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3,4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
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.	no

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
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.	4,5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	4, appendix 3
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).	5
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.	5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
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.	6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6

Section/topic	#	Checklist item	Reported on page #
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I2) for each meta-analysis.	6
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).	6
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	6-7
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.	7, 9 (Fig. 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.	7, 8 (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).	9
Results of individual	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.	9-11

studies			
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	9-11
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	12
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	12
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).	13-16
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	16
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	16
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role	17

		of funders for the systematic review.	

Appendix 3

Search strategy

Pubmed (407)

#1.	Diabetes Mellitus, Type 1[Mesh]
#2.	Type 1 Diabetes Mellitus[Title/Abstract]
#3.	T1DM[Title/Abstract]
#4.	Type 1 Diabetes[Title/Abstract]
#5.	OR/#1-4
#6.	closed-loop[Title/Abstract]
#7.	closed loop[Title/Abstract]
#8.	closing loop[Title/Abstract]
#9.	hybrid closed loop[Title/Abstract]
#10.	hybrid closed-loop[Title/Abstract]
#11.	artificial pancreas[Title/Abstract]
#12.	OR/#6-11
#13.	randomized controlled trial[Publication Type]
#14.	controlled clinical trial[Publication Type]
#15.	randomized[Title/Abstract]
#16.	randomly[Title/Abstract]
#17.	controlled[Title/Abstract]
#18.	trial[Title/Abstract]
#19.	random[Title/Abstract]
#20.	placebo[Title/Abstract]
#21.	OR/#13-20
#22.	#5 and #12 and #21

Cochrane Library（633）

#1 MeSH descriptor: [Diabetes Mellitus, Type 1] explode all trees

#2 MeSH descriptor: [Pancreas, Artificial] explode all trees

#3 ("Diabetes Mellitus, Type 1"):ti,ab,kw OR ("Type 1 Diabetes Mellitus"):ti,ab,kw OR ("T1DM"):ti,ab,kw OR ("Type 1 Diabetes"):ti,ab,kw OR ("diabetes mellitus type-I"):ti,ab,kw (Word variations have been searched)

#4 ("artificial pancreas"):ti,ab,kw OR ("closed-loop"):ti,ab,kw OR ("closed loop control system"):ti,ab,kw OR ("closed-loop control system"):ti,ab,kw OR ("hybrid closed loop"):ti,ab,kw (Word variations have been searched)

#5 #1 or #3

#6 #2 or #4

#7 #5 and #6

Embase （641）

#1 'insulin dependent diabetes mellitus'/exp

#2 't1dm' OR 'brittle diabetes' OR 'brittle diabetes mellitus' OR 'diabetes mellitus type OR 'diabetes mellitus type i' OR 'diabetes mellitus, brittle' OR 'diabetes mellitus, insulin dependent' OR 'diabetes mellitus, insulin-dependent' OR 'diabetes mellitus, juvenile onset' OR 'diabetes mellitus, type 1' OR 'diabetes mellitus, type i' OR 'diabetes type 1' OR 'diabetes type i' OR 'diabetes, juvenile' OR 'dm 1' OR 'early onset diabetes mellitus' OR 'iddm' OR 'insulin dependent diabetes' OR 'insulin dependent diabetes mellitus' OR 'juvenile diabetes' OR 'juvenile diabetes mellitus' OR 'juvenile onset diabetes' OR 'juvenile onset diabetes mellitus' OR 'ketoacidotic diabetes' OR 'labile diabetes mellitus' OR 'mckusick 22210' OR 'type 1 diabetes' OR 'type 1 diabetes mellitus' OR 'type i diabetes'i OR 'type i diabetes mellitus'

#3 #1 or #2

#4 'artificial pancreas'/exp

#5 'artificial endocrine pancreas' OR 'artificial pancreas' OR 'artificial pancreas islet' OR 'endocrine pancreas, artificial' OR 'pancreas, artificial' OR 'pancreas, artificial endocrine' (3134)

#6 ‘closed loop’ or ‘closed-loop’

#7 #4 or #5 or #6

#8 #3 and #7

#9 'clinical trial' or 'randomized controlled trial' or 'controlled clinical trial' or 'multicenter study' or 'phase 3 clinical trial' or 'phase 4 clinical trial'

#10 #8 and #9

Appendix 4 PMID or DOIs of studies that have been excluded at full-text review stage

Follow-up less than 8 weeks（n=55）

	Year	DOI
1	2021	10.1089/dia.2020.0589
2	2021	10.2337/dc20-2250
3	2021	10.2337/dc20-2106
4	2021	10.1177/1932296820986879
5	2021	10.1089/dia.2021.0037
6	2020	10.1111/dom.13898
7	2020	10.1089/dia.2020.0365
8	2020	10.1089/dia.2020.0546
9	2020	10.1089/dia.2020.0022
10	2019	10.2337/dc18-1881
11	2019	10.1371/journal.pone.0212013
12	2019	10.1111/dom.13898
13	2019	10.1089/dia.2019.0011
14	2019	10.1111/pedi.12867
15	2019	10.1111/dom.13585
16	2018	10.2337/dc18-0228
17	2018	10.1089/dia.2017.0346

18	2017	10.1111/dom.12852
19	2017	10.1111/dom.12880
20	2017	10.1016/S0140-6736(16)32567-3
21	2017	10.1007/s00125-017-4395-z
22	2017	10.1089/dia.2016.0424
23	2017	10.1210/jc.2017-00556
24	2017	10.2337/dc17-0883
25	2017	10.1016/S2213-8587(17)30001-3
26	2016	10.2337/dc15-2078
27	2016	10.1089/dia.2016.0288
28	2016	10.1016/S2213-8587(15)00489-1
29	2016	10.1111/dom.12707
30	2016	10.1016/j.diabet.2015.05.001
31	2016	10.1111/dom.12663
3	2016	10.2337/dc15-2815

2		
33	2016	10.2337/dc15-2468
34	2015	10.2337/dc13-0010
35	2015	10.1056/NEJMoa1314474
36	2015	10.1177/1932296815616134
37	2015	10.2337/dc14-3073
38	2015	10.1016/S2213-8587(14)70226-8
39	2015	10.1016/S2213-8587(15)00141-2
40	2015	10.1089/dia.2014.0259
41	2014	10.1111/pedi.12071
42	2014	10.2337/dc14-0835
43	2014	10.2337/dc14-0147
44	2014	10.2337/dc13-2911
45	2014	10.2337/dc13-2076
46	2014	10.2337/dc13-2644

47	2014	10.1111/dom.12324
48	2014	10.2337/dc13-1631
49	2014	10.2337/dc12-1079
50	2013	10.2337/dc12-1965
51	2013	10.1503/cmaj.121265
52	2013	10.2337/dc12-1079
53	2013	10.1089/dia.2013.0002
54	2012	10.1089/dia.2012.0004
55	2010	10.1016/S0140-6736(09)61998-X

Specific disease states(n=4)

	Year	DOI
1	2021	10.1111/dom.14214
2	2020	10.2337/dc19-1433
3	2017	10.1111/pedi.12410
4	1979	PMID: 220725

No control group or control group did not meet the inclusion criteria(n=15)

	Year	DOI
1	2021	10.1089/dia.2021.0097

2	2021	10.1111/dom.14355
3	2021	10.1016/S0140-6736(20)32514-9
4	2021	10.1089/dia.2020.0500
5	2020	10.1049/iet-syb.2020.0053
6	2020	10.1111/pedi.12962
7	2018	10.1089/dia.2018.0202
8	2017	10.1089/dia.2016.0461
9	2017	10.1089/dia.2016.0421
10	2016	10.1007/s00125-016-4107-0
11	2016	10.2337/dc15-2344
12	2016	10.1210/jc.2015-3003
13	2013	10.1089/dia.2013.0036
14	2013	10.2337/dc12-1956
15	1986	10.2337/diacare.9.2.124

The aim of the study was not to assess the effectiveness and safety of closed-loop insulin pumps(n=33)

	Year	DOI
1	2021	10.1089/dia.2020.0472
2	2021	10.2337/dc20-1729
3	2021	10.1089/dia.2020.0593
4	2020	10.1007/s00125-020-05244-y

5	2020	10.1016/j.jcjd.2019.08.003
6	2020	10.2337/dc19-2041
7	2020	10.1007/s11428-020-00614-x
8	2020	10.2337/dc19-0895
9	2019	10.1111/dme.13887
10	2019	10.1089/dia.2018.0328
11	2019	10.2196/14087
12	2018	10.1111/dom.13304
13	2018	10.1038/s41598-018-20785-4
14	2017	10.1109/TBME.2016.2590498
15	2017	10.1177/1932296816678631
16	2017	10.1089/dia.2016.0443
17	2017	10.1111/dme.13268
18	2017	10.2337/dc17-0500
19	2017	10.1089/dia.2016.0307
20	2017	10.1177/1932296817702656
21	2016	10.1111/dme.12823

22	2016	10.2337/dc16-1073
23	2016	10.1089/dia.2016.0311
24	2016	10.1089/dia.2016.0043
25	2016	10.1111/pedi.12230
26	2015	10.1111/dom.12549
27	2015	10.1210/jc.2015-2081
28	2015	10.1111/dme.12706
29	2014	10.1177/1932296814532238
30	2014	10.1089/dia.2014.0050
31	2014	10.1136/bmjdrc-2014-000025
32	2010	10.1177/193229681000400602
33	2010	10.1089/dia.2009.0084

Appendix 5

Data extraction form

Data extraction form			
Article title			
First author		Year of publication	
NCT		Document type	
Date of information extraction		Extractor	
Methodological characteristics			

Randomized sequence generation and allocation hiding	Randomized controlled trial：yes or no Crossover test：yes or no	Random allocation sequence generation method： Whether to hide the random sequence and its method：
Who is subject to blindness laws	Patients/intervener/evaluators of the outcome/ Analysts of statistics：	Basis for judgment：
Loss/dropout/withdrawal (n: number of lost visits; N: number of cases)		
Selective reporting outcomes	Yes or no basis for judgment：	
analysis of intentionality	Yes or no basis for judgment：	
Baseline information	Comparability： basis for judgment：	
Other bias		
Participant characteristics		
Source of Subjects		
Number of patients		
Sex (men/women)		
age		
Age category		
BMI(kg/m2）		
Duration of diabetes		
Duration of insulin treatment		
HbA1c %		

Interventions		
	experimental group	control group
location		
Follow-up time		
Research Methods		
specific measure	the name of the insulin pump algorithm： Single hormone/dual hormone： overnight/24h:	
Outcome indicators		
Main outcome indicators：		
Secondary outcome indicators：		
Result data table		
Indicator name	experimental group	control group
during 24-hour period		
the proportion (%) of time in		
In target range (TIR) (3.9-10.0mmol/L)		
above target range (TAR) (>10 mmol/L)		
below target range (TBR) (<3.9 mmol/L)		
glycated hemoglobin(HbA1c %)		
＞13.3 mmol/l		
low blood glucose index (LBGI)		

high blood glucose index (HBGI)		
coefficient of variation of glucose (CV)		
mean glucose (MG)		
total daily insulin dose		
During the day		
the proportion (%) of time in		
In target range (TIR) (3.9-10.0mmol/L)		
above target range (TAR) (>10 mmol/L)		
below target range (TBR) (<3.9 mmol/L)		
glycated hemoglobin(HbA1c %)		
＞13.3 mmol/l		
low blood glucose index (LBGI)		
high blood glucose index (HBGI)		
coefficient of variation of glucose (CV)		
mean glucose (MG)		
total daily insulin dose		
During the nighttime		
the proportion (%) of time in		
In target range (TIR)		

(3.9-10.0mmol/L)		
above target range (TAR) (>10 mmol/L)		
below target range (TBR) (<3.9 mmol/L)		
glycated hemoglobin(HbA1c %)		
＞13.3 mmol/l		
low blood glucose index (LBGI)		
high blood glucose index (HBGI)		
coefficient of variation of glucose (CV)		
mean glucose (MG)		
total daily insulin dose		
Adverse events		
Hypoglycemic event		
Hyperglycemia event		
Other adverse events		

Appendix 6

Overall risk of bias assessment

Key domains for assessment of risk of bias for the primary outcome:

Sequence generation (or randomised treatment order for cross-over studies)

Allocation concealment

Blinding

Selective reporting

Incomplete outcome data

Other bias

The overall risk of bias was assessed in compliance with the following rules:

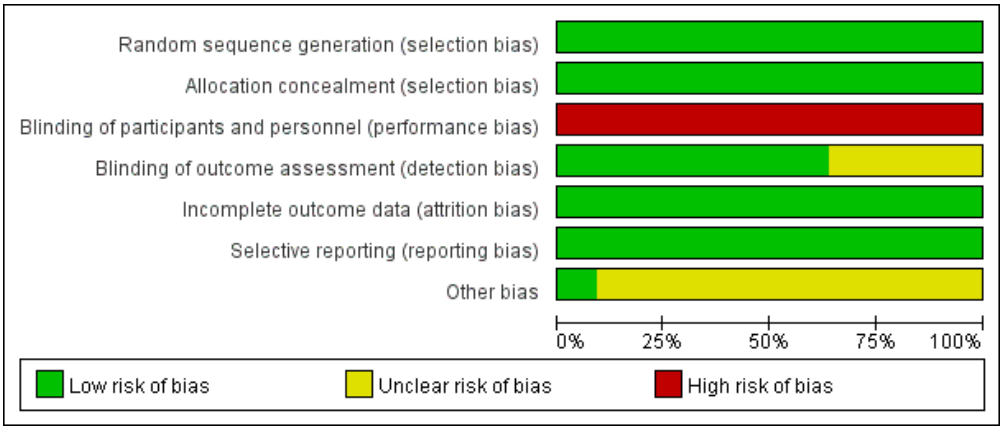
If a study was considered at high risk of bias for any of the aforementioned domains, the study was

characterised as “high risk study”

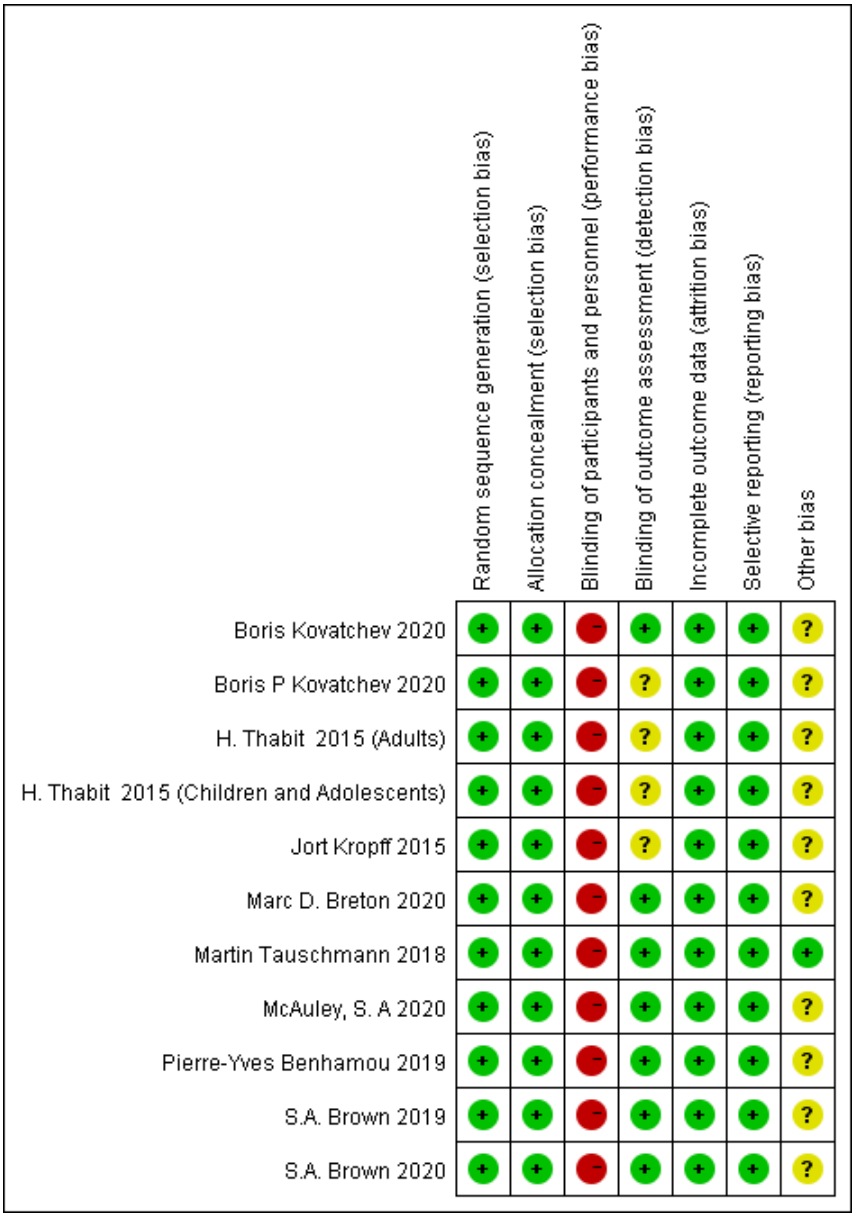
If a study was considered at low risk of bias for all aforementioned domains, the study was characterised as “low risk study”

In any other case the study was considered as “unclear risk study”

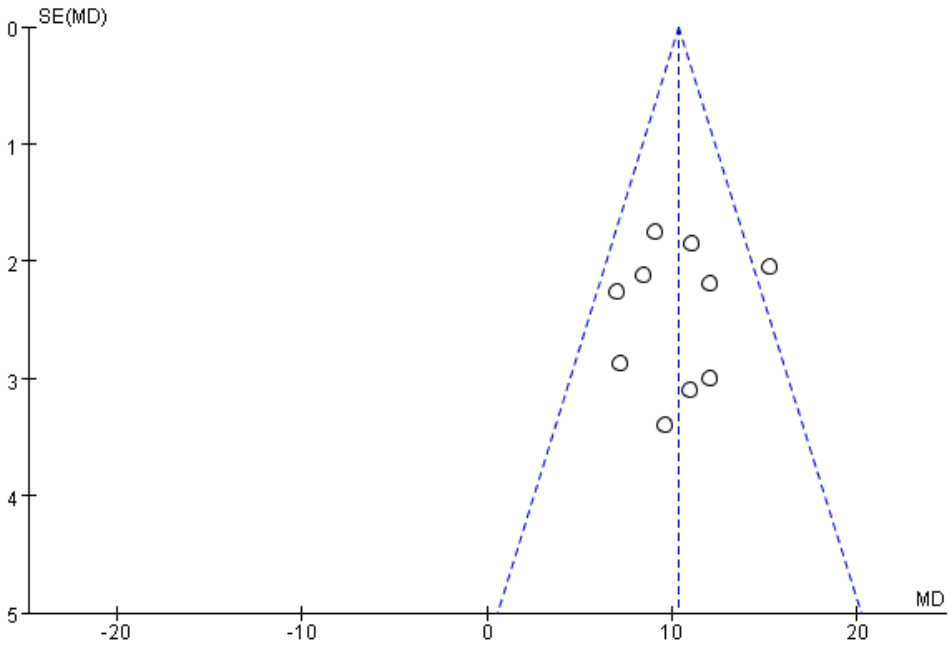
Appendix 7. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies



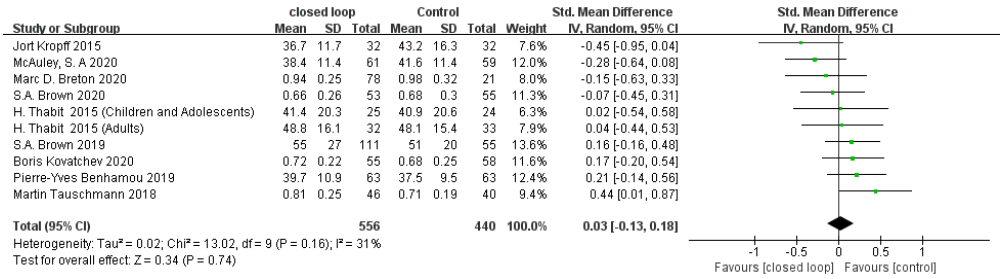
Appendix 8. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Appendix 9. Contour-enhanced funnel plot for studies assessing time spent in near normoglycaemia

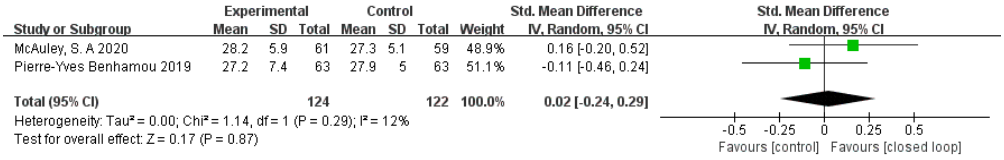


Appendix 10. Forest plot of Daily insulin dose

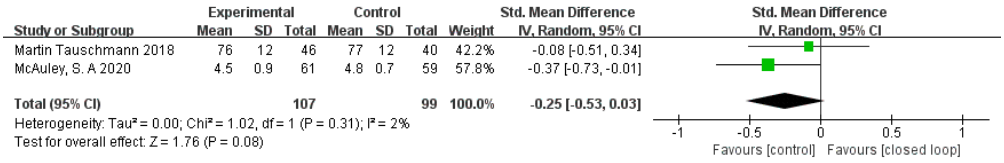


Appendix 11. Forest plot of satisfaction and Quality of Life.

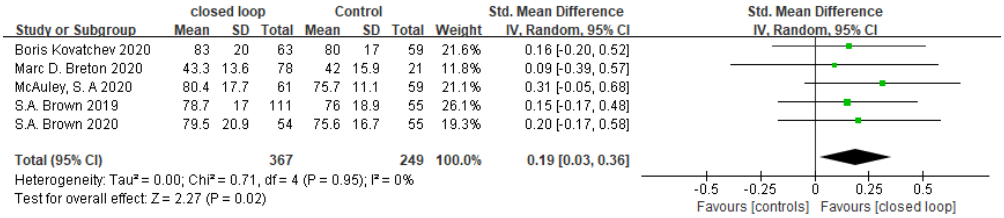
satisfaction with diabetes treatment



quality of life with diabetes



Appendix 12. Forest plot of Body weight

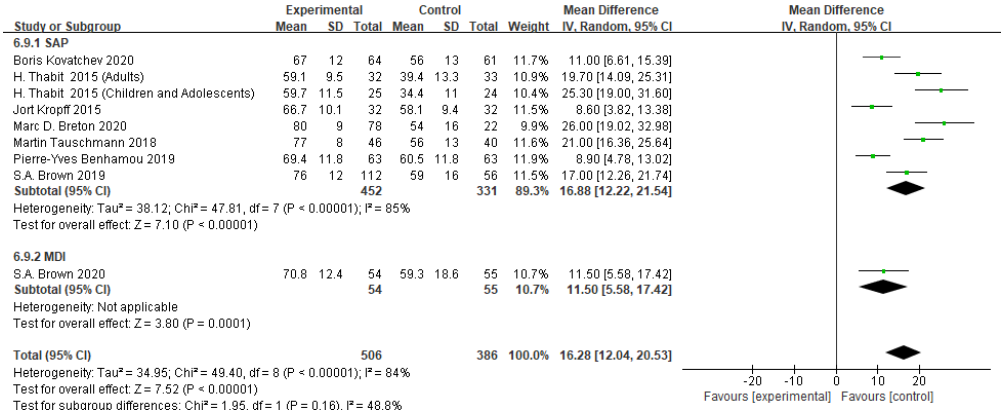


Appendix 13. The meta-regression by designed subgroups for time in target range (TIR) (70-180 mg/dl) at night

_meta_es	Coef.	Std. Err.	z	P>|z|	[95% Conf.	Interval]
agecategory	.8437925	.532501	1.58	0.113	-.1998902	1.887475
periodofuse	-.8946046	1.105487	-0.81	0.418	-3.06132	1.272111
studyduration	-.0897639	.0833949	-1.08	0.282	-.2532148	.0736871
algorithmtype	-.5916082	.5189248	-1.14	0.254	-1.608682	.4254658
studytype	1.281638	1.333926	0.96	0.337	-1.332809	3.896084
differentcontrolgroups	-1.998541	1.0922	-1.83	0.067	-4.139213	.1421311
_cons	3.558332	2.447912	1.45	0.146	-1.239488	8.356152

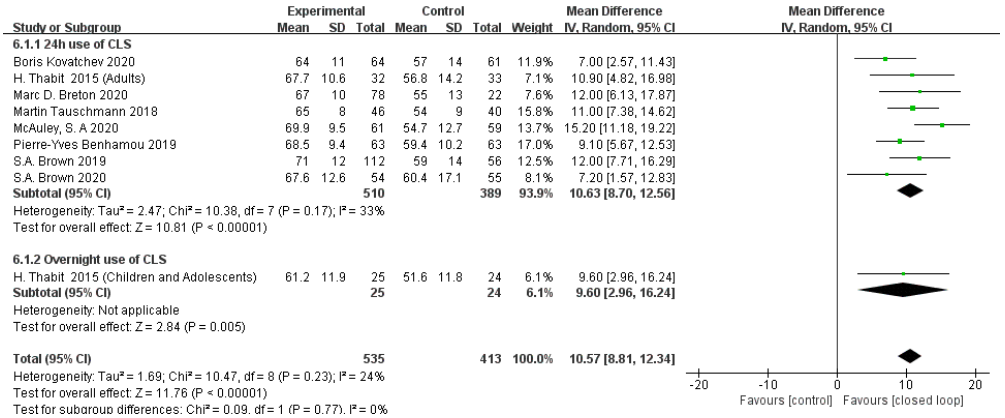
Test of residual homogeneity: Q_res = chi2(2) = **14.38** Prob > Q_res = **0.0008**

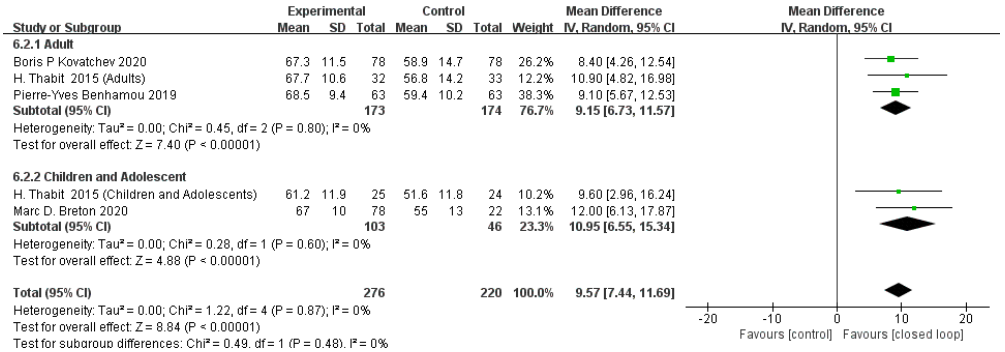
Appendix 14. Forest plots for subgroup analysis of nighttime TIR (70-180 mg/dl) indicators according to different control groups

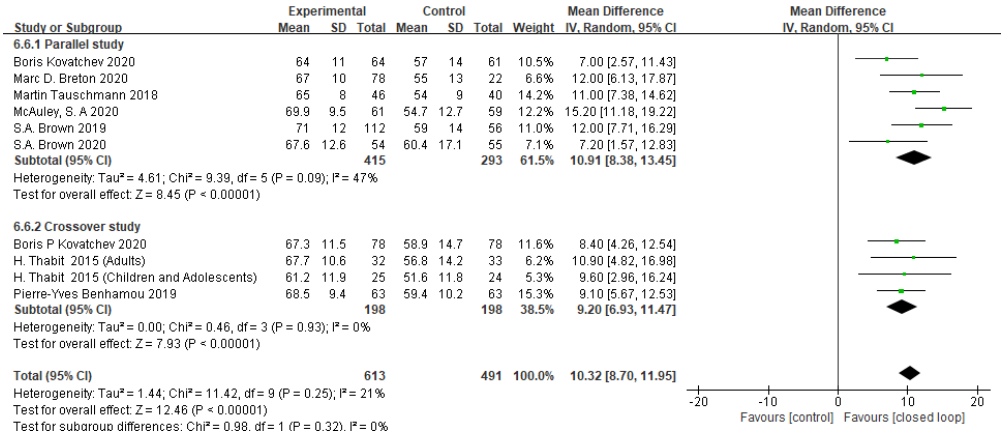


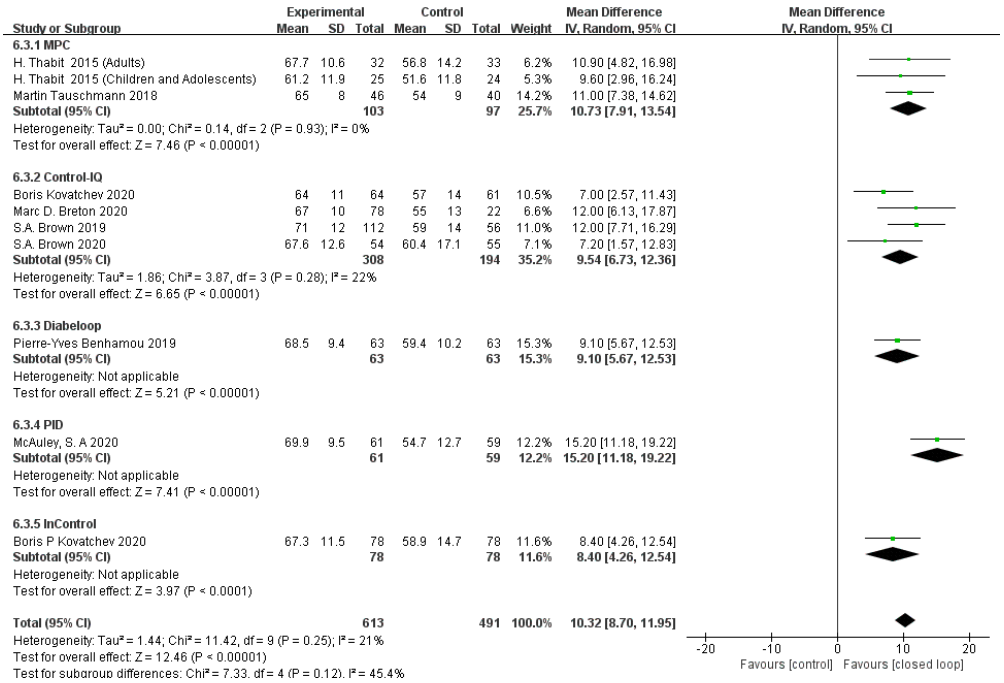
Appendix 15 Forest plot for the subgroup analyzed by designed subgroups for time in target

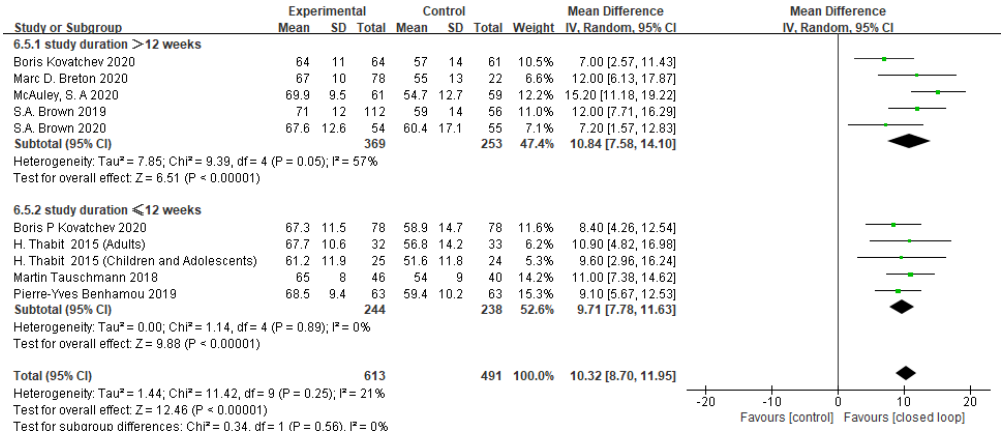
range (TIR) (70-180 mg/dl)

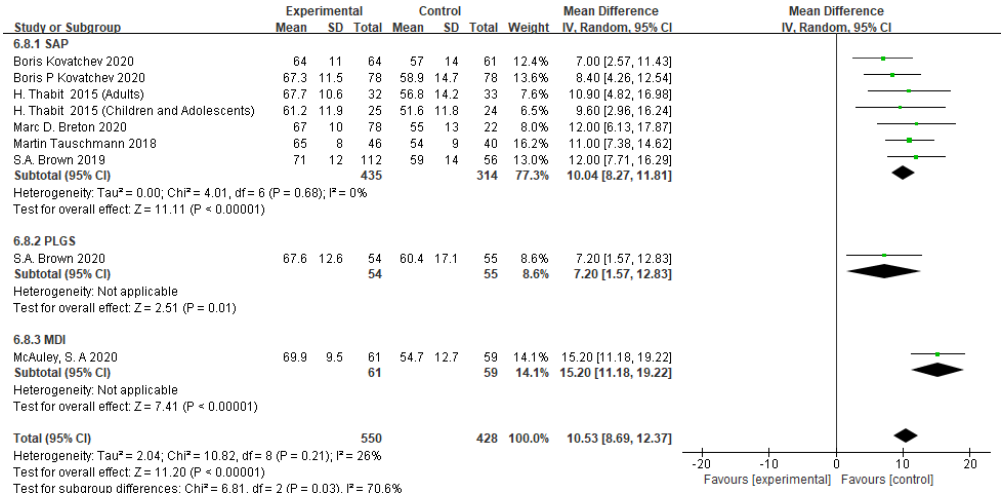






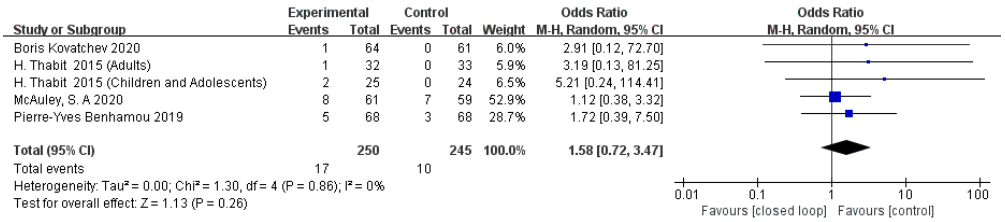

Experimental
Control
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
6.3.1 MPC
H. Thabit 2015 (Adults) 67.7 10.6 32 56.8 14.2 33 6.2% 10.90 [4.82, 16.98]
H. Thabit 2015 (Children and Adolescents) 61.2 11.9 25 51.6 11.8 24 5.3% 9.60 [2.96, 16.24]
Martin Tauschmann 2018 65 8 46 54 9 40 14.2% 11.00 [7.38, 14.62]
Subtotal (95% CI) 103 97 25.7% 10.73 [7.91, 13.54]
Heterogeneity: Tau² = 0.00; Chi² = 0.14, df = 2 (P = 0.93); I² = 0%
Test for overall effect: Z = 7.46 (P < 0.00001)
6.3.2 Control-IQ
Boris Kovatchev 2020 64 11 64 57 14 61 10.5% 7.00 [2.57, 11.43]
Marc D. Breton 2020 67 10 78 55 13 22 6.6% 12.00 [6.13, 17.87]
S.A. Brown 2019 71 12 112 59 14 56 11.0% 12.00 [7.71, 16.29]
S.A. Brown 2020 67.6 12.6 54 60.4 17.1 55 7.1% 7.20 [1.57, 12.83]
Subtotal (95% CI) 308 194 35.2% 9.54 [6.73, 12.36]
Heterogeneity: Tau² = 1.86; Chi² = 3.87, df = 3 (P = 0.28); I² = 22%
Test for overall effect: Z = 6.65 (P < 0.00001)
6.3.3 Diabeloop
Pierre-Yves Benhamou 2019 68.5 9.4 63 59.4 10.2 63 15.3% 9.10 [5.67, 12.53]
Subtotal (95% CI) 63 63 15.3% 9.10 [5.67, 12.53]
Heterogeneity: Not applicable
Test for overall effect: Z = 5.21 (P < 0.00001)
6.3.4 PID
McAuley, S. A 2020 69.9 9.5 61 54.7 12.7 59 12.2% 15.20 [11.18, 19.22]
Subtotal (95% CI) 61 59 12.2% 15.20 [11.18, 19.22]
Heterogeneity: Not applicable
Test for overall effect: Z = 7.41 (P < 0.00001)
6.3.5 InControl
Boris P Kovatchev 2020 67.3 11.5 78 58.9 14.7 78 11.6% 8.40 [4.26, 12.54]
Subtotal (95% CI) 78 78 11.6% 8.40 [4.26, 12.54]
Heterogeneity: Not applicable
Test for overall effect: Z = 3.97 (P < 0.0001)
Total (95% CI) 613 491 100.0% 10.32 [8.70, 11.95]
Heterogeneity: Tau² = 1.44; Chi² = 11.42, df = 9 (P = 0.25); I² = 21%
Test for overall effect: Z = 12.46 (P < 0.00001)
Test for subgroup differences: Chi² = 7.33, df = 4 (P = 0.12), I² = 45.4%
-20 -10 0 10 20
Favours [control] Favours [closed loop]


Experimental
Control
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
6.5.1 study duration >12 weeks
Boris Kovatchev 2020 64 11 64 57 14 61 10.5% 7.00 [2.57, 11.43]
Marc D. Breton 2020 67 10 78 55 13 22 6.6% 12.00 [6.13, 17.87]
McAuley, S. A 2020 69.9 9.5 61 54.7 12.7 59 12.2% 15.20 [11.18, 19.22]
S.A. Brown 2019 71 12 112 59 14 56 11.0% 12.00 [7.71, 16.29]
S.A. Brown 2020 67.6 12.6 54 60.4 17.1 55 7.1% 7.20 [1.57, 12.83]
Subtotal (95% CI) 369 253 47.4% 10.84 [7.58, 14.10]
Heterogeneity: Tau² = 7.85; Chi² = 9.39, df = 4 (P = 0.05); I² = 57%
Test for overall effect: Z = 6.51 (P < 0.00001)
6.5.2 study duration ⩽12 weeks
Boris P Kovatchev 2020 67.3 11.5 78 58.9 14.7 78 11.6% 8.40 [4.26, 12.54]
H. Thabit 2015 (Adults) 67.7 10.6 32 56.8 14.2 33 6.2% 10.90 [4.82, 16.98]
H. Thabit 2015 (Children and Adolescents) 61.2 11.9 25 51.6 11.8 24 5.3% 9.60 [2.96, 16.24]
Martin Tauschmann 2018 65 8 46 54 9 40 14.2% 11.00 [7.38, 14.62]
Pierre-Yves Benhamou 2019 68.5 9.4 63 59.4 10.2 63 15.3% 9.10 [5.67, 12.53]
Subtotal (95% CI) 244 238 52.6% 9.71 [7.78, 11.63]
Heterogeneity: Tau² = 0.00; Chi² = 1.14, df = 4 (P = 0.89); I² = 0%
Test for overall effect: Z = 9.88 (P < 0.00001)
Total (95% CI) 613 491 100.0% 10.32 [8.70, 11.95]
Heterogeneity: Tau² = 1.44; Chi² = 11.42, df = 9 (P = 0.25); I² = 21%
Test for overall effect: Z = 12.46 (P < 0.00001)
Test for subgroup differences: Chi² = 0.34, df = 1 (P = 0.56), I² = 0%
-20 -10 0 10 20
Favours [control] Favours [closed loop]

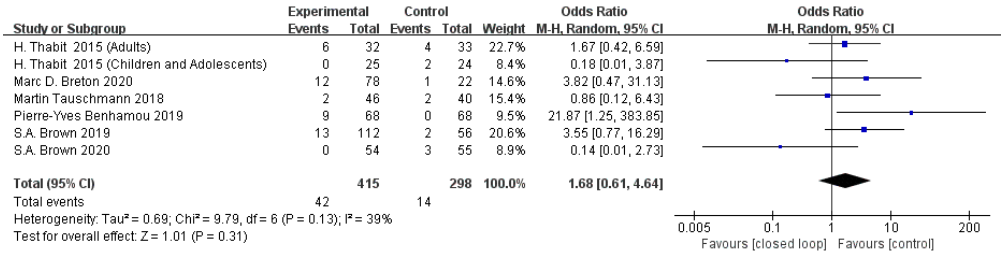

Experimental
Control
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
6.8.1 SAP
Boris Kovatchev 2020 64 11 64 57 14 61 12.4% 7.00 [2.57, 11.43]
Boris P Kovatchev 2020 67.3 11.5 78 58.9 14.7 78 13.6% 8.40 [4.26, 12.54]
H. Thabit 2015 (Adults) 67.7 10.6 32 56.8 14.2 33 7.6% 10.90 [4.82, 16.98]
H. Thabit 2015 (Children and Adolescents) 61.2 11.9 25 51.6 11.8 24 6.5% 9.60 [2.96, 16.24]
Marc D. Breton 2020 67 10 78 55 13 22 8.0% 12.00 [6.13, 17.87]
Martin Tauschmann 2018 65 8 46 54 9 40 16.2% 11.00 [7.38, 14.62]
S.A. Brown 2019 71 12 112 59 14 56 13.0% 12.00 [7.71, 16.29]
Subtotal (95% CI) 435 314 77.3% 10.04 [8.27, 11.81]
Heterogeneity: Tau² = 0.00; Chi² = 4.01, df = 6 (P = 0.68); I² = 0%
Test for overall effect: Z = 11.11 (P < 0.00001)
6.8.2 PLGS
S.A. Brown 2020 67.6 12.6 54 60.4 17.1 55 8.6% 7.20 [1.57, 12.83]
Subtotal (95% CI) 54 55 8.6% 7.20 [1.57, 12.83]
Heterogeneity: Not applicable
Test for overall effect: Z = 2.51 (P = 0.01)
6.8.3 MDI
McAuley, S. A 2020 69.9 9.5 61 54.7 12.7 59 14.1% 15.20 [11.18, 19.22]
Subtotal (95% CI) 61 59 14.1% 15.20 [11.18, 19.22]
Heterogeneity: Not applicable
Test for overall effect: Z = 7.41 (P < 0.00001)
Total (95% CI) 550 428 100.0% 10.53 [8.69, 12.37]
Heterogeneity: Tau² = 2.04; Chi² = 10.82, df = 8 (P = 0.21); I² = 26%
Test for overall effect: Z = 11.20 (P < 0.00001)
Test for subgroup differences: Chi² = 6.81, df = 2 (P = 0.03), I² = 70.6%
-20
-10
0
10
20
Favours [experimental]
Favours [control]

Appendix 16. Forest plot of serious adverse events

Severe hypoglycaemic events



hyperglycaemic events



diabetic ketoacidosis events