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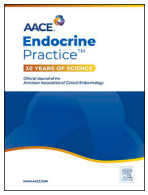

Review Article

Automated Insulin Delivery Systems in Cystic Fibrosis-Related Diabetes: A Systematic Review and Meta-Analysis

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ABSTRACT

Objectives: To assess the effects of automated insulin delivery systems (AIDs) on glycemic control and selected metabolic and pulmonary outcomes in people with cystic fibrosis related diabetes (pwCFRD).

Methods: We searched MEDLINE (via PubMed), Embase, and Cochrane Library for studies of AIDs in pwCFRD. Eligible studies included at least 14 days of follow-up and reported continuous glucose monitoring outcomes. The primary outcome was time in range (3.9-10.0 mmol/L or 70-180 mg/dL). Additional outcomes included time above range (>10.0 mmol/L or 180 mg/dL), time below range (<3.9 mmol/L or 70 mg/dL), average glucose, body mass index, and FEV_1. We performed single-arm meta-analyses using a random-effects model.

Results: Four studies ($n = 69$) met inclusion criteria. AIDs increased time in range by 9.55% (95% CI 1.49, 17.61; $P = .02$) at short-term (14-30 days) and 11.55% (95% CI 5.61, 17.50; $P < .001$) at long-term (≥12 weeks) follow-up, respectively. Time above range decreased by 8.41% (95% CI −15.59, −1.22; $P = .022$) and 12.96% (95% CI −17.67, −8.26; $P < .001$) at short- and long-term, respectively. Average glucose decreased by 1.01 mmol/L (18 mg/dL) (95% CI −1.98, −0.04; $P = .042$) and 1.12 mmol/L (20 mg/dL) (95% CI −1.70, −0.54; $P < .001$) at short- and long-term, respectively. AIDs did not change time below range, body mass index, and FEV_1.

Conclusions: AIDs improved glycemic control in pwCFRD without increasing hypoglycemia, with short-term benefits persisting over 12 weeks. Larger randomized trials are needed to confirm these findings.

Introduction

The prevalence of cystic fibrosis-related diabetes (CFRD) increases with age and affects nearly half of adults with cystic fibrosis (CF).[1] The most recent CF Foundation Clinical Care Guidelines recommended insulin as the preferred therapy to treat CFRD, since insulin improves glycemic control and has an anabolic effect that preserves weight and lung function in people with CFRD

Abbreviations: ADA, American Diabetes Association; AG, average glucose concentration; AIDs, automated insulin delivery systems; BMI, body mass index; CF, cystic fibrosis; CFRD, cystic fibrosis-related diabetes; CGM, continuous glucose monitoring; CI, confidence interval; FEV_1, forced expiratory volume in 1 s; IQR, interquartile range; MD, mean difference; MDI, multiple daily injections; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analysis; PROSPERO, International Prospective Register of Systematic Reviews; pwCFRD, people with CFRD; r, correlation coefficient; RCTs, randomized controlled trials; REML, restricted maximum-likelihood; RoB 2, Cochrane Risk of Bias 2 tool; ROBINS-I, Cochrane Risk of Bias in Nonrandomized Studies of Interventions tool; SD, standard deviation; TAR, time above range; TBR, time below range; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus; TIR, time in range.

B.L.S. and J.A. are considered joint first authors.

Registration: This study was prospectively registered in PROSPERO (International Prospective Register of Systematic Reviews) under protocol number CRD420251069070.

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(pwCFRD).[2] Current recommendations include insulin delivery through multiple daily injections or continuous subcutaneous insulin infusion (ie, non-automated insulin pump).[2-5]

The American Diabetes Association Standards of Care 2025 recommends individualizing the use of diabetes technology, with device selection based on each person's circumstances, preferences, and skills.[6] The guidelines also recommend early use of continuous glucose monitoring (CGM) in all types of diabetes, particularly for those using insulin.[7] The use of CGM has previously been validated in pwCFRD, demonstrating its utility in routine care and its ability to guide treatment decisions.[5] Automated insulin delivery systems (AIDs), also called hybrid closed-loop systems, are insulin pumps that use CGM data to automatically modulate basal insulin delivery, while requiring patients to bolus for meals.[8] Some systems can also deliver automated correction boluses.[8] AIDs have consistently increased time in range (TIR) in people with type 1 (T1DM) and type 2 diabetes mellitus (T2DM) and decreased mild and severe hypoglycemia in T1DM.[7,9] The American Diabetes Association currently recommends AIDs as first-line therapy for people with T1DM and as a consideration for people with T2DM on insulin therapy.[7] In pwCFRD, however, their use remains off label.

The maintenance of body weight preserves lung function in pwCFRD.[10,11] Historically, the diet recommended to pwCFRD focused on high calorie, high fat, and high salt, without limiting carbohydrates, making glycemic control more difficult to achieve.[11] However, these recommendations are evolving in the cystic fibrosis transmembrane conductance regulator (CFTR) modulator era.[12] PwCFRD face additional challenges in managing glucose, including reduced incretin signaling with pancreatic insufficiency and increased insulin resistance during pulmonary exacerbations or glucocorticoid use.[13] AID use in pwCFRD may add convenience and allow more flexible insulin dosing during acute illness, hospitalization, changes in insulin needs, feeding, and glucocorticoid use.

The current CF Foundation Clinical Care Guidelines for CFRD were published in 2010, before CGMs had sufficient accuracy to be recommended for insulin dosing and prior to FDA approval of AID.[2,14] As a result, these guidelines do not mention CGM or AIDs for pwCFRD. The management of CFRD has evolved and now includes more advanced diabetes technology. Unfortunately, current published data include a small number of studies with small sample sizes and heterogeneous designs. To close this gap, we conducted the first systematic review and meta-analysis evaluating the use of AIDs in pwCFRD, pooling the existing data across different CGM outcomes and providing a clearer evidence-based foundation for clinical decision making and future guideline updates.

Highlights

- Automated insulin delivery systems (AIDs) increased time in range (3.9-10.0 mmol/L)
- AIDs decreased time above range (>10.0 mmol/L)
- AIDs did not increase time below range (<3.9 mmol/L)
- Results were consistent at both short-term (14-30 days) and long-term (≥12 weeks)
- AIDs did not change forced expiratory volume in 1 sand body mass index

Clinical Relevance

Automated insulin delivery systems increased time in range and reduced hyperglycemia in cystic fibrosis related diabetes without increasing hypoglycemia, consistent with type 1 and type 2 diabetes studies. Benefits appeared early and persisted over longer follow up. Lung function and body mass index were unchanged.

Research Design and Methods

We performed a systematic review and meta-analysis in accordance with the Cochrane Handbook for Systematic Review of Interventions, version 6.5, 2024.[15] We report data in accordance with the 2020 PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines.[16]

Eligibility Criteria

We only included studies that met all the following criteria: (1) randomized controlled trials (RCTs), post hoc analyses of RCTs, randomized crossover trials, prospective cohorts, retrospective cohorts, or case series with at least 5 subjects; (2) enrollment of pwCFRD; (3) use of AIDs; and (4) follow-up of at least 14 days. We set this minimum follow-up interval based on prior studies demonstrating that 10-14 days of CGM data best correlate with longer-term glycemic metrics.[17] We also required studies to report glycemic parameters measured by CGM. We excluded studies published in languages other than English and those without a full-text publication.

Search Strategy and Data Extraction

Two authors (B.S. and Y.C.) independently searched MEDLINE (via PubMed), Embase, and the Cochrane Library from inception to 1 July 2025. The full search strategies for each database are provided in Supplementary Table 1. B.S. and Y.C. manually removed duplicates and selected studies using Rayyan reference manager software (Rayyan Systems Inc).[18] They also performed backward snowballing by screening the reference lists of relevant publications to identify additional studies.[19] Two authors (B.S. and M.T.) independently screened titles and abstracts and reviewed full-text articles according to the predefined eligibility criteria. After inclusion, B.S. and M.T. extracted baseline study characteristics. B.S. and Y.C. then independently extracted outcome data. For RCTs, we extracted data from the population(s) that used AIDs as intervention. We resolved disagreements by consensus with input from the senior author (M.A.).

Outcomes

The primary outcome was the CGM-measured percentage of time that glucose values were in range (3.9-10.0 mmol/L [70-180 mg/dL]). Other outcomes included percentage time above range (TAR) (>10.0 mmol/L [>180 mg/dL] and >13.9 mmol/L [>250 mg/dL]); percentage time below range (TBR) (<3.9 mmol/L [<70 mg/dL]); average glucose concentration (AG); body mass index (BMI); and forced expiratory volume in 1 s (FEV_1). We defined safety as an improvement in TIR without increase in TBR.

Because follow-up times varied across studies, we analyzed glucose outcomes at 2 timepoints. We defined short-term follow-up as the last visit occurring 14-30 days after the study began. We defined long-term follow-up as the final visit occurring at least 12 weeks after the study began. This allowed us to assess whether initial changes in glucose control persisted over time. The specific time point used as short-term and long-term follow-up for each study is specified in Supplementary Table 2. BMI and FEV_1 were analyzed at the last available follow-up.

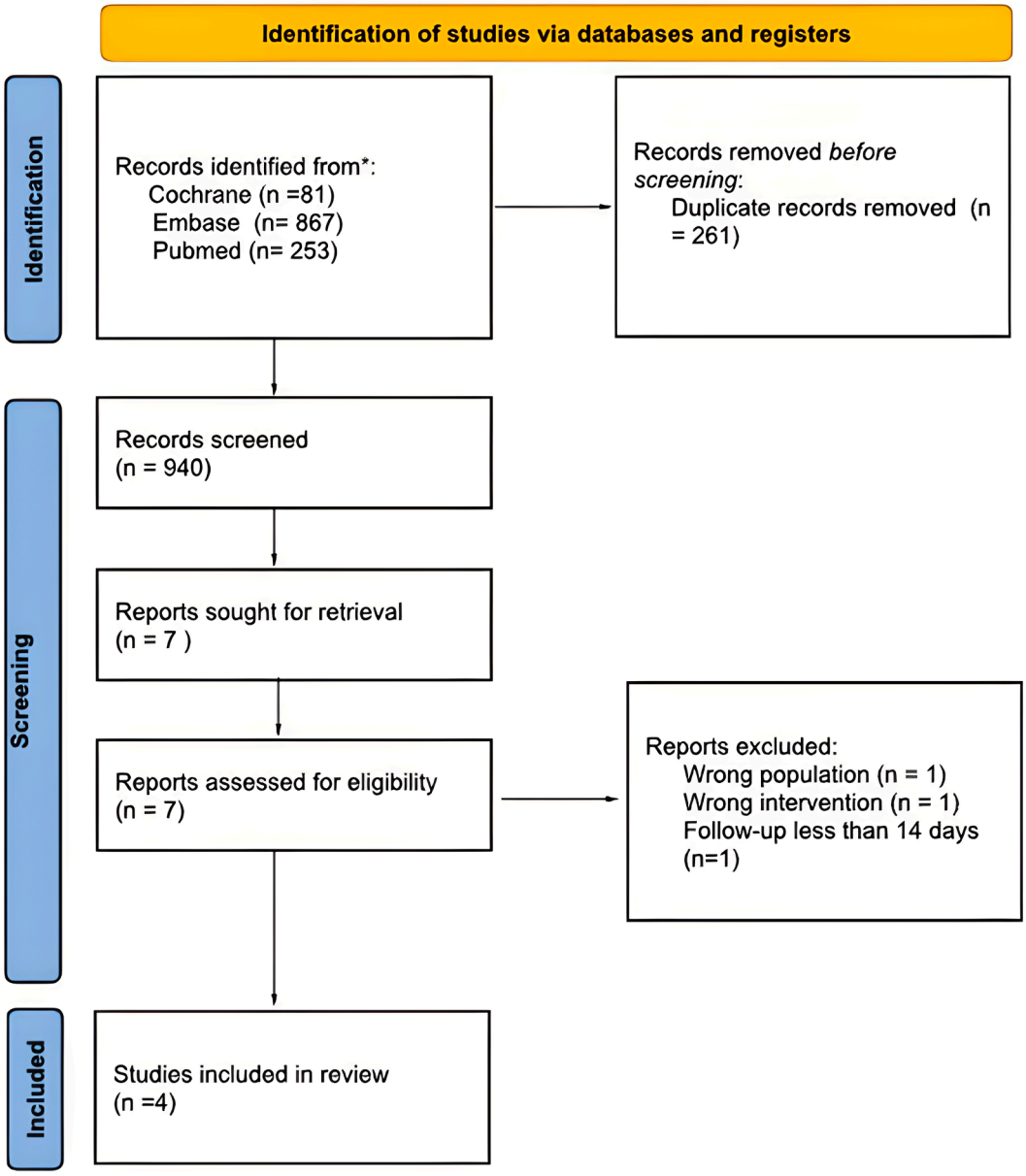


Fig. 1. PRISMA flow diagram of study screening and selection. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analysis.

Quality Assessment

Two authors (B.S. and M.T.) independently assessed risk of bias for included studies using the Cochrane Risk of Bias 2 tool (RoB 2).[20] We rated each domain as "low risk," "some concerns," or "high risk" of bias. For non-randomized studies, B.S. and M.T. used the Cochrane Risk of Bias in Nonrandomized Studies of Interventions tool (ROBINS-I).[21] This tool evaluates bias across 7 domains: (1) bias due to confounding; (2) bias in selection of participants; (3) bias in classification of interventions; (4) bias due to deviations from intended interventions; (5) bias due to missing data; (6) bias in measurement of the outcomes; and (7) bias in selection of the reported result.

Statistical Analysis

We performed a single-arm meta-analysis and calculated continuous outcomes as mean difference (MD) from baseline with standard deviation (SD) and 95% confidence interval (CI). A *P*-value <.05 was considered statistically significant. We used the restricted maximum-likelihood random-effects model for all analyses.[15]

We obtained the SD and the correlation coefficient (r) between final and baseline values using the reported *P*-value for the change, as recommended by the Cochrane Handbook for Systematic Reviews of Interventions.[15] When a *P*-value was not available, we calculated SD for the change using the median r from the other studies reporting the same outcome. We also performed a sensitivity analysis imputing different correlation coefficients: 0.5 (assuming a moderate correlation) and 0.8 (assuming a high correlation) (Supplementary Tables 3 and 4).[15]

When a study did not report the CI, we contacted the corresponding author to obtain this information. If the author did not provide the missing value, we used the CI from the study with the closest sample size for the same outcome. For outcomes reported as median with interquartile range (IQR), we calculated the mean

Table
Baseline Characteristics for the Included Studies

Study (y of publication)	*n*	Study design	AID	Duration (mo)	Age (y)	Female (%)	HbA1c (%)	BMI (Kg/m^2)	FEV1 (% predicted)	MDI (%)[a]	CFTR modulator (%)	Time in range (%)[b]
Bassi et al (2024)[27]	10	Observational	Tandem t:slim X2 and Minimed 780G	12	39.3 ± 12.7	30	7.31 ± 0.34	22.9 ± 3.1	79.90 ± 29.62	40	50	60.0 ± 20.0
Scully et al (2025)[28]	26	Observational	Omnipod 5	6	27.3 (18.5, 34.3)	65	6.8 (6, 7.6)	22.5 (20, 24.7)	87 (65, 103)	54	69	54.0 ± 22.3
Scully et al (2022)[29]	13	Observational	Tandem t:slim X2	3	38.5 ± 4.1	61.5	8.7 ± 0.5	24.2 ± 1.0	67 ± 7	38.5	76.9	54.3 ± 18.4
Sherwood et al (2024)[30]	20	RCT, crossover	iLet bionic pancreas	0.5	40 ± 13	50	7.4 ± 1.6	23.7 ± 3.5	70 ± 24	50	85	71.0 ± 16.0

Abbreviations: AID, automated insulin delivery system; BMI, body mass index; CFTR, cystic fibrosis transmembrane conductance regulator; FEV1, forced expiratory volume in 1 s; HbA1c, glycosylated hemoglobin; MDI, multiple daily insulin injections; n, number of participants; RCT, randomized controlled trial.
Results reported as number of patients, mean ± standard deviation (SD), median (quartile 1, quartile 3), or number of patients (%).
[a] Patients using MDI before AID initiation.
[b] Time in range defined as 3.9-10.0 mmol/L or 70-180 mg/dL; we reported data from the first 48 h of the AID arm for Sherwood et al, 2024; SD converted from originally reported 95% confidence interval or standard error, if SD was not provided.

and SD using the validated method proposed by Wan et al.[22] When studies reported separate ranges for TAR and TBR (10.0-13.9 mmol/L [180-250 mg/dL] and >13.9 mmol/L [>250 mg/dL] for TAR; 3-3.9 mmol/L [54-70 mg/dL] and <3.0 mmol/L [<54 mg/dL] for TBR), we combined these values as TAR (>10.0 mmol/L [>180 mg/dL]) and TBR (<3.9 mmol/L [<70 mg/dL]), respectively.

We assessed heterogeneity using the Chi^2 (χ^2) test and the I^2 statistic. We considered *P*-values <0.10 as statistically significant for the Chi^2 test. We regarded I^2 values of <25%, 25% to 49%, 50% to 74%, and ≥75% as indicating low, moderate, substantial, and considerable heterogeneity, respectively.[23] For analyses with moderate to considerable heterogeneity, we performed a leave-one-out analysis to assess the influence of individual studies on the pooled heterogeneity.[24] We performed all statistical analyses using R software, version 4.5.0 (R Foundation for Statistical Computing).[25] We used the meta package (function metagen) to conduct meta-analyses.[26]

Results

Study Selection and Characteristics

Figure 1 outlines the study screening and selection process. Our search of MEDLINE (via PubMed), Embase, and the Cochrane Library yielded 1201 results. After removing duplicates, we screened 940 titles and abstracts and reviewed the full texts of 7 studies. We included 4 studies with a total of 69 participants in this systematic review and meta-analysis. One study was an RCT, and the other 3 were retrospective observational studies.[27-30] We excluded 3 studies for the following reasons: 1 had only 1 week of follow-up, 1 did not meet population criteria, and 1 did not meet intervention criteria.[31-33] Table 1 summarizes key baseline characteristics of participants in the included studies.

Primary Outcome

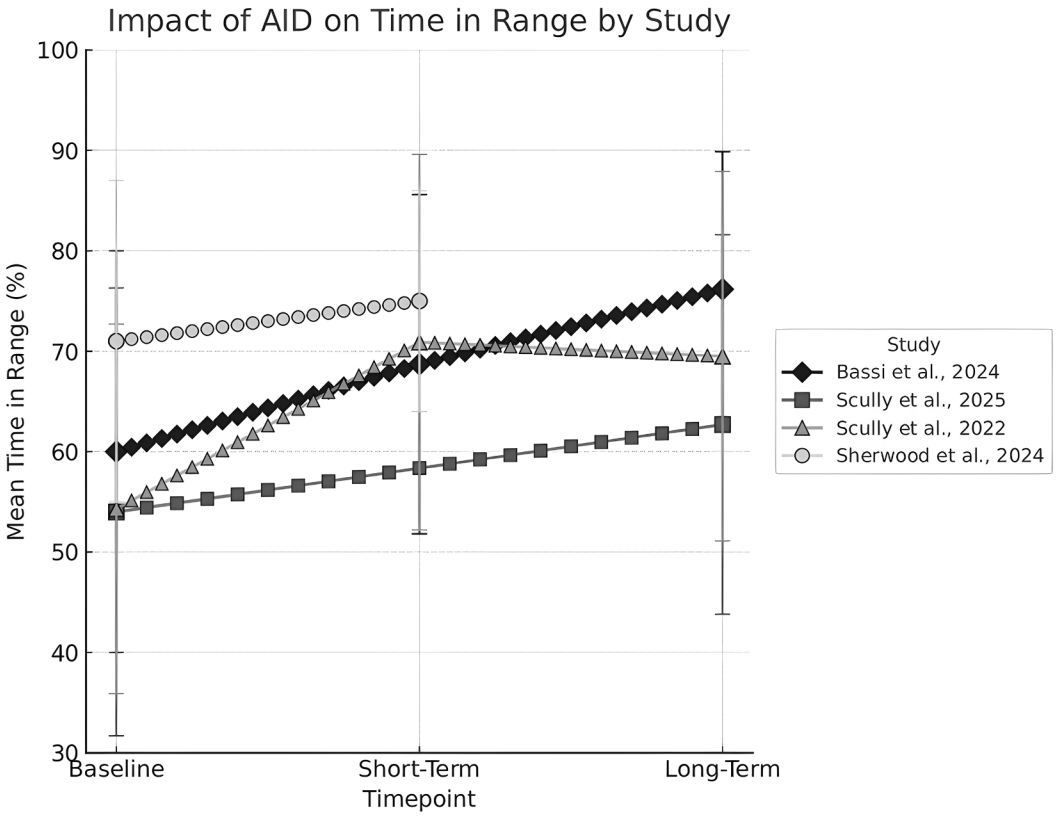
All 4 included studies of pwCFRD using AIDs reported time in range (TIR, 3.9-10.0 mmol/L [70-180 mg/dL]), the primary outcome of this review. Although not every individual study showed a statistically significant difference from baseline, all showed a trend towards increased TIR (Fig. 2).

In the pooled analysis, TIR increased significantly at short-term follow-up by 9.55% (95% CI 1.49, 17.61; $P = .02$; $I^2 = 71.3\%$; Fig. 3*A*) and at long-term follow-up by 11.55% (95% CI 5.61, 17.50; $P < .001$; $I^2 = 20.4\%$; Fig. 4*A*). Heterogeneity was low at long-term follow-up. Sensitivity analyses using different correlation coefficients did not change the significance of the findings (Supplementary Tables 3 and 4). Leave-one-out analysis for short term follow-up demonstrated low heterogeneity after exclusion of Scully et al, 2022 and Sherwood et al, 2024 (Supplementary Fig. 1).[29,30]

Additional Outcomes

Time Above Range (TAR)

We observed a trend toward reduction in TAR >10.0 mmol/L [>180 mg/dL] in individual studies of pwCFRD using AIDs (Supplementary Fig. 2), although not every study showed a significant reduction. In the pooled analysis, TAR decreased significantly at both short-term follow-up (MD −8.41%; 95% CI −15.59, −1.22; $P = .022$; $I^2 = 63.5\%$; Fig. 3*B*) and long-term follow-up (MD: −12.96%; 95% CI −17.67, −8.26; $P < .001$; $I^2 = 0.0\%$; Fig. 4*B*). Heterogeneity was low at long-term follow-up. Leave-one-out analysis for short-term follow-up demonstrated low heterogeneity after exclusion of Scully et al, 2022 (Supplementary Fig. 3).[29]



Study	Baseline	Short-Term	Long-Term
Bassi et al., 2024	60.00 ± 20.0	68.71 ± 16.9	76.17 ± 13.7
Scully et al., 2025	54.00 ± 22.3	NA	62.70 ± 18.9
Scully et al., 2022	54.30 ± 18.4	70.90 ± 18.7	69.50 ± 18.4
Sherwood et al., 2024	71.00 ± 16.0	75.00 ± 11.0	NA

Fig. 2. Impact of automated insulin delivery systems on mean time in range (%) for each timepoint by study. Outcomes are reported as mean ± standard deviation. Diamonds: Bassi et al, 2024; Squares: Scully et al, 2025; Triangles: Scully et al, 2022; Circles: Sherwood et al, 2024. NA, not available.

For TAR >13.9 mmol/L [>250 mg/dL], we did not observe a significant difference at short-term follow-up (MD −5.74%; 95% CI −13.05, 1.56; $P = .123$; $I^2 = 77.3\%$). At long-term follow-up, however, TAR >13.9 mmol/L decreased significantly by 8.82% (95% CI −13.84, −3.79; $P < .001$; $I^2 = 24.9\%$) (Supplementary Fig. 4). Leave-one-out analysis for short-term follow-up demonstrated low heterogeneity after exclusion of Sherwood et al, 2024 (Supplementary Fig. 5).[30]

Time Below Range (TBR)

We did not observe a difference in TBR <3.9 mmol/L [<70 mg/dL] in each of the individual studies (Supplementary Fig. 6). In the pooled analysis, there was no significant difference at either short-term follow-up (MD −0.48%; 95% CI −1.50, 0.55; $P = .361$; $I^2 = 49.8\%$) or long-term follow-up (MD 0.10%; 95% CI −0.35, 0.56; $P = .653$; $I^2 = 5.1\%$) compared with baseline (Figs. 3*C* and 4*C*). Leave-one-out analysis for short-term follow-up demonstrated low heterogeneity after exclusion of Bassi et al, 2024 (Supplementary Fig. 7).[27]

Average Glucose (AG)

AID use in pwCFRD significantly reduced average glucose (AG). In the pooled analysis, AG decreased by 1.01 mmol/L (18 mg/dL) after short-term follow-up (95% CI −1.98, −0.04; $P = .042$; $I^2 = 18.1\%$; Fig. 3*D*) and by 1.12 mmol/L (20 mg/dL) after long-term follow-up (95% CI −1.70, −0.54; $P < .001$; $I^2 = 0.0\%$; Fig. 4*D*).

Body Mass Index

Only 2 studies of pwCFRD using AIDs reported body mass index (BMI), both at long-term follow-up. Neither the individual analyses nor the pooled analysis showed significant difference (Supplementary Fig. 8*A*).

Pulmonary Function Test

Only 2 studies of pwCFRD using AIDs reported FEV_1 (% predicted), both at long-term follow-up. Neither the individual analyses nor the pooled analysis showed significant difference (Supplementary Fig. 8*B*).

Quality Assessment

We detailed the risk of bias assessment in Supplementary Figures 9 and 10. Using RoB 2, we rated Sherwood et al, 2024, as having low risk of bias.[30] According to ROBINS-I, all 3 observational

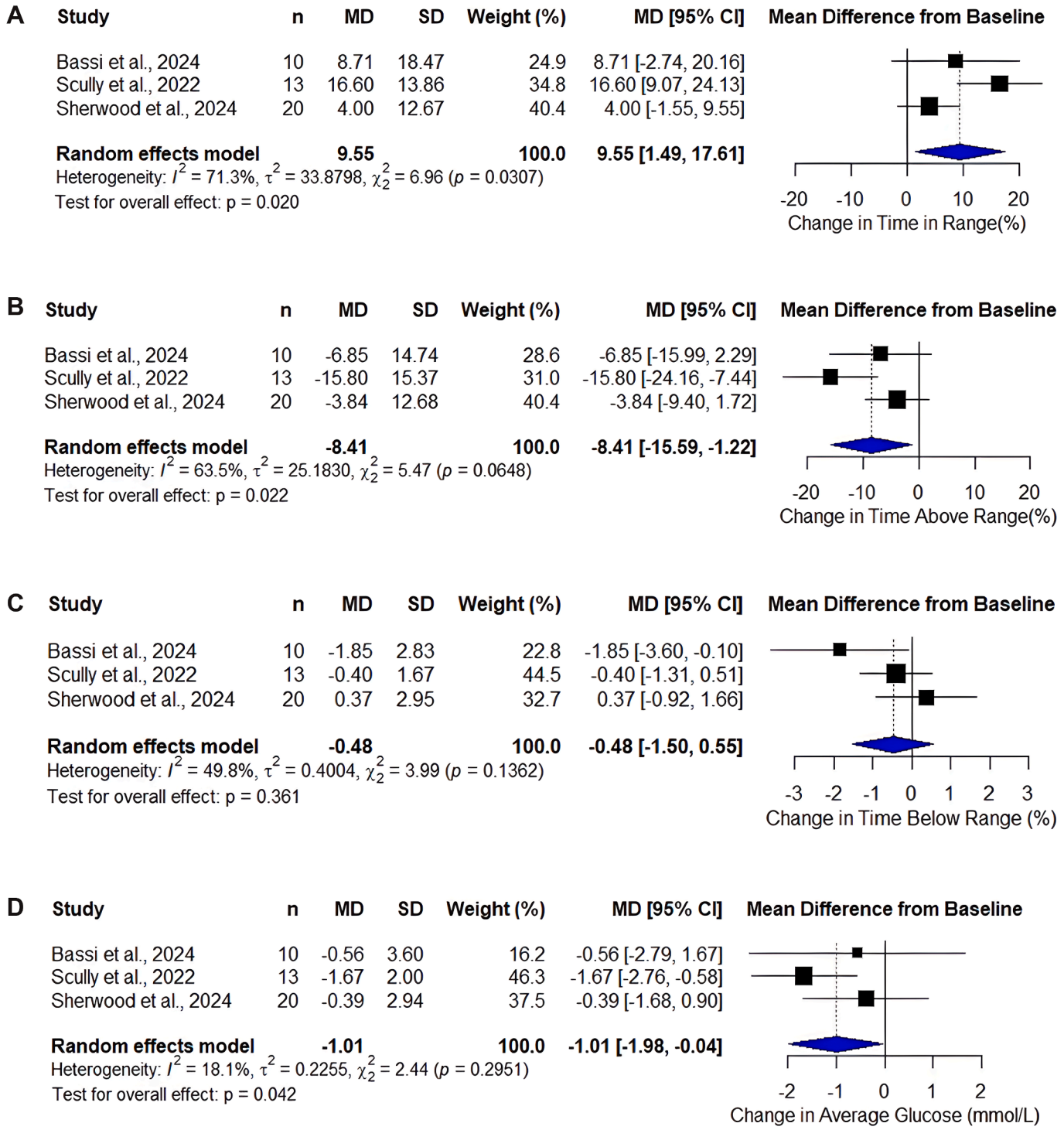


Fig. 3. At short-term follow-up, the use of automated insulin delivery systems: (*A*) improved time in range; (*B*) reduced time above range; (*C*) did not increase hypoglycemia (time below range); and (*D*) reduced average glucose level. CI, confidence interval; MD, mean difference; n, number of participants; SD, standard deviation.

studies were rated as having serious risk of bias due to the possibility of confounding.[27-29]

Discussion

This systematic review and single-arm meta-analysis is the first to summarize the effects of AIDs on glycemic outcomes in pwCFRD. We included one RCT and three retrospective studies, totaling 69 pwCFRD. In the pooled analysis, AID use was associated with improved TIR, decreased TAR, and lower average glucose from baseline to short-term follow-up, with benefits persisting at long-term follow-up. AID use in pwCFRD was not associated with significant changes in TBR, BMI, or FEV_1.

Prior studies have associated hyperglycemia with a decline in pulmonary function and nutritional status, but much of this evidence predates widespread CFTR modulator therapy.[34] Therefore,

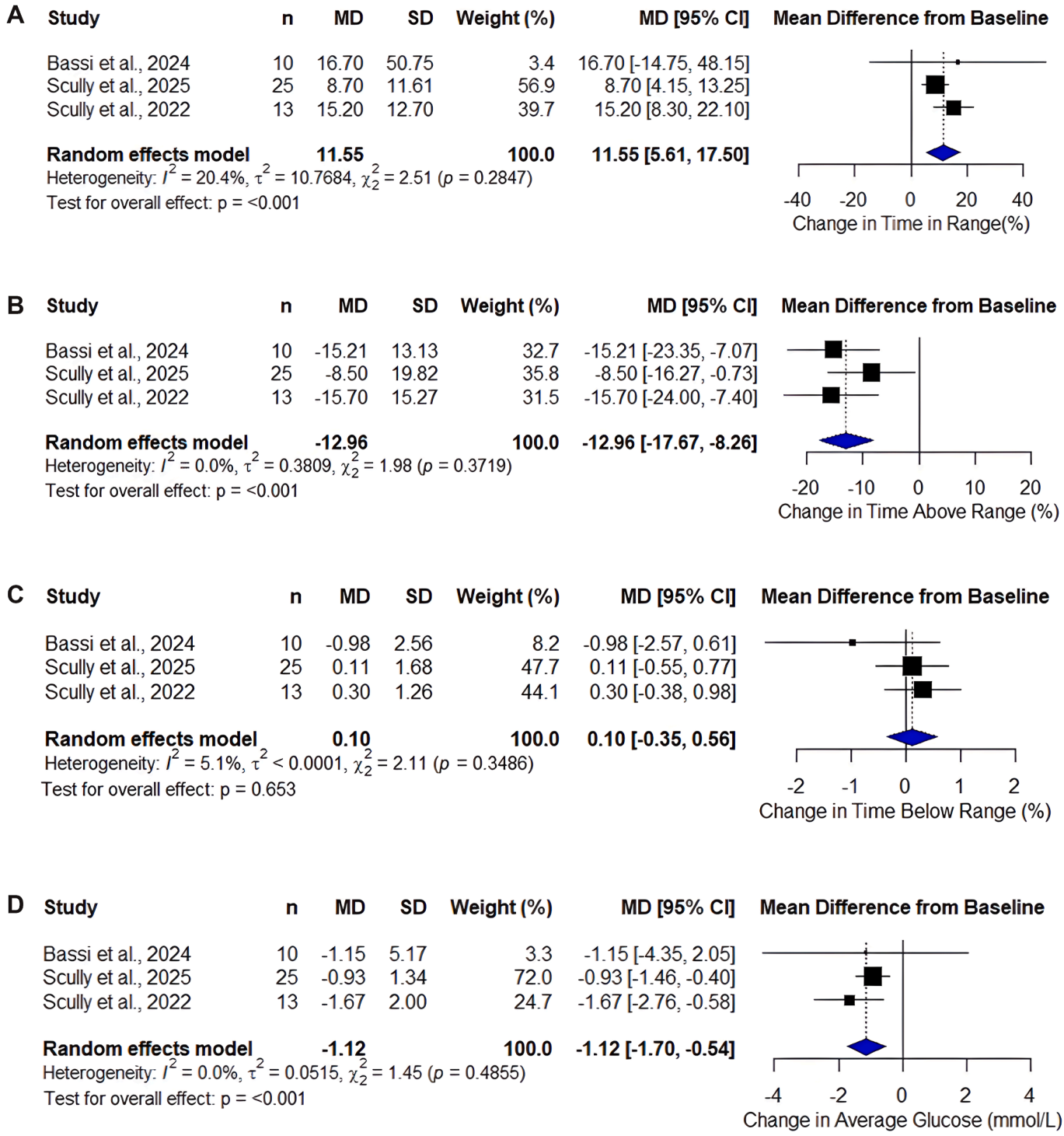


Fig. 4. At long-term follow-up, the use of automated insulin delivery systems: (*A*) improved time in range; (*B*) reduced time above range; (*C*) did not increase hypoglycemia (time below range); and (*D*) reduced average glucose level. CI, confidence interval; MD, mean difference; n, number of participants; SD, standard deviation.

the incremental benefit of improved glycemic control in the CFTR modulator era remains uncertain. AID systems may help reduce glycemic variability, lowering catabolic stress, reducing hypoglycemia, and helping preserve pulmonary function over time. Although AIDs are standard of care for people with T1DM and recommended for those with T2DM on insulin therapy, data supporting their use in pwCFRD remain sparse. PwCFRD are often under-represented in randomized trials and device studies, and AID use in this population is currently off label. Some have questioned whether residual endogenous insulin secretion in pwCFRD, combined with AID insulin delivery, could increase the risk of postprandial and fasting hypoglycemia.[35] However, our analysis showed that AID use in pwCFRD was safe and did not increase hypoglycemia (TBR). In some pwCFRD, the use of insulin therapy has unique complexities, including postprandial hypoglycemia, enteral feeding, and frequent glucocorticoid tapers. Therefore,

additional data are needed to confirm the efficacy and safety of AID in these scenarios.[36] Our analysis included only 69 pwCFRD, reflecting the rarity of this disease. Our results were consistent across studies, and AID use appeared adaptable and effective in maintaining glycemic outcomes, suggesting that the algorithms may adequately meet the metabolic demands of this population. Still, additional studies are needed to confirm these findings. Two large multicenter, randomized controlled trials (NCT06449677, NCT05562492) plan to enroll 150 and 128 patients, respectively, to better determine the safety and efficacy of AID in pwCFRD.

An important consideration when modifying therapy for pwCFRD is the potential for changes in body weight. With the widespread use of CFTR modulators in recent years, the nutritional status of pwCFRD has changed significantly, with reports of weight gain and a higher risk of metabolic syndrome.[37] In the included studies, 50 pwCFRD were taking CFTR modulators at the time of AID use. Only 2 studies reported BMI data, and the pooled analysis showed no difference in BMI among pwCFRD using AIDs. Weight neutrality with AID use is especially relevant because insulin resistance in CFRD can fluctuate with inflammation, infection, and glucocorticoid use, making conventional insulin regimens challenging.[38] In addition, AID use may help reduce treatment burden and provide greater flexibility for pwCFRD, particularly during periods of illness or glucocorticoid therapy.[39]

This study has some important limitations. 1) As with any meta-analysis, it is subject to biases from the included studies. 2) Few publications met our inclusion criteria, particularly randomized controlled trials. Notably, only one included study had a comparator group, making it impossible to conduct a comparative meta-analysis. 3) Twelve pwCFRD from 2 of the included studies were already using AIDs but switched systems at the start of follow-up, which may have reduced the magnitude of the observed effects.[28,30] 4) Variability in follow-up time points, AID algorithms, baseline glycemic control, and the timing of assessments may have contributed to the heterogeneity observed in short-term outcomes. 5) Because of the limited availability of data on this topic, it was not possible to perform subgroup analyses for different populations, such as adults and children, to better understand the specific impact of AIDs in each group. 6) Because this was a single-arm meta-analysis, evidence quality assessment with the GRADE (Grading of Recommendations Assessment, Development and Evaluation) tool could not be used. 7) According to ROBINS-I, all 3 retrospective studies included had a high risk of bias due to possible confounding, such as difference of baseline lung function, use of CFTR modulator therapy, and nutritional status.

Conclusions

This meta-analysis is the first to evaluate the safety and glycemic effects of AIDs in pwCFRD. In this analysis, AIDs improved glycemic control in pwCFRD without increasing hypoglycemia, with short-term benefits persisting over 12 weeks. Our results were consistent across all studies, supporting the robustness of our findings. Larger RCTs comparing AIDs with standard care in pwCFRD are undergoing and may be able to confirm these glycemic benefits as well as assess their impact on body weight, pulmonary function, patient satisfaction, patient-reported outcomes, and cost-effectiveness. Future studies are needed to better explore longer-term outcomes, specifically evaluating effects on lung function, hospitalization rates, microvascular and macrovascular complications, and survival, to determine the broader clinical impact of AID use in pwCFRD.

Disclosure

Marconi Abreu's spouse is a clinical educator for Sequel Meditech. The other authors declare that they have no relevant conflicts of interest to declare.

Author Contributions

B.S.: methodology, data extraction, statistical analysis, quality and certainty assessment, writing- original manuscript and reviews, and protocol design and coordination. J.A.: meaningful intellectual contribution on the proposed topic, manuscript writing, review, and editing. S.M.: meaningful intellectual contribution on the proposed topic, manuscript review, and editing. M.T.: data extraction, quality, and certainty assessment. Y.C.: study screening and selection, and data curation. G.C.: statistical analysis, quality and certainty assessment, manuscript review. M.A.: conceptualization, protocol design, methodology, and manuscript review and editing.

References

1. Kohler CL, Vigers T, Pyle L, et al. Trends in cystic fibrosis–related diabetes epidemiology between 2003 and 2018 from the U.S. cystic fibrosis foundation patient registry. *Diabetes Care*. 2025;48(7):1251–1259. https://doi.org/10.2337/dc25-0044.
2. Moran A, Brunzell C, Cohen RC, et al. Clinical care guidelines for cystic fibrosis–related diabetes. *Diabetes Care*. 2010;33(12):2697–2708. https://doi.org/10.2337/dc10-1768.
3. Dobson L, Sheldon CD, Hattersley AT. Validation of interstitial fluid continuous glucose monitoring in cystic fibrosis. *Diabetes Care*. 2003;26(6):1940–1941. https://doi.org/10.2337/diacare.26.6.1940-a.
4. Jefferies C, Solomon M, Perlman K, Sweezey N, Daneman D. Continuous glucose monitoring in adolescents with cystic fibrosis. *J Pediatr*. 2005;147(3):396–398. https://doi.org/10.1016/j.jpeds.2005.05.004.
5. O'Riordan SMP, Hindmarsh P, Hill NR, et al. Validation of continuous glucose monitoring in children and adolescents with cystic fibrosis. *Diabetes Care*. 2009;32(6):1020–1022. https://doi.org/10.2337/dc08-1925.
6. Putman MS, Norris AW, Hull RL, et al. Cystic fibrosis–related diabetes workshop: research priorities spanning disease pathophysiology, diagnosis, and outcomes. *Diabetes Care*. 2023;46(6):1112–1123. https://doi.org/10.2337/dc23-0380.
7. American Diabetes Association Professional Practice Committee, ElSayed NA, McCoy RG. 7. Diabetes technology: standards of care in Diabetes—2025. *Diabetes Care*. 2025;48(Supplement_1):S146–S166. https://doi.org/10.2337/dc25-S007.
8. Templer S. Closed-loop insulin delivery systems: past, present, and future directions. *Front Endocrinol*. 2022;13:919942. https://doi.org/10.3389/fendo.2022.919942.
9. Renard E, Joubert M, Villard O, et al. Safety and efficacy of sustained automated insulin delivery compared with sensor and pump therapy in adults with type 1 diabetes at high risk for hypoglycemia: a randomized controlled trial. *Diabetes Care*. 2023;46(12):2180–2187. https://doi.org/10.2337/dc23-0685.
10. Cano Megías M, Guisado Vasco P, González Albarrán O, Lamas Ferreiro A, Máiz Carro L. Association of the relative change in weight and body mass index with lung function in teenagers and adults with cystic fibrosis: influence of gender and diabetes. *Endocrinología Y Nutrición (English Edition)*. 2015;62(9):422–429. https://doi.org/10.1016/j.endoen.2015.11.005.
11. Stephenson AL, Mannik LA, Walsh S, et al. Longitudinal trends in nutritional status and the relation between lung function and BMI in cystic fibrosis: a population-based cohort study. *Am J Clin Nutr*. 2013;97(4):872–877. https://doi.org/10.3945/ajcn.112.051409.
12. Wilschanski M, Munck A, Carrion E, et al. ESPEN-ESPGHAN-ECFS guideline on nutrition care for cystic fibrosis. *Clin Nutr*. 2024;43(2):413–445. https://doi.org/10.1016/j.clnu.2023.12.017.
13. Granados A, Chan CL, Ode KL, Moheet A, Moran A, Holl R. Cystic fibrosis related diabetes: pathophysiology, screening and diagnosis. *J Cystic Fibrosis*. 2019;18:S3–S9. https://doi.org/10.1016/j.jcf.2019.08.016.
14. U.S. Food and Drug Administration. Premarket approval (PMA): Minimed 670G system. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P160017; 2016. Accessed September 26, 2025.
15. Higgins JPT, Thomas J, Chandler J, et al. In: *Cochrane handbook for systematic reviews of interventions*. Cochrane; 2024. Version 6.5. https://training.cochrane.org/handbook. Accessed September 24, 2025.

16. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021:n71. https://doi.org/10.1136/bmj.n71.
17. Cichosz SL, Jensen MH, Hejlesen O. Optimal data collection period for continuous glucose monitoring to assess long-term glycemic control: revisited. *J Diabetes Sci Technol*. 2023;17(3):690–695. https://doi.org/10.1177/19322968211069177.
18. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—A web and mobile app for systematic reviews. *Syst Rev*. 2016;5(1):210. https://doi.org/10.1186/s13643-016-0384-4.
19. Mourao E, Kalinowski M, Murta L, Mendes E, Wohlin C. Investigating the use of a hybrid search strategy for systematic reviews. In: *2017 ACM/IEEE International Symposium on Empirical Software Engineering and Measurement (ESEM)*. IEEE; 2017:193–198. https://doi.org/10.1109/ESEM.2017.30.
20. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*. 2019:l4898. https://doi.org/10.1136/bmj.l4898.
21. Sterne JA, Hernán MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ*. 2016:i4919. https://doi.org/10.1136/bmj.i4919.
22. Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. *BMC Med Res Methodol*. 2014;14(1):135. https://doi.org/10.1186/1471-2288-14-135.
23. Higgins JPT, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med*. 2002;21(11):1539–1558. https://doi.org/10.1002/sim.1186.
24. Lin L, Chu H, Hodges JS. Alternative measures of between-study heterogeneity in meta-analysis: reducing the impact of outlying studies. *Biometrics*. 2017;73(1):156–166. https://doi.org/10.1111/biom.12543.
25. R Core Team. In: *R: A language and environment for statistical computing*. R Foundation for Statistical Computing; 2025. https://www.R-project.org/. Accessed December 3, 2025.
26. Balduzzi S, Rücker G, Schwarzer G. How to perform a meta-analysis with R: a practical tutorial. *Evid Based Ment Health*. 2019;22(4):153–160. https://doi.org/10.1136/ebmental-2019-300117.
27. Bassi M, Franzone D, Dufour F, et al. Efficacy of advanced hybrid closed loop systems in cystic fibrosis related diabetes: a pilot study. *Front Endocrinol*. 2024;15:1347141. https://doi.org/10.3389/fendo.2024.1347141.
28. Scully KJ, Reed M, Douvas J, Putman MS, Marks BE. The effect of omnipod 5 automated insulin delivery on glycemic control in adolescents and adults with cystic fibrosis-related diabetes. *Diabetes Technol Ther*. 2025;27(9):711–718. https://doi.org/10.1089/dia.2025.0075.
29. Scully KJ, Palani G, Zheng H, Moheet A, Putman MS. The effect of control IQ hybrid closed loop technology on glycemic control in adolescents and adults with cystic fibrosis-related diabetes. *Diabetes Technol Ther*. 2022;24(6):446–452. https://doi.org/10.1089/dia.2021.0354.
30. Sherwood JS, Castellanos LE, O'Connor MY, et al. Randomized trial of the insulin-only iLet bionic pancreas for the treatment of cystic Fibrosis– related diabetes. *Diabetes Care*. 2024;47(1):101–108. https://doi.org/10.2337/dc23-1411.
31. Sherwood JS, Jafri RZ, Balliro CA, et al. Automated glycemic control with the bionic pancreas in cystic fibrosis-related diabetes: a pilot study. *J Cystic Fibrosis*. 2020;19(1):159–161. https://doi.org/10.1016/j.jcf.2019.08.002.
32. Grancini V, Cogliati I, Gaglio A, Resi V, Orsi E. Offlabel use of medtronic MiniMed 780G in the management of cystic fibrosis related diabetes in people requiring insulin total daily doses below 8 units: encouraging data from our population. *Acta Diabetol*. 2024;61(11):1483–1489. https://doi.org/10.1007/s00592-024-02329-7.
33. Grancini V, Alicandro G, Porcaro LL, et al. Effects of insulin therapy optimization with sensor augmented pumps on glycemic control and body composition in people with cystic fibrosis-related diabetes. *Front Endocrinol*. 2023;14:1228153. https://doi.org/10.3389/fendo.2023.1228153.
34. Perano S, Rayner CK, Couper J, Martin J, Horowitz M. Cystic fibrosis related diabetes—a new perspective on the optimal management of postprandial glycemia. *J Diabetes Its Complications*. 2014;28(6):904–911. https://doi.org/10.1016/j.jdiacomp.2014.06.012.
35. Marks BE, Williams KM, Sherwood JS, Putman MS. Practical aspects of diabetes technology use: continuous glucose monitors, insulin pumps, and automated insulin delivery systems. *J Clin Translational Endocrinol*. 2022;27:100282. https://doi.org/10.1016/j.jcte.2021.100282.
36. Scully KJ, Marks BE, Putman MS. Advances in diabetes technology to improve the lives of people with cystic fibrosis. *Diabetologia*. 2024;67(10):2143–2153. https://doi.org/10.1007/s00125-024-06223-3.
37. Ratti GA, Smith H, Mirfakhraee S, et al. Development of metabolic syndrome in people with cystic fibrosis one year after exposure to elexacaftor-tezacaftor-ivacaftor. *J Cystic Fibrosis*. 2025;24(1):47–52. https://doi.org/10.1016/j.jcf.2024.09.022.
38. Coderre L, Debieche L, Plourde J, Rabasa-Lhoret R, Lesage S. The potential causes of cystic fibrosis-related diabetes. *Front Endocrinol*. 2021;12:702823. https://doi.org/10.3389/fendo.2021.702823.
39. Marks BE, Kilberg MJ, Aliaj E, et al. Perceptions of diabetes technology use in cystic fibrosis-related diabetes management. *Diabetes Technol Ther*. 2021. https://doi.org/10.1089/dia.2021.0201.