Original Article

A comparison of HbA1c reduction among dipeptidyl peptidase-4 inhibitors (DPP-4) in patients with type 2 diabetes mellitus: A network meta-analysis of randomized controlled trials

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Abstract

Dipeptidyl peptidase-4 (DPP-4) inhibitors are widely used for glycemic management in type 2 diabetes mellitus (T2DM); however, their comparative efficacy in reducing glycated hemoglobin (HbA1c) remains uncertain because direct head-to-head evidence is limited. This study aimed to compare the effects of individual DPP-4 inhibitors on HbA1c reduction in patients with T2DM. A systematic review and network meta-analysis of randomized controlled trials was conducted using studies identified from PubMed, Embase, Web of Science, the Cochrane Library, and relevant reference lists up to February 20, 2026. Eligible studies compared alogliptin, linagliptin, saxagliptin, sitagliptin, or vildagliptin with placebo, either as monotherapy or as add-on treatment. Study quality was evaluated using the modified Jadad scale. Random-effects models were applied because substantial heterogeneity was identified, and comparative efficacy was ranked using P-scores. Forty-three randomized controlled trials were included. Compared with placebo, all evaluated DPP-4 inhibitors produced greater HbA1c reductions, with pooled mean differences of 0.49% for alogliptin, 0.41% for linagliptin, 0.36% for saxagliptin, 0.48% for sitagliptin, and 0.49% for vildagliptin. Network ranking indicated that alogliptin had the highest probability of providing the greatest HbA1c reduction (P-score: 0.9972), followed by linagliptin (0.7992), vildagliptin (0.6030), saxagliptin (0.3999), and sitagliptin (0.1950). No evidence of publication bias was detected. Alogliptin ranked highest for HbA1c reduction; however, substantial between-study heterogeneity, variations in follow-up duration and baseline characteristics, and the absence of comparative safety analyses warrant cautious interpretation. Treatment selection should therefore integrate glycemic efficacy with patient characteristics, safety, tolerability, and clinical context.

Keywords: Diabetes mellitus, vildagliptin, saxagliptin, alogliptin, sitagliptin

Introduction

The management of type 2 diabetes mellitus (T2DM) remains a major global health challenge. Standard guidelines for the management of T2DM have existed for at least two decades and have been updated periodically [1,2]. However, the existing guidelines have been unable to reduce the incidence of T2DM complications and mortality. In the last three decades, the elucidation of new

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potential treatments for T2DM has developed substantially [3], and over the past two decades, this effort has resulted in new treatment approaches, such as dipeptidyl peptidase-4 (DPP-4) inhibitors, sodium glucose transporter protein 2 (SGLT2) inhibitors [4], and glucagon-like peptide-1 (GLP-1) receptor agonists [5]. Those treatments, as either monotherapy or combination therapy, may be used in specific settings or complications, as commonly reported in real-world data. Of them, non-inferiority of efficacy has not been found among all treatments, either as monotherapy or in combination. Also, non-inferiority for safety has never been formally addressed [6]. However, evidence to guide the selection of the most appropriate agent within the same drug class remains limited.

DPP-4 inhibitors, commonly referred to as gliptins, are a class of antidiabetic agents that enhance glucose-dependent insulin secretion and suppress glucagon release. The drugs were first introduced for the management of T2DM in 2006 [3]. The primary mechanism of DPP-4 inhibitors is inhibition of DPP-4, an enzyme primarily involved in the metabolism of insulin and glucose. Inhibition may occur through interaction with residues in the catalytic site of the DPP-4 substrate, and through the formation of an enzyme-inhibitor complex [7]. Evidence suggests that DPP-4 inhibitors are superior for managing T2DM patients with cardiovascular diseases and have a favorable safety profile [3]. However, glucose-lowering efficacy may vary among individual DPP-4 inhibitors, and evidence from direct head-to-head comparisons remains limited [7]. Although several randomized controlled trials (RCTs) have evaluated the efficacy of DPP-4 inhibitors, their findings have been inconsistent [8-50]. Therefore, the aim of this study was to compare the effects of individual DPP-4 inhibitors on glycated hemoglobin (HbA1c) reduction in patients with T2DM using a network meta-analysis. Unlike conventional pairwise meta-analysis, which compares two interventions at a time, network meta-analysis integrates direct and indirect evidence across a connected network of trials, thereby enabling the simultaneous comparison and ranking of multiple treatments. This approach estimates the relative efficacy of different DPP-4 inhibitors, including comparisons for which direct head-to-head trials are unavailable.

Methods

Study design

A systematic review and network meta-analysis was conducted to compare the efficacy of DPP-4 inhibitors in reducing HbA1c levels among patients with T2DM. Relevant studies were identified through systematic searches of Web of Science, PubMed, the Cochrane Library, and Embase, and the required data were extracted for quantitative synthesis. The study was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [51].

Eligibility criteria

Eligible studies were required: (1) compare HbA1c levels between DPP-4 inhibitors and placebo in patients with T2DM and (2) report sufficient data to calculate the effect estimates. Reviews, letters to the editor, commentaries, non-randomized studies, and duplicate publications were excluded.

Article search and data curation

A systematic literature search was conducted through February 20, 2026, using Web of Science, Embase, PubMed, and the Cochrane Library. Before evaluating the primary outcome, potentially eligible DPP-4 inhibitors were identified for inclusion in the analysis. The search strategy was developed using terms adapted from Medical Subject Headings and included: (“DPP-4 inhibitors” OR “dipeptidyl peptidase-4 inhibitors” OR “alogliptin” OR “linagliptin” OR “saxagliptin” OR “sitagliptin” OR “vildagliptin”) AND (“HbA1c” OR “A1c” OR “hemoglobin A1c”) AND (“diabetes mellitus” OR “type 2 diabetes mellitus” OR “T2DM”). The search was restricted to articles published in English. The reference lists of relevant articles were also screened to identify additional eligible studies. When multiple publications reported data from the same study population, the publication with the largest sample size was included. Two authors (PAP, CG) independently extracted the following information from each eligible study: author and

publication year, study design, type of DPP-4 inhibitor, study setting, and HbA1c levels in the DPP-4 inhibitor and placebo groups.

Evaluation of article quality

Before inclusion, the methodological quality of eligible studies was independently assessed by two authors (PAP and CG) using the modified Jadad scale. Scores of 0–2, 3–4, and 5–8 indicated low, moderate, and high methodological quality, respectively [52]. Studies classified as low quality were excluded from the analysis.

Study variables

The primary outcome was the change in HbA1c levels, while the intervention of interest was treatment with a DPP-4 inhibitor. Based on the initial literature search conducted in Web of Science, Embase, PubMed, and the Cochrane Library, five DPP-4 inhibitors were considered eligible for inclusion in the analysis: alogliptin, linagliptin, saxagliptin, sitagliptin, and vildagliptin.

Statistical analysis

Publication bias and between-study heterogeneity were assessed before estimating the pooled effects. Publication bias was evaluated using Egger's regression test, with $p \leq 0.05$ indicating potential publication bias. Statistical heterogeneity was assessed using Cochran's Q test, with $p \leq 0.10$ indicating significant heterogeneity. A random-effects model was applied when heterogeneity was detected; otherwise, a fixed-effect model was used. The statistical significance of the pooled effect for each DPP-4 inhibitor was evaluated using the Z test, with $p \leq 0.05$ considered statistically significant. Effect estimates were expressed as mean differences (MDs) with 95% confidence intervals (CIs). To compare HbA1c reductions across individual DPP-4 inhibitors, a quantitative network meta-analysis was conducted using a random-effects model. Comparability between intervention and control groups was ensured by requiring equivalent background treatment. When a DPP-4 inhibitor was administered as monotherapy, the comparator group received placebo alone. When the inhibitor was administered as an add-on treatment, the same background therapy was required in both groups. Studies evaluating the same DPP-4 inhibitor were also required to use equivalent doses. The relative efficacy of alogliptin, linagliptin, saxagliptin, sitagliptin, and vildagliptin was estimated using MDs and corresponding 95% CIs. Treatment ranking was determined using P-scores, with higher P-scores indicating a greater probability of achieving a larger reduction in HbA1c. Confidence in the network estimates was evaluated using Confidence in Network Meta-Analysis software (CINeMA version 1.9.1, Bern, Switzerland). Pairwise meta-analyses were performed using Comprehensive Meta-Analysis software (version 2.1; Biostat, Englewood, NJ, USA), and pooled estimates were presented as forest plots.

Results

Studies selection

A total of 5,293 records were identified through database searching, and an additional 18 records were retrieved from other sources, resulting in 5,311 records after duplicate removal. During the screening stage, 5,233 records were excluded, leaving 78 full-text articles for eligibility assessment. Of these, 35 articles were excluded, comprising 12 review articles, seven commentaries, and 16 articles with inadequate data. Consequently, 43 studies were included in the meta-analysis evaluating the effects of DPP-4 inhibitors on HbA1c reduction [8-50]. The study selection process is presented in **Figure 1**. All included studies were classified as high quality based on the modified Jadad scale, and the characteristics of the included studies are summarized in **Table 1**.

Table 1. Baseline characteristics of studies included in our analysis

Study	Study design	Sample size	Dipeptidyl peptidase 4 inhibitors	Study setting	Follow-up period	Modified Jadad score
Abe *et al.*, 2016 [8]	RCT	82	Saxagliptin 5 mg	Saxagliptin vs placebo as add-on to insulin	24 weeks	6
Aschner *et al.*, 2006 [9]	RCT	473	Sitagliptin 100 mg	Sitagliptin vs placebo	24 weeks	8
Barzilai *et al.*, 2011 [10]	RCT	192	Sitagliptin 100 mg	Sitagliptin vs placebo as add-on to standard treatment	24 weeks	8
Bryzinski *et al.*, 2014 [11]	RCT	3567	Saxagliptin 5 mg	Saxagliptin vs placebo as add-on to sulfonylurea	24 weeks	6
Charbonnel *et al.*, 2006 [12]	RCT	677	Sitagliptin 100 mg	Sitagliptin vs placebo as add-on to metformin	24 weeks	8
Chien *et al.*, 2011 [13]	RCT	97	Sitagliptin 100 mg	Sitagliptin vs placebo as add-on to sulfonylurea	24 weeks	5
DeFronzo *et al.*, 2008 [14]	RCT	195	Alogliptin 25 mg	Alogliptin vs placebo	26 weeks	7
Dejager *et al.*, 2007 [15]	RCT	312	Vildagliptin 50 mg	Vildagliptin vs placebo	24 weeks	7
Del-Prato *et al.*, 2011 [16]	RCT	496	Linagliptin 5 mg	Linagliptin vs placebo as add-on to standard treatment	24 weeks	7
Dobs *et al.*, 2013 [17]	RCT	256	Sitagliptin 100 mg	Sitagliptin vs placebo as add-on to metformin	54 weeks	8
Farngren *et al.*, 2012 [18]	RCT	28	Vildagliptin 50 mg	Vildagliptin vs placebo as add-on to insulin	4 weeks	5
Fonseca *et al.*, 2007 [19]	RCT	296	Vildagliptin 50 mg	Vildagliptin vs placebo as add-on to insulin	24 weeks	6
Fonseca *et al.*, 2013 [20]	RCT	313	Sitagliptin 100 mg	Sitagliptin vs placebo as add-on to pioglitazone	26 weeks	7
Garber *et al.*, 2008 [21]	RCT	276	Vildagliptin 50 mg	Vildagliptin vs placebo as add-on to glimepiride	24 weeks	7
Gomis *et al.*, 2011 [22]	RCT	389	Linagliptin 5 mg	Linagliptin vs placebo as add-on to pioglitazone	24 weeks	6
Haak *et al.*, 2012 [23]	RCT	287	Linagliptin 5 mg	Linagliptin vs placebo as add-on to metformin	24 weeks	7
Hollander *et al.*, 2011 [24]	RCT	370	Saxagliptin 5 mg	Saxagliptin vs placebo as add-on to thiazolidinedione	76 weeks	6
Isik *et al.*, 2017 [25]	RCT	205	Sitagliptin 100 mg	Sitagliptin vs placebo as add-on to metformin	6 months	6
Kanazawa *et al.*, 2017 [26]	RCT	71	Vildagliptin 50 mg	Vildagliptin vs placebo as add-on to insulin	24 months	5
Kawamori *et al.*, 2012 [27]	RCT	239	Linagliptin 5 mg	Linagliptin vs placebo as add-on to voglibose	26 weeks	6
Kikuchi *et al.*, 2009 [28]	RCT	148	Vildagliptin 50 mg	Vildagliptin vs placebo	12 weeks	6
Li *et al.*, 2020 [29]	RCT	88	Sitagliptin 100 mg	Sitagliptin vs placebo as add-on to acarbose	24 weeks	6
Nauck *et al.*, 2009 [30]	RCT	314	Alogliptin 25 mg	Alogliptin vs placebo as add-on to metformin	26 weeks	8
Owens *et al.*, 2011 [31]	RCT	1040	Linagliptin 5 mg	Linagliptin vs placebo as add-on to metformin and sulfonylurea	24 weeks	6
Pan *et al.*, 2012 [32]	RCT	551	Saxagliptin 5 mg	Saxagliptin vs placebo as add-on to metformin	24 weeks	6
Pratley *et al.*, 2009 [33]	RCT	297	Alogliptin 25 mg	Alogliptin vs placebo as add-on to glyburide	26 weeks	8
Raz *et al.*, 2006 [35]	RCT	296	Sitagliptin 100 mg	Sitagliptin vs placebo	18 weeks	8
Raz *et al.*, 2008 [34]	RCT	187	Sitagliptin 100 mg	Sitagliptin vs placebo as add-on to metformin	30 weeks	7
Rezki *et al.*, 2020 [36]	RCT	24	Saxagliptin 5 mg	Saxagliptin vs placebo	12 weeks	6
Rosenstock *et al.*, 2009 [37]	RCT	195	Saxagliptin 5 mg	Saxagliptin vs placebo	24 weeks	7
Rosenstock *et al.*, 2010 [38]	RCT	327	Alogliptin 25 mg	Alogliptin vs placebo as add-on to pioglitazone	26 weeks	6
Scalzo *et al.*, 2019 [39]	RCT	24	Sitagliptin 100 mg	Sitagliptin vs placebo as add-on to sulfonylurea	3 months	5
Scherbaum *et al.*, 2008 [40]	RCT	131	Vildagliptin 50 mg	Vildagliptin vs placebo	52 weeks	6
Scherbaum *et al.*, 2008 [41]	RCT	306	Vildagliptin 50 mg	Vildagliptin vs placebo	52 weeks	6
Sjöstrand *et al.*, 2014 [42]	RCT	429	Saxagliptin 5 mg	Saxagliptin vs placebo as add-on to metformin	24 weeks	6
Strain *et al.*, 2013 [43]	RCT	274	Vildagliptin 50 mg	Vildagliptin vs placebo	24 weeks	8
Tanimura-Inagaki *et al.*, 2020 [44]	RCT	164	Sitagliptin 100 mg	Sitagliptin vs placebo as add-on to sulfonylurea	6 months	5
Taskinen *et al.*, 2011 [45]	RCT	700	Linagliptin 5 mg	Linagliptin vs placebo as add-on to metformin	24 weeks	6
Vilsbøll *et al.*, 2010 [46]	RCT	641	Sitagliptin 100 mg	Sitagliptin vs placebo as add-on to insulin	24 weeks	8
White *et al.*, 2013 [47]	RCT	5380	Alogliptin 25 mg	Alogliptin vs placebo as add-on to insulin	36 months	6
Williams-Herman *et al.*, 2010 [48]	RCT	372	Sitagliptin 100 mg	Sitagliptin vs placebo as add-on to metformin	104 weeks	8
Yang *et al.*, 2011 [49]	RCT	570	Saxagliptin 5 mg	Saxagliptin vs placebo as add-on to metformin	24 weeks	8
Yoon *et al.*, 2011 [50]	RCT	520	Sitagliptin 100 mg	Sitagliptin vs placebo as add-on to pioglitazone	24 weeks	6

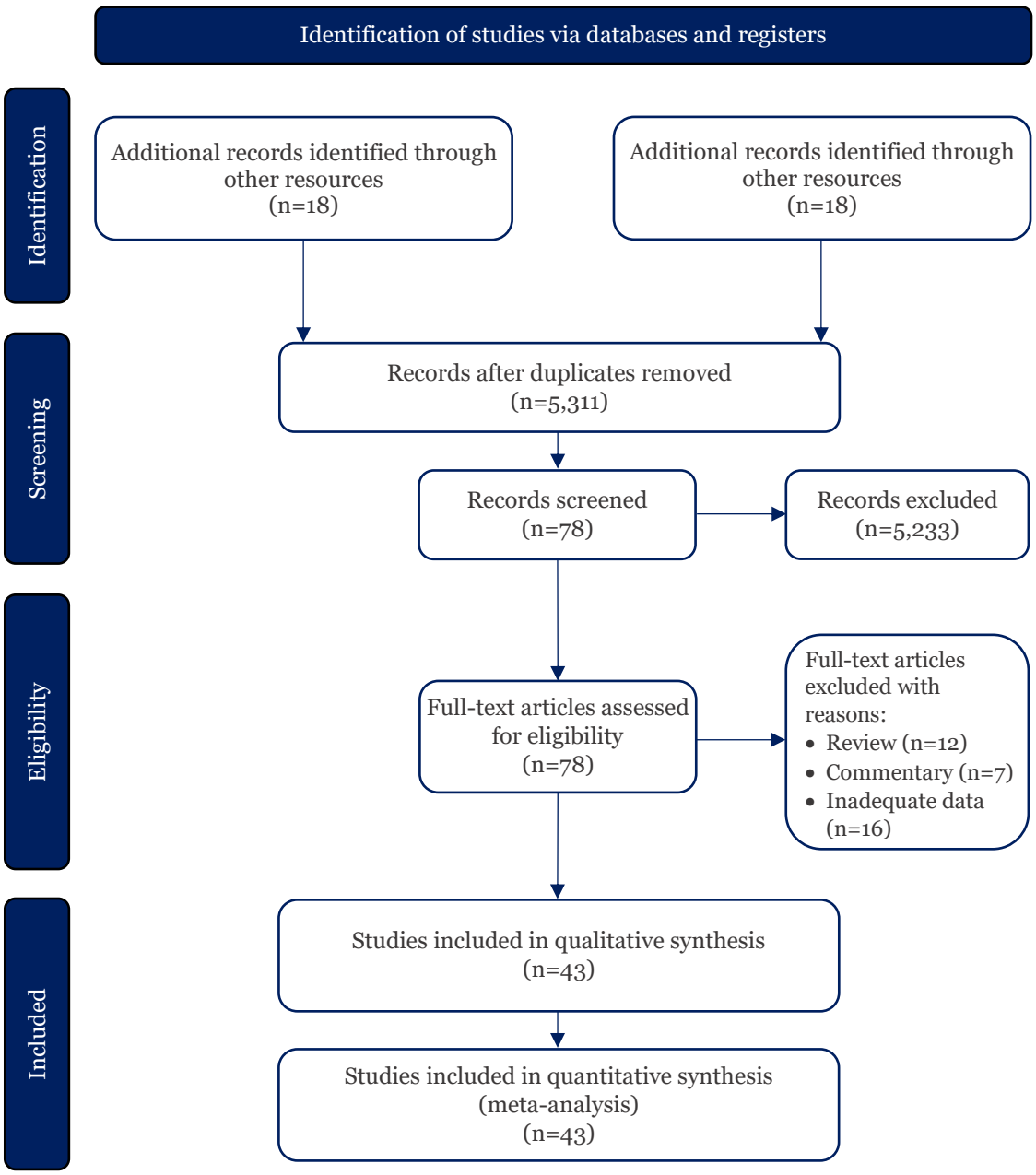


Figure 1. Flow diagram of the study selection process.

Efficacy of DPP-4 inhibitors in reducing the levels of HbA1C

Five studies [14,30,33,38,47] compared changes in HbA1c levels between alogliptin and placebo (**Figure 2A**). The pooled analysis showed that alogliptin produced a greater reduction in HbA1c than placebo, with an MD of 0.49% (**Table 2**). Similarly, six studies [16,22,23,27,31,45] evaluating linagliptin demonstrated a greater HbA1c reduction than placebo (MD: 0.41%) (**Figure 2B** and **Table 2**). Saxagliptin was also associated with a greater reduction in HbA1c compared with placebo (MD: 0.36%) (**Figure 2C** and **Table 2**). The corresponding reductions for sitagliptin and vildagliptin were 0.48% and 0.49%, respectively, compared with placebo (**Figure 2D**, **Figure 2E** and **Table 2**).

Table 2. Summary of pairwise meta-analysis of HbA1c reduction with DPP-4 inhibitors compared with placebo

DPP4 inhibitors	Number of studies	Change of HbA1C levels (%), mean±SD		Mean difference (MD)	*p* Egger	*p* Het	*p*-value
		DPP4 inhibitor	Placebo				
Alogliptin	5	0.75±0.55	0.26±0.50	0.49	0.1680	<0.0001	<0.0001

DPP4 inhibitors	Number of studies	Change of HbA1C levels (%), mean±SD		Mean difference (MD)	*p* Egger	*p* Het	*p*-value
		DPP4 inhibitor	Placebo				
Linagliptin	6	0.72±0.42	0.31±0.30	0.41	0.2110	<0.0001	<0.0001
Saxagliptin	8	0.65±0.31	0.24±0.13	0.36	0.0740	<0.0001	<0.0001
Sitagliptin	15	0.87±0.56	0.37±0.44	0.48	0.2040	<0.0001	<0.0001
Vildagliptin	9	0.62±0.33	0.13±0.09	0.49	0.2980	<0.0001	<0.0001

DPP4: dipeptidyl peptidase 4; *p* Het: *p* heterogeneity; SD: standard deviation

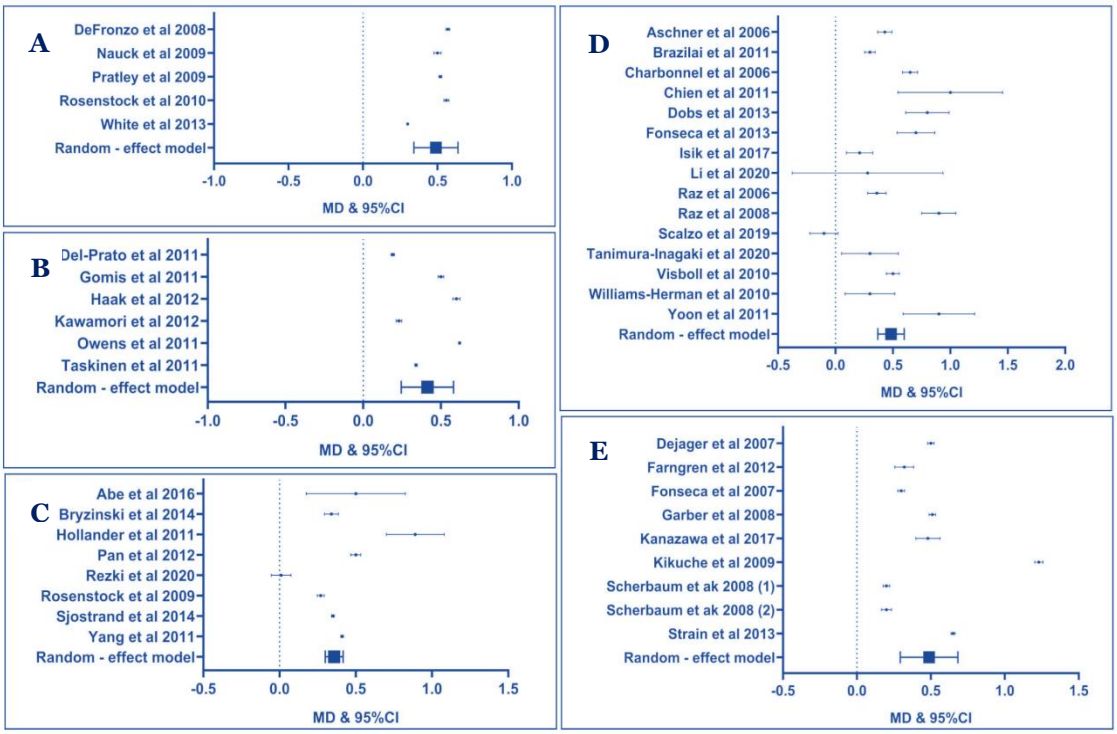
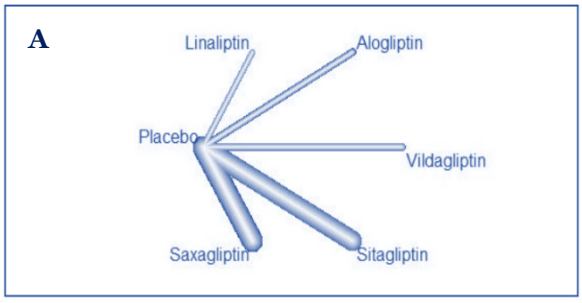


Figure 2. Forest plots of glycated hemoglobin (HbA1c) reduction with individual dipeptidyl peptidase-4 (DPP-4) inhibitors compared with placebo: (A) alogliptin [14,30,33,38,47]; (B) linagliptin [16,22,23,27,31,45]; (C) saxagliptin [8,11,24,32,36,37,42,49]; (D) sitagliptin [9,10,12,13,17,20,25,29,34,35,39,44,46,48,50]; and (E) vildagliptin [15,18,19,21,26,28,40,41,43].

In the network ranking analysis, alogliptin had the highest P-score (0.9972), followed by linagliptin (0.7992), vildagliptin (0.6030), saxagliptin (0.3999), and sitagliptin (0.1950) (**Figure 3**). These findings indicated that alogliptin had the highest probability of achieving the greatest HbA1c reduction among the evaluated DPP-4 inhibitors.



B

DPP4 - inhibitors	P - score
Alogliptin	0.9972
Linagliptin	0.7992
Vildagliptin	0.6030
Saxagliptin	0.3999
Sitagliptin	0.1950

Figure 3. Network meta-analysis and ranking of dipeptidyl peptidase-4 (DPP-4) inhibitors for reducing glycated hemoglobin (HbA1c) levels. (A) Network plot illustrating comparisons among individual DPP-4 inhibitors; thicker connecting lines represent comparisons with larger sample sizes. (B) P-score ranking of the evaluated DPP-4 inhibitors, with higher P-scores indicating greater relative efficacy in reducing HbA1c levels.

Heterogeneity and publication bias

Significant heterogeneity was detected across all pairwise meta-analyses; therefore, pooled effect estimates were calculated using random-effects models. Publication bias was assessed using Egger's regression test, which showed no evidence of significant publication bias for any evaluated DPP-4 inhibitor (**Table 2**).

Discussion

This network meta-analysis demonstrated that all evaluated DPP-4 inhibitors were associated with greater reductions in HbA1c levels than placebo. In the comparative ranking analysis, alogliptin, linagliptin, and vildagliptin ranked higher than saxagliptin and sitagliptin, with alogliptin having the highest P-score. Nevertheless, these rankings represent the relative probabilities derived from the available direct and indirect evidence and should not be interpreted as definitive proof of clinical superiority, particularly given the substantial heterogeneity across the included studies.

The present findings are generally consistent with those reported by previous studies [53,54] that identified differences in glycemic efficacy among individual DPP-4 inhibitors. A study reported that vildagliptin was associated with greater reductions in insulin requirements and improved glycemic control compared with sitagliptin and linagliptin [53]. Similarly, another study demonstrated variation among DPP-4 inhibitors in achieving glycemic targets [54]. In contrast, a study reported broadly comparable efficacy among DPP-4 inhibitors administered as monotherapy or combination therapy [55]. These differences may reflect variations in study selection, network structure, background treatment, drug combinations, follow-up duration, baseline HbA1c levels, and participant characteristics. In the present analysis, studies involving add-on therapy were included only when the background treatment was comparable between the intervention and control groups, which may have reduced confounding attributable to unequal concomitant therapies.

Although DPP-4 inhibitors share a common glucose-lowering mechanism, their molecular interactions, binding kinetics, pharmacodynamic profiles, and duration of enzyme inhibition may differ. These pharmacological differences could partly explain the observed variation in HbA1c reduction. DPP-4 inhibition prevents the degradation of incretin hormones, particularly glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1, thereby enhancing glucose-dependent insulin secretion and suppressing glucagon release. Vildagliptin exhibits prolonged substrate-like binding to the catalytic site of DPP-4, whereas sitagliptin acts through competitive inhibition, potentially resulting in differences in the magnitude and duration of enzyme inhibition [56]. Nevertheless, the clinical relevance of these mechanistic differences remains uncertain, and the treatment rankings observed in this meta-analysis should not be attributed solely to pharmacological properties.

An important strength of this study was the simultaneous comparison of five DPP-4 inhibitors by integrating direct and indirect evidence within a network meta-analytic framework. The analysis also applied predefined comparability criteria for background therapy and drug dose and was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. These features improve the transparency and interpretability of the findings. Clinically, the results suggest that alogliptin, linagliptin, and vildagliptin may provide comparatively greater HbA1c reductions than saxagliptin and sitagliptin. However, treatment selection should not be based exclusively on HbA1c reduction. Patient characteristics, comorbidities, renal and hepatic function, potential drug interactions, tolerability, accessibility, and safety should also be considered.

The present analysis evaluated glycemic efficacy but did not compare adverse events among individual DPP-4 inhibitors. Previous reports have raised concerns regarding pancreatitis following sitagliptin treatment, while separate safety evaluations have examined adverse events associated with vildagliptin [57,58]. However, these findings do not provide sufficient evidence for direct comparative safety conclusions. Therefore, the efficacy rankings reported in this study should not be interpreted as recommendations to preferentially prescribe one DPP-4 inhibitor over another without considering the overall benefit–risk profile. Further adequately powered

head-to-head randomized controlled trials are required to compare both efficacy and safety across individual agents.

Several limitations should be acknowledged. First, potentially influential patient-level factors, including body mass index, diabetes-related complications, baseline laboratory characteristics, previous treatment response, and concomitant drug use, could not be incorporated into the analysis. Second, the number of studies and sample sizes differed across treatment comparisons, which may have affected the precision of the pooled estimates and treatment rankings. Third, variation in study settings and participant characteristics may have contributed to the substantial between-study heterogeneity. Fourth, follow-up durations varied considerably, precluding meaningful subgroup analyses according to treatment duration. Fifth, baseline HbA1c levels differed among the included studies and may have influenced the magnitude of treatment response. Consequently, although comparable intervention and background-treatment conditions were required within individual trials, the findings should be interpreted cautiously because residual clinical and methodological heterogeneity remained.

Conclusion

All evaluated DPP-4 inhibitors were associated with greater reductions in HbA1c levels than placebo in patients with T2DM. In the network meta-analysis, alogliptin, linagliptin, and vildagliptin ranked higher than saxagliptin and sitagliptin, with alogliptin showing the highest probability of achieving the greatest HbA1c reduction. However, these findings should be interpreted cautiously because of substantial between-study heterogeneity and variations in study characteristics. Further head-to-head trials comparing both efficacy and safety are warranted before definitive treatment preferences can be established.

Ethics approval

Not required.

Acknowledgments

None.

Competing interests

The authors declare that there are no conflicts of interest.

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Underlying data

All data generated or analysed during this systematic review and meta-analysis are presented in the article and its supplementary materials. The complete data-extraction dataset and statistical analysis outputs are available from the corresponding author upon request.

Declaration of artificial intelligence use

Artificial intelligence tool, ChatGPT, was used for language refinement, including improvement of grammar, sentence structure, and readability. Authors confirm that all AI-assisted processes were critically reviewed by the authors to ensure the integrity and reliability of the results. The final decisions and interpretations presented in this article were made solely by the authors.

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