ONLINE-ONLY SUPPLEMENTAL MATERIAL

18 **1. Supplemental Table S1. 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.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5,6
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
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.	6
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.	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
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
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
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
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7
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.	7

Section/topic	#	Checklist item	Reported on page #
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).	7
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	NA
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.	8
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.	8
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).	8
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.	8
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	10
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	8
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	NA
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).	10
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).	12
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	13
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.	14

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

Search strategy for PubMed

diabetes AND insulin AND titration AND (investigator OR physician) AND randomized

Supplemental Table S2. Risk of bias summary: review of authors' judgments about each risk of bias item for each randomized controlled trial.

	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data addressed	Selective reporting	Funding
Davies, 2005 (17)	unclear	unclear	low	low	low	low	high
Meneghini, 2007 (18)	unclear	unclear	low	low	low	low	high
Garg, 2015 (19)	unclear	low	low	low	low	low	high
Yale, 2017 (20)	unclear	unclear	low	low	low	low	high
Russell-Jones, 2019 (21)	unclear	low	low	low	low	low	high
Bonadonna, 2020 (22)	unclear	low	low	low	low	low	high

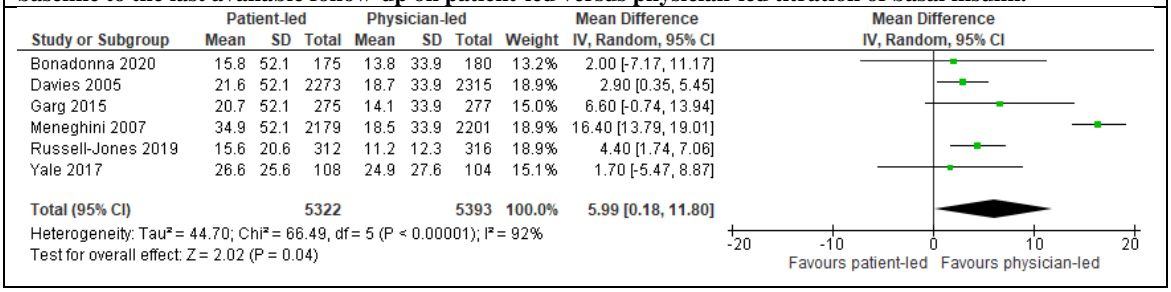
30 **Supplemental Table S3. Algorithms for titration of basal insulin in included studies.**

	Patient-led titration		Physician-led titration	
Davies, 2005 (17)	Target: FPG ≤ 100 mg/dl SMBG: not reported Frequency of titration: every 3 days Algorithm: titration based on mean FPG for the previous 3 consecutive days only in the absence of blood glucose levels <72 mg/dl		Target: FPG ≤ 100 mg/dl SMBG: not reported Frequency of titration: weekly Algorithm: titration based on mean FPG for the previous 3 consecutive days only in the absence of blood glucose levels <72 mg/dl	
	FPG	Titration	FPG	Titration
	100-120 mg/dl	0-2 IU/day (at physician's discretion)	100-120 mg/dl	0-2 IU/day (at physician's discretion)
	120-140 mg/dl	+2 IU/day	120-140 mg/dl	+2 IU/day
	140-180 mg/dl	+2 IU/day	140-180 mg/dl	+4 IU/day
	>180 mg/dl	+2 IU/day	>180 mg/dl	+6-8 IU/day (at physician's discretion)
	Other data: subject dose adjustments were reviewed by the investigator at clinical visits or over the telephone.			
Meneghini, 2007 (18)	Target: FPG 80-110 mg/dl SMBG: daily for dose titration Frequency of titration: every 3 days Algorithm: titration based on the average of 3 FPGs		Target: FPG 80-110 mg/dl SMBG: 6 days before 12 and 26 weeks visits Frequency of titration: at the discretion of the investigator Algorithm: not reported. Titration was performed by the investigator according to the standard-of-care practice.	
	FPG	Titration		
	<80 mg/dl	-3 IU/day		
	80-110 mg/dl	No change		
	>110 mg/dl	+3 IU/day		
Garg, 2015 (19)	Target: FPG of 110 mg/dl SMBG: unclear Frequency of titration: twice per week Algorithm: titration based on median FPG for the previous 3 consecutive days		Target: FPG of 110 mg/dl SMBG: daily fasting SMBG over 3 consecutive days before visits at baseline and weeks 6, 12, 16, and 24 and 7-point BG profile at baseline and every 4 weeks Frequency of titration: at 2, 4, 6, 12, 16, and 24 weeks visits Algorithm: titration based on median FPG for the previous 3 consecutive days	
	FPG	Titration	FPG	Titration
	≤ 56 mg/dl	at physician's discretion	≤ 56 mg/dl	at physician's discretion
	≤ 70 mg/dl or symptomatic hypoglycemia	-2 IU/day	≤ 70 mg/dl or symptomatic hypoglycemia	-2 IU/day
	70-110 mg/dl	No change	70-110 mg/dl	No change
	110-160 mg/dl	+2 IU/day	110-160 mg/dl	+2 IU/day
	>160 mg/dl	+4 IU/day	>160 mg/dl	+4 IU/day

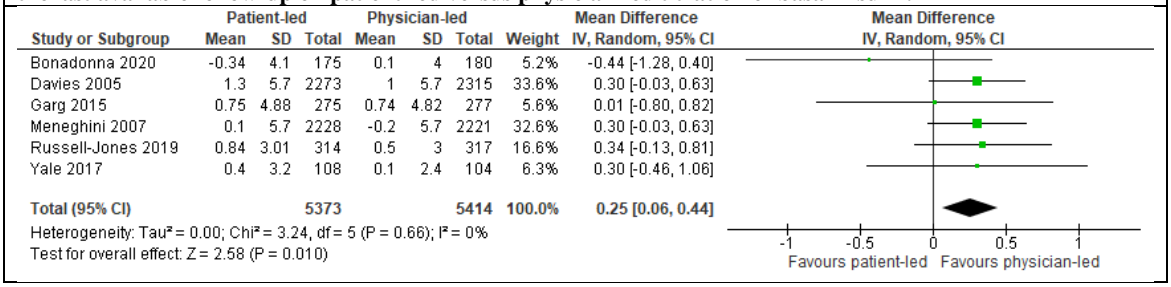
	Patient-led titration		Physician-led titration	
Yale, 2017 (20)	Target: FPG 80-100 mg/dl SMBG: Frequency of titration: daily Algorithm: titration based on daily FPG		Target: FPG 80-100 mg/dl SMBG: Frequency of titration: at least once weekly but no more often than every 3 days Algorithm: titration based on median FPG for the previous 3 consecutive days	
	FPG	Titration	FPG	Titration
	<100 mg/dl >100 mg/dl	no change +1 IU/day	<60 mg/dl or occurrence of ≥2 symptomatic or 1 severe hypoglycemia episode in the preceding week 60-80 mg/dl 80-100 mg/dl 100-140 mg/dl >140 mg/dl	-3 IU/day or at physician's discretion -3 IU/day no change +3 IU/day +6 IU/day
Russell-Jones, 2019 (21)	Target: FPG 80-130 mg/dl SMBG: unclear Frequency of titration: every 3-4 days Algorithm: titration based on median FPG for the previous 3-4 consecutive days		Target: FPG 80-130 mg/dl SMBG: unclear Frequency of titration: weekly for the first 8 weeks, bi-weekly until week 12, and then monthly until week 24 Algorithm: titration based on median FPG for the previous 3-4 consecutive days	
	FPG	Titration	FPG	Titration
	<80 mg/dl 80-130 mg/dl >130 mg/dl	-3 IU/day no change +3 IU/day	<80 mg/dl 80-130 mg/dl >130 mg/dl	-3 IU/day or at physician's discretion no change +3 IU/day

	Patient-led titration		Physician-led titration	
Bonadonna, 2020 (22)	Target: FPG 80-110 mg/dl in the absence of hypoglycemia SMBG: daily fasting SMBG until it was stable at target. Thereafter, fasting pre-breakfast SMBG was mandatory on at least 3 consecutive days per week and 7-point SMBG profile was performed at week 12 and week 24 Frequency of titration: weekly or even more frequently (but no more often than every 3–4 days) Algorithm: titration based on median FPG for the previous 3 consecutive days		Target: FPG 80-110 mg/dl in the absence of hypo-glycemia SMBG: daily fasting SMBG until it was stable at target. Thereafter, fasting pre-breakfast SMBG was mandatory on at least 3 consecutive days per week and 7-point SMBG profile was performed at week 12 and week 24 Frequency of titration: weekly until week 12, and then every 2 weeks until week 24 Algorithm: titration based on median FPG for the previous 3 consecutive days	
	FPG	Titration	FPG	Titration
	<54 mg or occurrence of ≥2 symptomatic or 1 severe hypoglycemic episode(s) in the preceding week	contact physician	<54 mg or occurrence of ≥2 symptomatic or 1 severe hypoglycemic episode(s) in the preceding week	at physician's discretion
	<80 mg/dl	-2 IU/day	<80 mg/dl	-2 IU/day
	80-110 mg/dl	no change	80-110 mg/dl	no change
	110-180 mg/dl	+2 IU/day	110-180 mg/dl	+2 IU/day
	>180 mg/dl	+4 IU/day	>180 mg/dl	+4 IU/day
	Other data: patients received from the study-nurse a specific, detailed, educational session regarding self-adjustment of insulin. Nurse phone calls were scheduled to collect glycemic values and relevant information from self-managed patients and to verifycorrect algorithm application, but nurses were instructed to exert no influence on insulin titration			

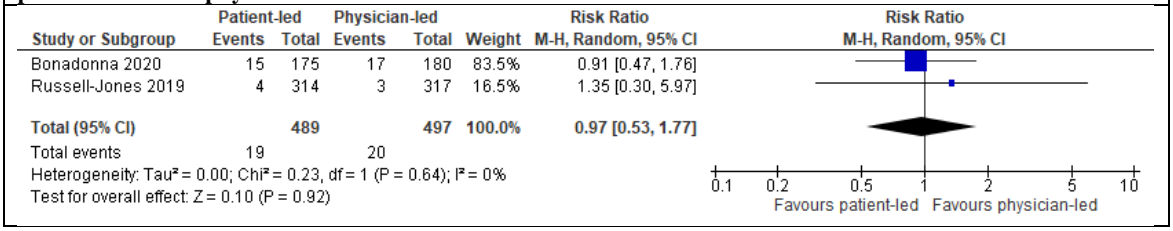
Supplemental Figure S1. Forest plot of meta-analysis for difference in change in daily basal insulin dose from baseline to the last available follow-up on patient-led versus physician-led titration of basal insulin.



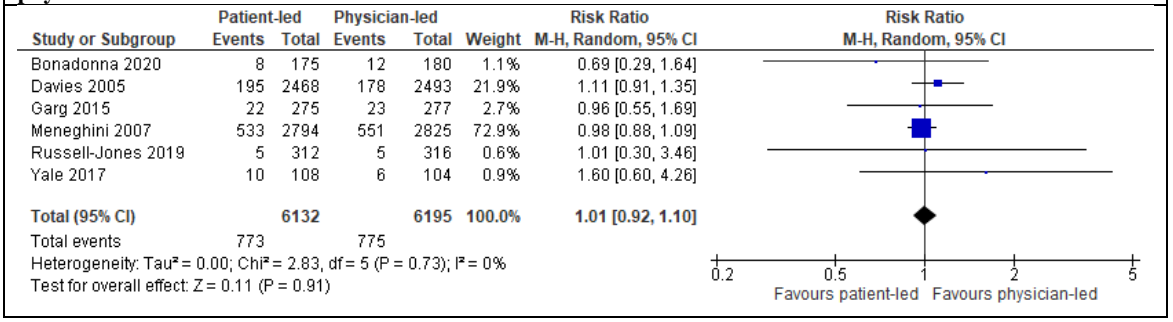
Supplemental Figure S2. Forest plot of meta-analysis for difference in change in body weight from baseline to the last available follow-up on patient-led versus physician-led titration of basal insulin.



Supplemental Figure S3. Forest plot of meta-analysis for relative risk of requiring rescue medication on patient-led versus physician-led titration of basal insulin.



Supplemental Figure S4. Forest plot of meta-analysis for relative risk of discontinuation on patient-led versus physician-led titration of basal insulin.



Supplemental Table S4. Patient-reported outcomes.

	Scale	More favorable findings in patient-led titration	No difference	More favorable findings in physician-led titration
Davies, 2005 (17)	Not assessed.	NA	NA	NA
Meneghini, 2007 (18)	Not assessed.	NA	NA	NA
Garg, 2015 (19)	Diabetes Treatment Satisfaction Questionnaire (DTSQ) EuroQol (EQ-5D)		x x	
Yale, 2017 (20)	Diabetes Treatment Satisfaction Questionnaire (DTSQ)		x	
Russell-Jones, 2019 (21)	Diabetes Distress Scale (DDS) Diabetes Empowerment Scale (DES)		x x	
Bonadonna, 2020 (22)	Diabetes Empowerment Scale short-form (DES-SF) Diabetes Treatment Satisfaction Questionnaire (DTSQ) Problem Areas in Diabetes Scale-5 (PAID5)		x x x	

48 **Supplemental Table S5. Publication bias.**

Endpoint	Egger's test
Difference in change in HbA1c	0.574
Difference in change in fasting plasma glucose	0.099
Difference in change in daily basal insulin dose	0.680
Difference in change in body weight	0.122
Relative risk of any hypoglycemia	0.917
Relative risk of level 3 hypoglycemia	0.554
Relative risk of requiring rescue medication	NA
Relative risk of discontinuation	0.787

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