**Supplementary Appendix**

**Efficacy and hypoglycemic risk of sitagliptin in obese/overweight patients with** **type 2 diabetes compared with GLP-1 receptor agonists: a meta-analysis**

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**Table S1: Search strategy**

|  |  |
| --- | --- |
| **Search strategy** | **database** |
| (((((((((((“semaglutide”) OR “lixisenatide”) OR “albiglutide”) OR “dulaglutide”) OR “liraglutide”) OR “exenatide”) OR “GLP-1 RAs”) OR “glucagon-like-peptide-1 receptor agonists”)) AND ((("DM") OR "diabetic") OR "diabetes")) AND ((("obes\*") OR "over weight") OR "overweight")) AND ((("Januvia") OR "MK0431") OR "sitagliptin") | PubMed |
| ('dm' OR 'diabetes' OR 'diabetic') AND ('overweight' OR 'over weight' OR 'obes\*') AND ('sitagliptin' OR 'mk0431' OR 'januvia') AND ('lixisenatide' OR 'semaglutide' OR 'albiglutide' OR 'dulaglutide' OR 'liraglutide' OR 'exenatide' OR 'glp-1 ras' OR 'glucagon-like-peptide-1 receptor agonists') | EMBASE |
| "obese" OR "overweight" | Studies With Results | Interventional Studies | diabetes | Sitagliptin | ClinicalTrials.gov |
| #1 "MK0431" (Word variations have been searched) #2 "sitagliptin" (Word variations have been searched)  #3 "januvia" (Word variations have been searched) #4 #1 or #2 or #3  #5 "diabetes" (Word variations have been searched) #6 "diabetic" (Word variations have been searched)  #7 "DM" (Word variations have been searched) #8 #5 or #6 or #7  #9 "obse\*" (Word variations have been searched) #10 "overweight" (Word variations have been searched)  #11 "over weight" (Word variations have been searched) #12 #9 or #10 or #11  #13 #12 and #8  #14 "semaglutide" (Word variations have been searched) #15 "lixisenatide" (Word variations have been searched)  #16 "albiglutide" (Word variations have been searched) #17 "dulaglutide" (Word variations have been searched)  #18 "liraglutide" (Word variations have been searched) #19 "exenatide" (Word variations have been searched)  #20 "GLP-1 RAs" (Word variations have been searched)  #21 "glucagon-like-peptide-1 receptor agonists" (Word variations have been searched)  #22 #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21  #23 #4 and #22 and #13 | Cochrane Library |

**Table S2: The reasons for study exclusion**

| **No.** | **Excluded studies** | **Reason for exclusion** |
| --- | --- | --- |
| 1 | Bailey TS, Takács R, Tinahones FJ, et al. Efﬁcacy and safety of switching from sitagliptin to liraglutide in subjects with type 2 diabetes (LIRA-SWITCH): a randomized, double-blind, double-dummy, active-controlled 26-week trial. Diabetes, Obesity and Metabolism. 2016. 18: 1191-1198 | No data to extract |
| 2 | Htike ZZ, Yates T, Brady EM, et al. Rationale and design of the randomised controlled trial to assess the impact of liraglutide on cardiac function and structure in young adults with type 2 diabetes (the LYDIA study). Cardiovascular Diabetology. 2016. 15: 102-111. | No data to extract |
| 3 | Kusama M, Nakashima e, Yuchi Y, et al. Long-term clinical efficacy and safety of GLP-1 analogue liraglutide vs. DPP-4 inhibitor sitagliptin in Japanese obese adults with type 2 diabetes. Journal of Diabetes. 2013: 139 | No data to extract |
| 4 | SeinoY, Terauchi Y, Osonoi T, et al. Safety and efficacy of semaglutide once weekly vs sitagliptin once daily, both as monotherapy in Japanese people with type 2 diabetes. Diabetes, Obesity and Metabolism. 2018. 20: 378-388 | the average BMI of participants<30mg/m2 |
| 5 | Yamada Y, Senda M, Naito Y, et al. Reduction of postprandial glucose by lixisenatide vs sitagliptin treatment in Japanese patients with type 2 diabetes on background insulin glargine: A randomized phase IV study (NEXTAGE Study). Diabetes, Obesity and Metabolism. 2017. 19: 1252-1259. | the average BMI of participants<30mg/m2 |
| 6 | Weinstock RS, Guerci B, Umpierrez G, et al. Safety and efficacy of once-weekly dulaglutide versus sitagliptin after 2 years in metformin-treated patients with type 2 diabetes (AWARD-5): a randomized, phase III study. Diabetes, Obesity and Metabolism. 2015. 17: 849-858. | It is the same trial with study by Skrivanek et al. |
| 7 | Zang L, Liu Y, Luo Y, et al. Efficacy and safety of liraglutide versus sitagliptin, both in combination with metformin, in Chinese patients with type 2 diabetes: a 26-week, open-label, randomized, active comparator clinical trial. Diabetes, Obesity and Metabolism. 2016. 18: 803-811. | the average BMI of participants<30mg/m2 |

**Table S3: Raw data of interventional group**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author,**  **year** | **Change in HbA1c**  **(%)** | | | **Change in FPG**  **(mmol/l)** | | | **Change in PPG**  **(mmol/l)** | | | **Change in body weight**  **(kg)** | | | **Change in SBP**  **(mmHg)** | | | **Change in DBP**  **(mmHg)** | | | **number of participants achieving an HbA1c goal of < 6.5%** | | **number of participants achieving an HbA1c goal of < 7.0%** | | **Number of patients experiencing hypoglycemia** | |
|  | **#**  **mean** | **N\*** | **SD** | **#**  **mean** | **N\*** | **SD** | **#**  **mean** | **N\*** | **SD** | **#**  **mean** | **N\*** | **SD** | **#**  **mean** | **N\*** | **SD** | **#**  **mean** | **N\*** | **SD** | **N\*** | **Total\*** | **N\*** | **Total\*** | **N\*** | **Total\*** |
| $Berg, 2011 | NR | NR | NR | -1.57 | 67 | 1.23 | -2.47 | 68 | 1.98 | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | 1 | 71 |
| $Bergenstal,2010 | -0.92 | 162 | 1.26 | -0.91 | 161 | 2.66 | NR | NR | NR | -0.77 | 163 | 4.12 | 0.2 | 163 | 12.13 | -0.4 | 163 | 7.28 | 26 | 166 | 51 | 166 | 5 | 166 |
| $Gaal,2014 | -0.7 | 160 | 1.26 | -0.69 | 161 | 2.51 | -1.44 | 139 | 4.52 | -1.17 | 160 | 3.79 | NR | NR | NR | NR | NR | NR | 42 | 160 | 64 | 160 | 3 | 161 |
| $Gadde,2017 | -0.625 | 122 | 1.46 | -0.628 | 122 | 2.83 | -1.31 | 31 | 4.01 | -1.2 | 122 | 3.31 | 0.8 | 122 | 12.15 | 0.2 | 122 | 7.73 | NR | NR | 39 | 122 | 7 | 122 |
| $Skrivanek,2014 | -0.61 | 311 | 0.88 | -0.97 | 308 | 1.93 | NR | NR | NR | -1.46 | 314 | 3.19 | -1.94 | 315 | 11.71 | -1.06 | 315 | 7.45 | 68 | 312 | 118 | 312 | 14 | 315 |
| $Russell-Jones,2012 | -1.15 | 142 | 0.95 | -1.13 | 120 | 1.97 | NR | NR | NR | -0.76 | 141 | 3.09 | -1.81 | 141 | 11.40 | -0.45 | 141 | 7.36 | NR | NR | 65 | 143 | 0 | 163 |
| &Charbonel,2013 | -0.8 | 269 | 1.01 | -1.1 | 269 | 2.17 | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | 91 | 269 | 169 | 269 | 39 | 326 |
| $Prately,2010 | -0.9 | 210 | 1.01 | -0.83 | 210 | 2.17 | NR | NR | NR | -0.96 | 215 | 3.96 | -0.94 | 213 | 12.99 | -1.78 | 213 | 8.76 | 26 | 219 | 48 | 219 | 21 | 219 |

**Table S4:** **Raw data of control group**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author,**  **year** | **Change in HbA1c**  **(%)** | | | **Change in FPG**  **(mmol/l)** | | | **Change in PPG**  **(mmol/l)** | | | **Change in body weight**  **(kg)** | | | **Change in SBP**  **(mmHg)** | | | **Change in DBP**  **(mmHg)** | | | **number of participants achieving an HbA1c goal of < 6.5%** | | **number of participants achieving an HbA1c goal of < 7.0%** | | **Number of patients experiencing hypoglycemia** | |
|  | **#**  **Mean** | **N\*** | **SD** | **#**  **mean** | **N\*** | **SD** | **#**  **mean** | **N\*** | **SD** | **#**  **mean** | **N\*** | **SD** | **#**  **mean** | **N\*** | **SD** | **#**  **mean** | **N\*** | **SD** | **N\*** | **total** | **N\*** | **Total\*** | **N\*** | **Total\*** |
| $Berg, 2011 | NR | NR | NR | -1.61 | 68 | 1.24 | -6.02 | 69 | 1.99 | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | 3 | 70 |
| $Bergenstal,2010 | -1.55 | 159 | 1.26 | -1.76 | 155 | 2.61 | NR | NR | NR | -2.31 | 160 | 4.09 | -3.6 | 160 | 12.27 | -1.4 | 160 | 7.21 | 62 | 160 | 94 | 160 | 2 | 160 |
| $Gaal,2014 | -0.7 | 150 | 1.22 | -0.45 | 153 | 2.35 | -3.35 | 129 | 4.24 | -2.51 | 152 | 3.62 | NR | NR | NR | NR | NR | NR | 36 | 150 | 61 | 150 | 1 | 158 |
| $Gadde,2017 | -1.13 | 181 | 1.47 | -1.18 | 181 | 2.89 | -3.31 | 44 | 3.85 | -1.1 | 181 | 4.04 | 1.2 | 181 | 12.11 | 1 | 181 | 8.07 | NR | NR | 78 | 181 | 4 | 181 |
| $Skrivanek,2014 | -1.22 | 301 | 0.87 | -2.38 | 297 | 2.07 | NR | NR | NR | -3.18 | 303 | 3.13 | -1.73 | 304 | 11.68 | -0.43 | 304 | 7.50 | 141 | 302 | 184 | 302 | 34 | 304 |
| $Russell-Jones,2012 | -1.53 | 218 | 1.03 | -2.25 | 198 | 1.97 | NR | NR | NR | -2.04 | 215 | 3.08 | -1.25 | 215 | 11.58 | -0.5 | 215 | 7.48 | NR | NR | 145 | 226 | 5 | 248 |
| &Charbonel,2013 | -1.2 | 253 | 1.02 | -2.3 | 252 | 2.17 | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | 97 | 253 | 183 | 253 | 13 | 324 |
| $Prately,2010 | -1.24 | 211 | 1.02 | -1.87 | 210 | 2.17 | NR | NR | NR | -2.86 | 215 | 3.96 | -0.55 | 213 | 12.99 | -0.71 | 213 | 8.76 | 51 | 221 | 95 | 221 | 30 | 221 |

**HbA1c=hemoglobin A1c, FPG=fasting plasma glucose, PPG=postprandial plasma glucose, SBP= systolic blood pressure, DBP= diastolic blood pressure, NR=not reported**

**\*No. of participants analyzed and data obtained from** [**www.clinicaltrials.gov**](http://www.clinicaltrials.gov)

**#Least squares mean**

**$Data obtained from www.clinicaltrials.gov**

**[SD] calculated from SE and sample size**

**&Data obtained from another study**

**Table S5: Exposures of included studies**

|  |  |  |
| --- | --- | --- |
| **Author,**  **year** | **Intervention and administration** | **Control and administration** |
| Berg,  2011 | Sitagliptin: oral administration100mg once daily in the morning  Placebo: subcutaneous injection (5ug to 10ug) twice a day | Exenatide: subcutaneous injection (5ug to 10ug) twice a day  Placebo: oral administration 100mg once daily in the morning |
| Bergenstal,  2010 | 100mg oral sitagliptin once daily plus placebo as a once weekly injection | 2mg exenatide as a once weekly injection plus oral placebo once daily |
| Gaal,  2014 | sitagliptin 100 mg capsule orally QD up to Week 24 along with volume matching lixisenatide placebo 10 mcg QD for 1 week, followed by 15 mcg QD for 1 week, then 20 mcg QD up to Week 24. | lixisenatide 10 microgram (mcg) once daily (QD) for 1 week, followed by 15 mcg QD for 1 week, then 20 mcg QD up to Week 24 along with placebo matching to sitagliptin 100 milligram (mg) capsule orally QD up to Week 24 |
| Pratley,  2010 | Once-daily dose of sitagliptin 100 mg (tablets) with at least 1500 mg metformin/day (tablets) for 26 weeks | Once-daily subcutaneous dose of liraglutide 1.2 mg with at least 1500 mg metformin/day (tablets) for 26 weeks. |
| Charbonel,  2013 | Sitagliptin 100 mg tablet orally once daily for 26 weeks. Participants continued their stable dose of metformin >=1500 mg orally daily. Participants may have received glimepiride orally for glycemic control. | Liraglutide subcutaneous injection once daily for 26 weeks (starting dose 0.6 mg daily up-titrated to 1.2 mg daily on Day 8). Participants continued their stable dose of metformin >=1500 mg orally daily. Participants may have had their liraglutide dose up titrated to 1.8 mg daily for glycemic control |
| Russell-Jones,  2012 | Sitagliptin 100 mg daily plus placebo once weekly subcutaneous injection | Exenatide (subcutaneous injection) 2mg once weekly plus placebo oral once daily |
| Skrivanek,2014  NCT00734474 | Sitagliptin: 100-milligrams (mg) tablet, administered orally, once daily Placebo: solution, subcutaneous (SC) injection, once weekly  Metformin: at least 1500 milligrams per day (mg/day), administered orally | LY2189265 (Dulaglutide): 1.5 milligrams (mg), subcutaneous (SC) injection, once weekly  Placebo: tablet, administered orally, once daily  Metformin: at least 1500 milligrams per day (mg/day), administered orally |
| Gadde, 2017  NCT01652729 | Sitagliptin 100mg oral tablet once daily | Exenatide once weekly suspension 2mg subcutaneous injection |

**Table S6: Definition of hypoglycemia**

| **Author, year** | **Mild, symptoms or moderate** | **severe** |
| --- | --- | --- |
| Berg,2011 | Minor hypoglycemia was defined as self-reported transient symptoms of hypoglycemia and a blood glucose <3mmol/l. | Major hypoglycemia was defined as any episode consistent with hypoglycemia resulting in the loss of consciousness or seizure or documented hypoglycemia < 3mmol/l requiring assistance. |
| Bergenstal,2010 | Minor hypoglycemia: symptoms consistent with hypoglycemia and blood glucose concentration <3mmol/l prior to treatment and not classified as major hypoglycemia. | Major hypoglycemia: events that, in the judgment of the investigator or physician, resulted in loss of consciousness, seizure, coma, or other change in mental status consistent with neuroglycopenia, in which symptoms resolved after administration of intramuscular glucagon or intravenous glucose, required third-party assistance, and was accompanied by a blood glucose concentration < 3mmol/l prior to treatment. |
| Gaal,2014 | Symptomatic hypoglycemia was an event with clinical symptoms that were considered to result from a hypoglycemic episode with an accompanying plasma glucose less than 60 mg/dL (3.3 mmol/L) or associated with prompt recovery after oral carbohydrate, intravenous glucose, or glucagon administration if no plasma glucose measurement was available. | Severe symptomatic hypoglycemia was symptomatic hypoglycemia event in which the patient required the assistance of another person and was associated with either a plasma glucose level below 36 mg/dL (2.0 mmol/L) or prompt recovery after oral carbohydrate, intravenous glucose, or glucagon administration, if no plasma glucose measurement was available. |
| Skrivanek,2014 | documented symptomatic (defined as any time a participant feels that he/she is experiencing symptoms and/or signs associated with hypoglycemia and has a plasma glucose level of ≤3.9 mmol/L, asymptomatic (defined as episodes not accompanied by typical symptoms of hypoglycemia but with a measured plasma glucose of ≤3.9 mmol/L), nocturnal (defined as any episode that occurred between bedtime and waking), or probable symptomatic (defined as episodes during which symptoms of hypoglycemia were not accompanied by a plasma glucose determination). | severe (defined as episodes requiring assistance from another person to actively administer resuscitative actions), |
| Pratley, 2010  NCT00700817 | Minor if able to treat her/himself and plasma glucose below 3.1 mmol/L  Symptoms only if able to treat her/himself and no plasma glucose measurement or plasma glucose higher than or equal to 3.1 mmol/L. | Major if unable to treat her/himself. |
| Gadde, 2017  NCT01652729 | Minor hypoglycemia was defined as a non-major hypoglycemia event with symptoms of hypoglycemia and a glucose concentration of <54 mg/dL. If a hypoglycemia event did not meet symptomatic or blood glucose criteria for a major or minor event, it was classified as symptoms of hypoglycemia | Major hypoglycemia was defined as an event that resulted in loss of consciousness, seizure or coma that resolved after administration of glucagon or glucose, or any event that required third-party assistance to resolve because of severe impairment in consciousness or behavior and was associated with a glucose concentration of <54 mg/dL |
| Charbonel,2013  NCT01296412 | Any episode considered likely to represent symptomatic hypoglycemia by the investigator was to be captured as an AE of symptomatic hypoglycemia  At the discretion of the investigator, an asymptomatic blood glucose value ≤3.9 mmol/l (70 mg/dl) could be reported as an AE of asymptomatic hypoglycemia | Hypoglycemia was classified as severe if a patient required medical or non-medical assistance or exhibited a markedly depressed level of consciousness (including loss of consciousness or seizure) |
| Russell-Jones,2012  NCT00676338 | inor hypoglycemia is defined as a sign or symptom associated with hypoglycemia that is either self-treated by the patient or resolves on its own AND has a concurrent finger stick blood glucose <3.0 mmol/L (54 mg/dL) and not classified as major hypoglycemia | Major hypoglycemia is defined as any event that has symptoms consistent with hypoglycemia resulting in loss of consciousness or seizure that shows prompt recovery in response to administration of glucagon or glucose, or documented hypoglycemia (blood glucose <3.0 mmol/L [54 mg/dL]) requiring the assistance of another person because of severe impairment in consciousness or behavior (whether or not symptoms of hypoglycemia are detected by the patient) |

**Table S7: Summary of sensitivity analyses using a fixed effects model**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Outcome** | **No. of studies contributing data** | **Risk Ratio (95% CI), sitagliptin vs GLP-1 receptor agonists** | **Mean Difference (95% CI), sitagliptin vs GLP-1 receptor agonists** | **No. of participants of**  **experimental group** | **No. of participants of**  **control group** | **I2 heterogeneity, %** | **P** |
| Decrease in HbA1c | 7 |  | 0.44 [0.37, 0.52] | 1376 | 1473 | 68 | P < 0.00001 |
| Patients achieving HbA1c goal of <7.0% | 7 | 0.70 [0.65, 0.76] |  | 1391 | 1493 | 80 | P < 0.00001 |
| Decrease in FPG | 8 |  | 0.89 [0.74, 1.05] | 1418 | 1514 | 86 | P<0.00001 |
| Decrease in PPG | 3 |  | 2.99 [2.45, 3.52] | 238 | 242 | 75 | P < 0.00001 |
| Decrease in body weigh | 6 |  | 1.34 [1.07, 1.61] | 1115 | 1226 | 85 | P < 0.00001 |
| Decrease in SBP | 5 |  | 0.30 [-0.76, 1.35] | 954 | 1073 | 50 | 0.58 |
| Decrease in DBP | 5 |  | -0.30 [-0.98, 0.37] | 954 | 1073 | 5 | 0.38 |
| Participants experiencing hypoglycemia | 8 | 1.00 [0.76, 1.33] |  | 1543 | 1666 | 77 | 0.98 |

**HbA1c=hemoglobin A1c, FPG=fasting plasma glucose, PPG=postprandial plasma glucose, SBP= systolic blood pressure, DBP= diastolic blood pressure**

**Table S8: Summary of sensitivity analyses omitting one study at a time**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Outcome** | **No. of studies contributing data** | **Risk Ratio (95% CI), sitagliptin vs GLP-1 receptor agonists** | **Mean Difference (95% CI), sitagliptin vs GLP-1 receptor agonists** | **No. of participants of**  **experimental group** | **No. of participants of**  **control group** | **I2 heterogeneity, %** | **P** |
| **Exclude study by Berg et al** | | | | | | | |
| Decrease in FPG | 7 |  | 0.89 [0.51, 1.28] | 1351 | 1446 | 80 | <0.00001 |
| Decrease in PPG | 2 |  | 1.93 [1.02, 2.84] | 170 | 173 | 0 | <0.0001 |
| Participants experiencing hypoglycemia | 7 | 1.20 [0.53, 2.71] |  | 1472 | 1596 | 80 | 0.66 |
| **Exclude study by Bergenstal et al** | | | | | | | |
| Decrease in HbA1c | 6 |  | 0.39 [0.23, 0.54] | 1214 | 1314 | 71 | <0.00001 |
| Patients achieving HbA1c goal of <7.0% | 6 | 0.73 [0.61, 0.87] |  | 1225 | 1333 | 78 | 0.0005 |
| Decrease in FPG | 7 |  | 0.76 [0.30, 1.23] | 1257 | 1359 | 88 | 0.001 |
| Decrease in body weigh | 5 |  | 1.22 [0.49, 1.95] | 952 | 1066 | 84 | 0.001 |
| Decrease in SBP | 4 |  | -0.36 [-1.51, 0.79] | 791 | 913 | 0 | 0.54 |
| Decrease in DBP | 4 |  | -0.59 [-1.34, 0.15] | 791 | 913 | 0 | 0.12 |
| Participants experiencing hypoglycemia | 7 | 0.98 [0.43, 2.27] |  | 1377 | 1506 | 79 | 0.97 |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Outcome** | **No. of studies contributing data** | **Risk Ratio (95% CI), sitagliptin vs GLP-1 receptor agonists** | **Mean Difference (95% CI), sitagliptin vs GLP-1 receptor agonists** | **No. of participants of**  **experimental group** | **No. of participants of**  **control group** | **I2 heterogeneity, %** | **P** |
| **Exclude study by Charbonnel et al** | | | | | | | |
| Decrease in HbA1c | 6 |  | 0.42 [0.24, 0.59] | 1107 | 1220 | 73 | <0.00001 |
| Patients achieving HbA1c goal of <7.0% | 6 | 0.66 [0.56, 0.79] |  | 1122 | 1240 | 69 | <0.00001 |
| Decrease in FPG | 7 |  | 0.71 [0.23, 1.19] | 1149 | 1262 | 87 | 0.004 |
| Participants experiencing hypoglycemia | 7 | 0.84 [0.42, 1.65] |  | 1217 | 1342 | 55 | 0.60 |
| **Exclude study by Gaal et al** | | | | | | | |
| Decrease in HbA1c | 6 |  | 0.47 [0.37, 0.58] | 1216 | 1323 | 39 | <0.00001 |
| Patients achieving HbA1c goal of <7.0% | 6 | 0.66 [0.55, 0.80] |  | 1231 | 1343 | 80 | <0.0001 |
| Decrease in FPG | 7 |  | 0.92 [0.55, 1.29] | 1257 | 1361 | 81 | <0.00001 |
| Decrease in PPG | 2 |  | 3.01 [1.57, 4.46] | 99 | 113 | 60 | <0.0001 |
| Decrease in body weigh | 5 |  | 1.44 [0.59, 2.29] | 955 | 1074 | 88 | 0.0008 |
| Participants experiencing hypoglycemia | 7 | 1.00 [0.44, 2.26] |  | 1382 | 1508 | 80 | 1.00 |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Outcome** | **No. of studies contributing data** | **Risk Ratio (95% CI), sitagliptin vs GLP-1 receptor agonists** | **Mean Difference (95% CI), sitagliptin vs GLP-1 receptor agonists** | **No. of participants of**  **experimental group** | **No. of participants of**  **control group** | **I2 heterogeneity, %** | **P** |
| **Exclude study by Gadde et al** | | | | | | | |
| Decrease in HbA1c | 6 |  | 0.40 [0.25, 0.56] | 1254 | 1292 | 73 | <0.00001 |
| Patients achieving HbA1c goal of <7.0% | 6 | 0.69 [0.56, 0.84] |  | 1269 | 1312 | 83 | 0.0003 |
| Decrease in FPG | 7 |  | 0.80 [0.35, 1.26] | 1296 | 1333 | 88 | 0.0006 |
| Decrease in PPG | 2 |  | 2.78 [1.18, 4.39] | 207 | 198 | 85 | 0.0007 |
| Decrease in body weigh | 5 |  | 1.71 [1.33, 2.09] | 993 | 1045 | 33 | <0.00001 |
| Decrease in SBP | 4 |  | 0.56 [-1.30, 2.42] | 832 | 892 | 61 | 0.55 |
| Decrease in DBP | 4 |  | -0.20 [-1.04, 0.63] | 832 | 892 | 22 | 0.63 |
| Participants experiencing hypoglycemia | 7 | 0.94 [0.41, 2.20] |  | 1421 | 1485 | 78 | 0.89 |
| **Exclude study by Prately et al** | | | | | | | |
| Decrease in HbA1c | 6 |  | 0.43 [0.26, 0.60] | 1166 | 1262 | 72 | <0.00001 |
| Patients achieving HbA1c goal of <7.0% | 6 | 0.73 [0.61, 0.87] |  | 1172 | 1272 | 78 | 0.0005 |
| Decrease in FPG | 7 |  | 0.73 [0.25, 1.22] | 1208 | 1304 | 88 | 0.003 |
| Decrease in body weigh | 5 |  | 1.33 [0.50, 2.16] | 900 | 1011 | 87 | 0.002 |
| Decrease in SBP | 4 |  | 0.58 [-1.32, 2.49] | 741 | 860 | 61 | 0.55 |
| Decrease in DBP | 4 |  | -0.14 [-0.92, 0.63] | 741 | 860 | 7 | 0.71 |
| Participants experiencing hypoglycemia | 7 | 1.17 [0.43, 3.18] |  | 1324 | 1445 | 78 | 0.76 |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Outcome** | **No. of studies contributing data** | **Risk Ratio (95% CI), sitagliptin vs GLP-1 receptor agonists** | **Mean Difference (95% CI), sitagliptin vs GLP-1 receptor agonists** | **No. of participants of**  **experimental group** | **No. of participants of**  **control group** | **I2 heterogeneity, %** | **P** |
| **Exclude study by Russell-Jones et al** | | | | | | | |
| Decrease in HbA1c | 6 |  | 0.42 [0.25, 0.59] | 1234 | 1255 | 73 | <0.00001 |
| Patients achieving HbA1c goal of <7.0% | 6 | 0.69 [0.56, 0.86] |  | 1248 | 1267 | 83 | 0.0008 |
| Decrease in FPG | 7 |  | 0.71 [0.24, 1.18] | 1298 | 1316 | 87 | 0.003 |
| Decrease in body weigh | 5 |  | 1.46 [0.57, 2.34] | 974 | 1011 | 88 | 0.001 |
| Decrease in SBP | 4 |  | 0.63 [-1.26, 2.51] | 813 | 858 | 59 | 0.51 |
| Decrease in DBP | 4 |  | -0.37 [-1.25, 0.50] | 813 | 858 | 24 | 0.40 |
| Participants experiencing hypoglycemia | 7 | 1.22 [0.55, 2.69] |  | 1380 | 1418 | 79 | 0.62 |
| **Exclude study by Skrivanek et al** | | | | | | | |
| Decrease in HbA1c | 6 |  | 0.37 [0.23, 0.51] | 1065 | 1172 | 55 | <0.00001 |
| Patients achieving HbA1c goal of <7.0% | 6 | 0.71 [0.58, 0.87] |  | 1079 | 1190 | 80 | 0.001 |
| Decrease in FPG | 7 |  | 0.68 [0.24, 1.11] | 1110 | 1217 | 83 | 0.002 |
| Decrease in body weigh | 5 |  | 1.36 [0.47, 2.26] | 801 | 923 | 87 | 0.003 |
| Decrease in SBP | 4 |  | 0.59 [-1.46, 2.63] | 639 | 769 | 60 | 0.57 |
| Decrease in DBP | 4 |  | -0.16 [-1.08, 0.77] | 639 | 769 | 20 | 0.74 |
| Participants experiencing hypoglycemia | 7 | 1.38 [0.62, 3.06] |  | 1228 | 1362 | 67 | 0.43 |

**HbA1c=hemoglobin A1c, FPG=fasting plasma glucose, PPG=postprandial plasma glucose, SBP= systolic blood pressure, DBP= diastolic blood pressure**