Supplemental Material

Supplementary Methods

Supplementary Methods 1a. Additional Information.

Additional information on the search strategies, study exclusions as well as exclusion criteria of included studies are presented in Supplemental Methods 2a-2c and Supplementary Table S1 and Table S2 respectively. The risk of bias assessment for Randomised Controlled Trials included in the review and results from the Newcastle Ottawa Scale as applied to the non-randomised studies included is presented in Supplementary Table S3 and Table S4 respectively. Analysis Approaches and methods used to control confounding in the non-randomised studies is presented in Supplementary Table S5.

Forest plots for outcomes for HbA1c change from baseline in mmol/mol, proportion achieving a HbA1c < 6.5% by study end and change from baseline in Body Mass Index are presented in Supplementary Figures S1-S2.

Supplementary Methods 2a. Search Strategy in EMBASE.

Database: Embase <1980 to 2015 Week 43>
Search Strategy:
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1 exp metformin/ (39879)
2 metformin.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (41520)
3 glucophage.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (1473)
4 dimethylbiguanidine.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (3)
5 dimethylguanylguanidine.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (2)
6 1 or 2 or 3 or 4 or 5 (41532)
7 exp sitagliptin/ (5031)
8 sitagliptin.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (5216)
9 Januvia.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (698)
10 ("Mk 0431" or mk 431 or mk0431 or mk431 or ono 5435 or ono5435).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (193)
11 ristaben.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (8)
12 sitagliptine.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (48)
13 tesavel.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (12)
14 xelevia.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (32)
15 Glactiv.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (7)
16 or/7-15 (5228)
17 6 and 16 (3046)
18 exp sulfonylurea/ (10374)
19 sulphonylurea*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (2940)
20 sulphonylureas.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (1328)
21 sulfonylurea*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (22171)
22 sulfonylurea.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (20994)
23 (sulfonurea or sulfonyl urea or sulfonylcarbamide or sulphonurea).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (168)
24 or/18-23 (23245)
25 17 and 24 (1651)
26 Clinical study/ (70420)
27 Case control study.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (133957)

28 Family study/ (10937)
29 Longitudinal study/ (82511)
30 Retrospective study/ (432735)
31 Prospective study/ (311493)
32 Randomized controlled trials/ (85652)
33 31 not 32 (309109)
34 Cohort analysis/ (220411)
35 (Cohort adj (study or studies)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (150359)
36 (Case control adj (study or studies)).tw. (88705)
37 (follow up adj (study or studies)).tw. (47930)
38 (observational adj (study or studies)).tw. (82562)
39 (epidemiologic$ adj (study or studies)).tw. (80707)
40 (cross sectional adj (study or studies)).tw. (109506)
41 or/26-30,33-40 (1421985)
42 Clinical trial/ (852134)
43 Randomized controlled trial/ (386850)
44 Randomization/ (68432)
45 Single blind procedure/ (21172)
46 Double blind procedure/ (124394)
47 Crossover procedure/ (44827)
48 Placebo/ (264947)
49 Randomi?ed controlled trial$.tw. (125572)
50 Rct.tw. (18572)
51 Random allocation.tw. (1460)
52 Randomly allocated.tw. (23491)
53 Allocated randomly.tw. (2066)
54 (allocated adj2 random).tw. (739)
55 Single blind$.tw. (16493)
56 Double blind$.tw. (155737)
57 ((treble or triple) adj blind$).tw. (496)
58 Placebo$.tw. (222385)
59 Prospective study/ (311493)
60 or/42-59 (1514373)
61 Case study/ (34294)
62 Case report.tw. (292773)
63 Abstract report/ or letter/ (941827)
64 or/61-63 (1262329)
65 60 not 64 (1474343)
66 41 or 65 (2525050)
67 25 and 66 (992)

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Supplementary Methods 2b. Search Strategy in MEDLINE.

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>
Search Strategy:
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1 exp Metformin/ (8560)
2 metformin.mp. (13210)
3 glucophage.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (94)
4 dimethylbiguanidine.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1)
5 dimethylguanylguanidine.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (2)
6 1 or 2 or 3 or 4 or 5 (13226)
7 sitagliptin.mp. (1351)
8 Januvia.mp. (43)
9 ("Mk 0431" or mk 431 or mk0431 or mk431 or ono 5435 or ono5435).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (25)
10 ristaben.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (0)
11 sitagliptine.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (22)
12 tesavel.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (2)
13 xelevia.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1)
14 Glactiv.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (2)
15 or/7-14 (1363)
16 6 and 15 (436)
17 exp Sulfonylurea Compounds/ (16939)
18 sulphonylurea*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (2125)
19 sulphonylureas.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (981)
20 sulfonylurea*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (9629)

21 (sulfonurea or sulfonyl urea or sulfonylcarbamide or sulphonurea).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (114)
22 or/17-21 (21242)
23 16 and 22 (150)
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Supplementary Methods 2c. Search Strategy in CENTRAL.

ID	Search
#1	"Metformin"
#2	"glucophage"
#3	"dimethylbiguanidine"
#4	"dimethylguanylguanidine"
#5	#1 or #2 or #3 or #4
#6	"sitagliptin"
#7	"Januvia"
#8	("Mk 0431" or mk 431 or mk0431 or mk431 or ono 5435 or ono5435)
#9	"ristaben"
#10	"sitagliptine"
#11	"tesavel"
#12	"xelevia"
#13	"Glactiv"
#14	#6 or #7 or #8 or #9 or #10 or #11 or #12 or #13
#15	#5 and #14
#16	"sulphonylurea"
#17	"sulphonylurea$"
#18	"sulfonylurea"
#19	"sulfonylurea*"
#20	(sulfonurea or sulfonyl urea or sulfonylcarbamide or sulphonurea)
#21	#16 or #17 or #18 or #19 or #20
#22	#15 and #21 in Trials

Table S1 Rationale for exclusion of studies following review of full publications.

Studies excluded	Rationale for exclusion
1. The incidence of hypoglycaemia in Muslim patients with type 2 diabetes treated with sitagliptin or a sulphonylurea during Ramadan: a randomised trial [1]	**Unsuitable comparator** - Patients were not required to be on metformin
2. Sitagliptin Use in Patients With Diabetes and Heart Failure [2]	**Unsuitable comparator** - Patients were not required to be on metformin and sulphonylurea not used.
3. Safety and effectiveness of non-insulin glucose-lowering agents in the treatment of people with type 2 diabetes who observe Ramadan: a systematic review and meta-analysis [3]	**Review/Meta-analysis only**
4. Roadmap for oral antidiabetic therapy when sulfonylurea-metformin combination failed[4]	**Unsuitable comparator** – No sulphonylurea comparator group
5. Combination Therapy with a Dipeptidyl Peptidase-4 Inhibitor, Sulfonylurea, and Metformin Markedly Improves HbA1c Levels in Japanese Patients with Type 2 Diabetes Mellitus[5]	**Unsuitable comparator** - Case series with 3 patients and unsuitable comparators.
6. Comparative Study of Three DPP-4 Inhibitors, Namely Sitagliptin, Vildagliptin, and Alogliptin, in Japanese Type 2 Diabetic Patients: The COSVA Randomized, Controlled Trial[6]	**Unsuitable comparator** - No sulphonylurea comparator group
7. Real world clinical effectiveness of sitagliptin therapy for management of type 2 diabetes: a retrospective database analysis[7]	**Unsuitable comparator -** No sulphonylurea comparator group
8. The tolerability and safety of DPP-4 inhibitors for the treatment of older people with type 2 diabetes mellitus: an observational study[8]	**Unsuitable comparator -** No sulphonylurea comparator group
9. A single centre retrospective 12 months follow up study of safety and efficacy of sitagliptin[9]	**Unsuitable comparator** - Conference abstract where multiple unclear comparison groups
10. Retrospective Analysis on the Efficacy, Safety and Treatment Failure Group of Sitagliptin for Mean 10-Month Duration[10]	**Unsuitable comparator** - No sulphonylurea comparator group
11. Effect of sitagliptin on cardiovascular outcomes in type 2 diabetes[11]	**Unsuitable comparator** - No sulphonylurea comparator group
12. Comparative safety and effectiveness of sitagliptin in patients with type 2 diabetes: retrospective population based cohort study[12]	**Unsuitable comparator -** No sulphonylurea comparator group
13. Sitagliptin After Ischemic Stroke in Type 2 Diabetic Patients: A Nationwide Cohort Study[13]	**Unsuitable comparator -** No sulphonylurea comparator group
14. Hypoglycaemia in patients with type 2 diabetes from India and Malaysia treated with sitagliptin or a sulfonylurea during Ramadan: a randomized, pragmatic study[14]	**Unsuitable comparator -** No sulphonylurea comparator group
15. Cardiovascular Outcomes of Sitagliptin in Type 2 Diabetic Patients with Acute Myocardial Infarction, a Population-Based Cohort Study in Taiwan[15]	**Unsuitable comparator** - Comparator group could be on a multitude of different medicines not just sulphonylureas
16. Lower risk of hypoglycaemia with sitagliptin compared to glipizide when either is added to metformin therapy: a pre-specified analysis adjusting for the most recently measured HbA1c value[16]	**Safety only** – No efficacy/effectiveness outcome reported. Only hypoglycaemia incidence reported.

Studies excluded	Rationale for exclusion
17. A comparison of the effects of the DPP-4 inhibitor sitagliptin and the sulfonylurea glimepiride on metabolic parameters and endothelial function[17]	**Unsuitable comparator** – Patients not required to be on metformin.
18. Duration of maintenance of dual therapy with metformin and sitagliptin in type 2 diabetes[18]	**Conference abstract only** with full study reported elsewhere and included.
19. Comparative Efficacy of Adding Sitagliptin to Metformin, Sulfonylurea or Dual Therapy: A Propensity Score-Weighted Cohort Study[19]	**Unsuitable comparator –** Comparator involve sitagliptin and sulphonylurea used together not sulphonylurea and metformin.
20. Treatment maintenance duration of dual therapy with metformin and sitagliptin in type 2 diabetes-real-world data from odyssee study.[20]	**Conference abstract only** with full study reported elsewhere and included.
21. Assessing time to insulin use among type 2 diabetes patients treated with sitagliptin or sulfonylurea plus metformin dual therapy[21]	**Conference abstract only** with full study reported elsewhere and included.
22. Clinical efficacy of sitagliptin as add-on to metformin, sulphonylurea or metformin sulphonylurea combined therapy: A propensity score matched cohort study[22]	**Unsuitable comparator** and **Conference abstract** only
23. To compare the hypoglycaemic effect of sitagliptin/ metformin combination vs glimepiride in type II diabetes patients during Ramadan[23]	**Safety only** – hypoglycaemia only outcome reported
24. Sitagliptin more effectively achieves a composite endpoint for A1C reduction, lack of hypoglycemia and no body weight gain compared with glipizide[24]	**Unsuitable composite** endpoint reported only
25. Efficacy and safety of the dipeptidyl peptidase-4 inhibitor sitagliptin, in patients with type 2 diabetes mellitus inadequately controlled on glimepiride alone or on glimepiride and metformin[25]	**Unsuitable comparator** arm consisting of use of combination of sitagliptin and glimepiride together
26. Efficacy and tolerability of the dipeptidyl peptidase-4 inhibitor sitagliptin as monotherapy over 12 weeks in patients with type 2 diabetes[26]	**Unsuitable comparator** – placebo controlled
27. Diabetes mellitus in the young: Gliptins or sulfonylurea after metformin?[27]	**Unclear diagnosis -** Patients not confirmed as having Type 2 Diabetes Mellitus and may have any type of diabetes
28. Comparison on adding sitagliptin or glimepiride in poorly controlled overweight type 2 diabetes with oral metformin[28]	Publication only available in **Chinese**
29. A comparison of glycaemic effects of sitagliptin and sulfonylureas in elderly patients with type 2 diabetes mellitus[29]	**Pooled Study** of elderly patients from three trials

Table S2 Major exclusion criteria across included studies

Author & Publication date	Major Exclusion Criteria
Ahren et al (2014)[30]	Type 1 Diabetes, used any anti-diabetic besides metformin within 12 weeks of screening had renal function impairment prohibiting the use of metformin or had a fasting
Arech. et al (2010)[31]	Type 1 Diabetes, pregnancy, current symptomatic heart failure (NYHA Class III or IV), symptomatic biliary disease or history of pancreatitis, recent clinically significant cardiovascular and/or cerebrovascular disease (≤2 months before screening), treated gastroparesis, history of GI surgery thought to significantly affect upper GI function, history of most cancers not in remission for at least 3 years, personal or family history of medullary thyroid carcinoma or multiple endocrine neoplasia type 2, resting systolic blood pressure >160 mmHg and/or diastolic blood pressure >100 mmHg, lipase above the upper limit of normal (ULN), hemoglobinopathy that could affect HbA1c, and alanine aminotransferase or aspartate aminotransferase more than 2.5 times the ULN.
Kim et al (2013)[32]	Major hepatopathy, ischemic heart disease or cerebrovascular disease or a history of such disease, a creatinine level > 0.133mmol/L, treatment with agents other than metformin or other medicine that might influence blood glucose and steroid levels and major diabetes complications (chronic renal insufficiency, proliferative retinopathy, stroke)
Koren et al (2012)§[33]	Creatinine clearance < 30mL/min, a history of treatment with incretins or sulfonylurea during the last 3 months, treatment with nitrates, uncontrolled heart failure, uncontrolled hypertension, and/or any change in the hypertensive medications within 1 month prior to starting the study, malignancy, and pregnancy
Nauck et al (2007)[34]	Type 1 Diabetes, renal impairment, insulin use within 8 weeks of screening, Fasting Plasma Glucose >15mmol/l, and if on non-stable doses of lipid lowering, anti-hypertensive, thyroid medications, hormone replacement therapy or birth control medication.
Seck et al (2010)†[35]	Type 1 Diabetes, renal impairment, insulin use within 8 weeks of screening, Fasting Plasma Glucose >15mmol/l, and if on non-stable doses of lipid lowering, anti-hypertensive, thyroid medications, hormone replacement therapy or birth control medication.
Sriva. et al (2012)[36]	Type 1 Diabetes, evidence of cardiac failure, evidence of hepatic or renal insufficiency or other terminal illnesses
Derosa et al(2015)[37]	Patients with a history of ketoacidosis, unstable or rapidly progressive diabetic retinopathy,nephropathy, neuropathy; impaired hepatic function, impaired renal function, severe anemia, New York Heart Association class I–IV congestive heart failure, history of myocardial infarction or stroke, cerebrovascular conditions within 6 months before study enrolment, history of cancer and pancreatitis
Inzuc. et al (2015)[38]	Type 1 Diabetes, gestational or secondary diabetes, non-metformin anti-diabetic use and no prescription for other OADs in the first 90 days after the index date.
Lee et al (2013)[39]	Recent (≤6 months) history of major cardiovascular event; current hepatic, renal, hematologic, or gastrointestinal disease or those that had undergone systemic corticosteroid treatment in the previous 12 weeks.
Suraj et al (2015)[40]	Type 1 Diabetes, on insulin, with secondary diabetes, experiencing complications on or during treatment plan, known or suspected hypersensitivity to study drugs, co-morbid illness such as cardiovascular diseae, renal failure and liver disease.
Valen. et al (2015)[41]	No exclusion criteria specified

Table S3 Risk of Bias Assessment for included Randomised Controlled Trials

RCT Study Bias Domain	Selection Bias	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other
	Sequence generation	Allocation Concealment	Blinded to Participants/ personnel	Blinded to Outcome Assessors	Incomplete outcome data	Selective outcome reporting	Other bias
Ahren et al [30]	Unc	Unc	Low	Low	Low	Low	Low
Arechaveleta et al [31]	Low	Low	Low	Low	Unc	Low	Low
Kim et al [32]	Unc	Unc	Low	Low	Low	High	Low
Koren et al [33]	High	High	High	Low	Low	Low	Low
Nauck et al [34]	Low	Low	Low	Low	Low	Low	Low
Seck et al [35]	Low	Low	Low	Low	Unc	Low	Low
Srivastava et al [36]	Low	Low	High	Low	Unc	Unc	High

Low, Low risk of Bias; High, High Risk of Bias; Unc, Unclear Risk of Bias

Table S4 Quality Assessment of non-randomised observational studies using Newcastle Ottawa Scale

Non-randomised Study	Study Design	Selection (Out of 4)	Comparability (Out of 2)	Outcome (Out of 3)	Evidence Quality (low/moderate/high)
Derosa et al [37]	Prospective Cohort	* * *	*	* *	Low
Inzucchi et al [38]	Retrospective Cohort	* * * *	* *	* * *	High
Lee et al [39]	Prospective Cohort	* * *	* *	* *	Moderate
Suraj et al [40]	Prospective Cohort	* * * *		*	Low
Valensi et al [41]	Prospective Cohort	* * * *	* *	* * *	High

Table S5 Analysis Approaches and methods used to control confounding in non-randomised observational studies

Non-Randomised Study	Study Design	Analysis Approach	Confounders Accounted for	Potential Confounders Not Accounted for
Derosa et al [37]	Prospective Cohort	Matched analysis for age, sex and diabetes duration, Strict inclusion criteria and though limited data provided on baseline characteristics, the groups were well matched for characteristics reported.	Age, sex, diabetes duration as discussed	There were several additional variables Derosa et al did not control for in their analysis which could have introduced confounding in their presented results. These include confounders relating to diet, socioeconomic status, concomitant medication and comorbidities
Inzucchi et al [38]	Retrospective Cohort	The authors incorporate several design features to minimise bias and account for confounders 1. Large sample size from large database 2. Propensity Score matching analysis to ensure more accurate comparison. 3. Prespecified sensitivity analysis conducted exploring impact of missing data and subgroups	Propensity score matching created 3864 matched pairs with no significant differences in baseline characteristics across a wide range of baseline demographic, geographical, laboratory measurements as well as comorbidities.	We did not identify any further confounders that Inzucchi et al had not already accounted for in analysis.
Lee et al [39]	Prospective Cohort	Strict inclusion criteria meant that despite lack of randomisation, no significant difference was evident in baseline characteristics reported.	No confounders adjusted for in analysis however Ki lee et al have demonstrated that baseline characteristics were highly similar for demographic and anthropometric characteristics	There were several additional variables Lee et al did not control for in their analysis which could have introduced confounding in their presented results. These include confounders relating to diet, socioeconomic status,

Non-Randomised Study	Study Design	Analysis Approach	Confounders Accounted for	Potential Confounders Not Accounted for
				concomitant medication and comorbidities (most comorbid individuals were however excluded by Lee et al through their study exclusion criteria – see Table S2)
Suraj et al [40]	Prospective Cohort	Several differences were evident in baseline characteristics including across gender, fasting plasma glucose, diabetes duration and no adjustments made in final analysis	No adjustments made to account for confounding in final analysis	Suraj et al did not undertake any adjustments to account for potential confounding relating to demographic variables such as age, sex, HbA1c and metformin dose. There may be other confounders too relating to concomitant prescribed medications and certain comorbidities which were not accounted for as well (though some of these individuals may have been excluded by Suraj et al by their study exclusion criteria – see Table S2)
Valensi et al [41]	Prospective Cohort	The authors incorporate several design features to minimise bias and account for confounders 1. Physicians were asked to enrol individuals that were deemed by their judgement equally eligible for sitagliptin or sulphonylurea 2. Propensity Score was generated using a broad range of demographic, clinical measures e.g. HbA1c etc., comorbidity and treatment confounders and used to adjust final analysis	Propensity scores were calculated for an extensive range of potential confounding characteristics and used to adjust final analysis	We did not identify any further confounders that Valensi et al had not already accounted for in analysis.

Non-Randomised Study	Study Design	Analysis Approach	Confounders Accounted for	Potential Confounders Not Accounted for
		3. Time varying confounders which may have introduced bias after study initiation were also analysed 4. Several sensitivity analysis were conducted exploring impact of missing data		

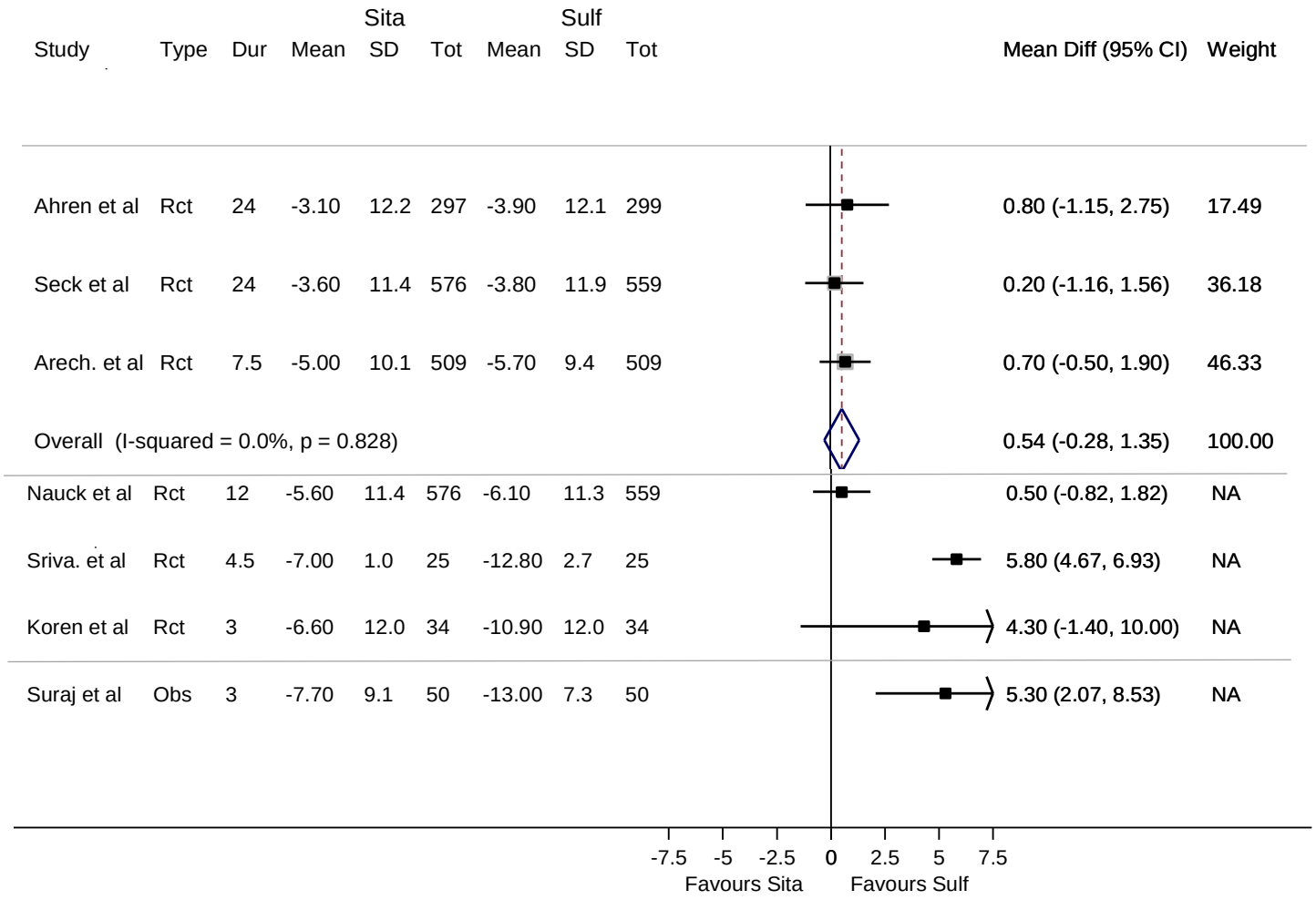

Figure S1. Forest Plots comparing sitagliptin and sulphonylureas for change from baseline in HbA1c (mmol/mol)

Rct, Randomized controlled trial; Obs, Non-randomised Observational study; Dur, duration in months; SD, Standard deviation; Tot, total participants; Mean Diff, mean difference; NA, not applicable. Note: Weights present are from Fixed effects meta-analysis though Random-effects estimates were identical. Tau^2=0%

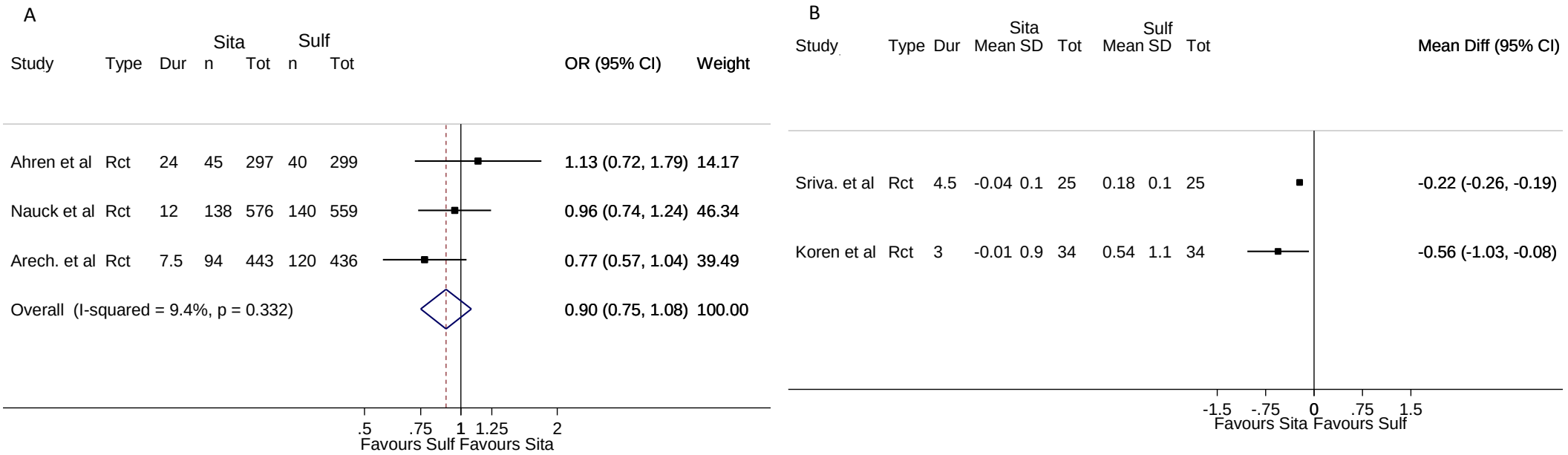

Figure S2. Forest Plots comparing sitagliptin and sulphonylureas for proportions achieving a HbA1c < 6.5% at end of study (A) and for change from baseline in Body Mass Index, kg/m2 (B).

Rct, Randomized controlled trial; Obs, Non-randomised Observational study ; Dur, duration in months; SD, Standard deviation; Tot, total participants; Mean Diff, mean difference. Note: Weights where present are from Fixed effects meta-analysis though Random-effects estimates were identical. Tau^2=0% for meta-analysis

Supplemental References

1. Al Sifri S, Basiounny A, Echtay A, et al. The incidence of hypoglycaemia in Muslim patients with type 2 diabetes treated with sitagliptin or a sulphonylurea during Ramadan: a randomised trial. *Int J Clin Pract* 2011;65(11):1132-40. doi: 10.1111/j.1742-1241.2011.02797.x
2. Weir DL, McAlister FA, Senthilselvan A, et al. Sitagliptin Use in Patients With Diabetes and Heart Failure. A Population-Based Retrospective Cohort Study. *JACC: Heart Failure* 2014;2(6):573-82.
3. Gray LJ, Dales J, Brady EM, et al. Safety and effectiveness of non-insulin glucose-lowering agents in the treatment of people with type 2 diabetes who observe Ramadan: A systematic review and meta-analysis. *Diabetes Obes Metab* 2015;17(7):639-48.
4. Mesci B, Tekin M, Oguz A, et al. Roadmap for oral antidiabetic therapy when sulfonylurea-metformin combination failed. *Obes Rev* 2011;12(7):568-9. doi: 10.1111/j.1467-789X.2011.00891.x
5. Hirao K, Maeda H, Shirabe S, et al. Combination Therapy with a Dipeptidyl Peptidase-4 Inhibitor, Sulfonylurea, and Metformin Markedly Improves HbA1c Levels in Japanese Patients with Type 2 Diabetes Mellitus. *Japanese Clinical Medicine* 2012;3:1-7.
6. Takihata M, Nakamura A, Terauchi Y. Comparative study of three DPP-4 inhibitors, namely sitagliptin, vildagliptin, and alogliptin, in japanese type 2 diabetic patients: The cosva randomized, controlled trial. *Diabetes* 2014;63:A264. doi: 10.2337/db14-833-1316
7. Wade R, Pawaskar MD, Quimbo RA, et al. Real world clinical effectiveness of sitagliptin therapy for management of type 2 diabetes: A retrospective database analysis. *Value Health* 2009;12 (7):A401.
8. Viljoen A, Meek CL, Gadsby R, et al. The tolerability and safety of DPP-4 inhibitors for the treatment of older people with type 2 diabetes mellitus: An observational study. *British Journal of Diabetes and Vascular Disease* 2013;13(4):187-91.
9. Patel K, Krishnan A, Khan E. A single centre retrospective 12 months follow up study of safety and efficacy of sitagliptin. *Diabetes* 2010;Conference Publication.
10. Kim WJ, Park CY, Jeong EH, et al. Retrospective analysis on the efficacy, safety and treatment failure group of sitagliptin for mean 10-month duration. *Diabetes Metab J* 2011;35(3):290-7.
11. Goossen K, Graber S. Longer term safety of dipeptidyl peptidase-4 inhibitors in patients with type 2 diabetes mellitus: systematic review and meta-analysis. *Diabetes Obes Metab* 2012;14(12):1061-72. doi: 10.1111/j.1463-1326.2012.01610.x
12. Eurich DT, Simpson S, Senthilselvan A, et al. Comparative safety and effectiveness of sitagliptin in patients with type 2 diabetes: Retrospective population based cohort study. *BMJ* 2013;346(7908).
13. Chen DY, Wang SH, Mao CT, et al. Sitagliptin after ischemic stroke in type 2 diabetic patients: A nationwide cohort study. *Medicine (United States)* 2015;94(28).
14. Aravind SR, Ismail SB, Balamurugan R, et al. Hypoglycemia in patients with type 2 diabetes from India and Malaysia treated with sitagliptin or a sulfonylurea during Ramadan: A randomized, pragmatic study. *Curr Med Res Opin* 2012;28(8):1289-96. doi: http://dx.doi.org/10.1185/03007995.2012.707119
15. Wang SH, Chen DY, Lin YS, et al. Cardiovascular outcomes of sitagliptin in type 2 diabetic patients with acute myocardial infarction, a population-based cohort study in Taiwan. *PLoS One* 2015;10(6).
16. Krobot KJ, Ferrante SA, Davies MJ, et al. Lower risk of hypoglycemia with sitagliptin compared to glipizide when either is added to metformin therapy: a pre-specified analysis adjusting for the most recently measured HbA(1c) value. *Curr Med Res Opin* 2012;28(8):1281-7.

17. Nomoto H, Miyoshi H, Nakamura A, et al. A comparison of the effects of the DPP-4 inhibitor sitagliptin and the sulfonylurea glimepiride on metabolic parameters and endothelial function. *Diabetologia* 2014;57(1 suppl. 1):S355-s56. doi: 10.1007/s00125-014-3355-0
18. Valensi P, De Pouvourville G, Benard N, et al. Duration of maintenance of dual therapy with metformin and sitagliptin in type 2 diabetes: The Odyssee observational study. *Diabetologia* 2014;1):S367.
19. Mamza J, Mehta R, Donnelly R, et al. Comparative Efficacy of Adding Sitagliptin to Metformin, Sulfonylurea or Dual Therapy: A Propensity Score-Weighted Cohort Study. *Diabetes Ther* 2015;6(2):213-26.
20. Leproust S, Dallongeville J, Valensi P, et al. Treatment maintenance duration of dual therapy with metformin and sitagliptin in type 2 diabetes-real-world data from odyssee study. *Value Health* 2014;17 (7):A334-A35.
21. Inzucchi SE, Qiu Y, Rajpathak S, et al. Assessing time to insulin use among type 2 diabetes patients treated with sitagliptin or sulfonylurea plus metformin dual therapy. *Diabetologia* 2014;1):S365-S66.
22. Idris I, Mehta R, Donnelly R, et al. Clinical efficacy of sitagliptin as add-on to metformin, sulphonylurea or metforminsulphonylurea combined therapy: A propensity score matched cohort study. *Diabet Med* 2015;32:159-60.
23. Abid R, Zahid M. To compare the hypoglycaemic effect of sitagliptin/ metformin combination vs glimiperide in type II diabetes patients during Ramadan. *Medical Forum Monthly* 2013;24(10):43-6.
24. Seck TL, Engel SS, Williams-Herman DE, et al. Sitagliptin more effectively achieves a composite endpoint for A1C reduction, lack of hypoglycemia and no body weight gain compared with glipizide. *Diabetes Res Clin Pract* 2011;93(1):e15-7.
25. Charbonnel B, Karasik A, Liu J, et al. Efficacy and safety of the dipeptidyl peptidase-4 inhibitor sitagliptin added to ongoing metformin therapy in patients with type 2 diabetes inadequately controlled with metformin alone. *Diabetes Care* 2006;29(12):2638-43. doi: 10.2337/dc06-0706
26. Scott R, Wu M, Sanchez M, et al. Efficacy and tolerability of the dipeptidyl peptidase-4 inhibitor sitagliptin as monotherapy over 12 weeks in patients with type 2 diabetes. *Int J Clin Pract* 2007;61(1):171-80. doi: 10.1111/j.1742-1241.2006.01246.x
27. Muthukrishnan J, Dawra S, Marwaha V, et al. Diabetes mellitus in the young: Gliptins or sulfonylurea after metformin? *Indian J Endocrinol Metab* 2012;16(Suppl 2):S474-6.
28. Li W, Lin M, Zhang X. Comparison on adding sitagliptin or glimepiride in poorly controlled overweight type 2 diabetes with oral metformin (In Chinese). *Zhongguo Yi Yuan Yao Xue Za Zhi* 2012;32:792–94.
29. Shankar RR, Xu L, Golm GT, et al. A comparison of glycaemic effects of sitagliptin and sulfonylureas in elderly patients with type 2 diabetes mellitus. *Int J Clin Pract* 2015;69(6):626-31.
30. Ahren B, Johnson SL, Stewart M, et al. HARMONY 3: 104-week randomized, double-blind, placebo- and active-controlled trial assessing the efficacy and safety of albiglutide compared with placebo, sitagliptin, and glimepiride in patients with type 2 diabetes taking metformin. *Diabetes Care* 2014;37(8):2141-8.
31. Arechavaleta R, Seck T, Chen Y, et al. Efficacy and safety of treatment with sitagliptin or glimepiride in patients with type 2 diabetes inadequately controlled on metformin monotherapy: a randomized, double-blind, non-inferiority trial. *Diabetes Obes Metab* 2011;13(2):160-8. doi: 10.1111/j.1463-1326.2010.01334.x
32. Kim HS, Shin JA, Lee SH, et al. A comparative study of the effects of a dipeptidyl peptidase-IV inhibitor and sulfonylurea on glucose variability in patients with type 2 diabetes with inadequate glycemic control on metformin. *Diabetes Technol Ther* 2013;15(10):810-6.

33. Koren S, Shemesh-Bar L, Tirosh A, et al. The effect of sitagliptin versus glibenclamide on arterial stiffness, blood pressure, lipids, and inflammation in type 2 diabetes mellitus patients. *Diabetes Technol Ther* 2012;14(7):561-7.
34. Nauck MA, Meininger G, Sheng D, et al. Efficacy and safety of the dipeptidyl peptidase-4 inhibitor, sitagliptin, compared with the sulfonylurea, glipizide, in patients with type 2 diabetes inadequately controlled on metformin alone: a randomized, double-blind, non-inferiority trial. *Diabetes Obes Metab* 2007; 9(2).
35. Seck T, Nauck M, Sheng D, et al. Safety and efficacy of treatment with sitagliptin or glipizide in patients with type 2 diabetes inadequately controlled on metformin: a 2-year study. *Int J Clin Pract* 2010;64(5):562-76.
36. Srivastava S, Saxena GN, Keshwani P, et al. Comparing the efficacy and safety profile of sitagliptin versus glimepiride in patients of type 2 diabetes mellitus inadequately controlled with metformin alone. *Journal of Association of Physicians of India* 2012;60(3):27-30.
37. Derosa G, D'Angelo A, Maffioli P. Sitagliptin in type 2 diabetes mellitus: Efficacy after five years of therapy. *Pharmacol Res* 2015;100:127-34.
38. Inzucchi SE, Tunceli K, Qiu Y, et al. Progression to insulin therapy among patients with type 2 diabetes treated with sitagliptin or sulphonylurea plus metformin dual therapy. *Diabetes Obes Metab* 2015;17(10):956-64.
39. Lee YK, Song SO, Kim KJ, et al. Glycemic effectiveness of metformin-based dual-combination therapies with sulphonylurea, pioglitazone, or DPP4-inhibitor in drug-naive Korean type 2 diabetic patients. *Diabetes Metab J* 2013;37(6):465-74. doi: 10.4093/dmj.2013.37.6.465
40. Suraj B, Tripathi CD, Biswas K, et al. A Comparative Evaluation of Safety, Efficacy and Cost Effectiveness of Three Add on Treatment Regimens in Type 2 Diabetics; Not Controlled by Metformin Alone. *Research Journal of Pharmacy and Technology* 2015;8(1):44-50.
41. Valensi P, de Pouvourville G, Benard N, et al. Treatment maintenance duration of dual therapy with metformin and sitagliptin in type 2 diabetes: The ODYSSEE observational study. *Diabetes Metab* 2015;41(3):231-38.