Appendix 2 (as supplied by the authors): Characteristics of randomized controlled trials included in the evaluation of fractures

Study	Design	Participants	Thiazolidinedione and comparator	Treatment duration	Fracture in thiazol-idinedione arm	Fractures in control arm	Monitoring for adverse effects
Kahn 2006 (ADOPT)[1, 2]	Double-blind, adequate allocation concealment	Type 2 dDiabetes mellitus, diagnosed within past 3 years, treated with diet and exercise only. Mean age 56 years.	Rosiglitazone versus metformin or glibenclamide	4 years	Women: 60/ 645 Men: 32/811	Women: 51/1195 Men: 57/1700	Investigators looked for adverse events at every study visit. Patients were asked to report number of emergency room visits and hospitalizations, and any days where their activity had been restricted. Baseline characteristics were similar between both groups for ethnicity, disease duration, HbA_{1c} and BMI.
Dormandy 2006 (PROActiv)[3,4]	Double-blind, adequate allocation concealment	Type 2 diabetes (median duration 8 years), with known vascular disease. Mean age 62 years. About one-third was on insulin.	Pioglitazone versus placebo	3.5 years	Women: 44/870* Men: 30/1735*	Women: 23/905* Men: 37/1728*	Investigators enquired about adverse events at every study visit. Trial monitors also regularly checked the patients' trial records to ensure that serious adverse events were being reported. Serious events were then checked against the clinical notes. Baseline characteristics were similar between both groups for ethnicity, disease duration, HbA_{1c} and BMI.
AVM100264[5]	Double-blind, unclear allocation concealment	Type 2 diabetes mellitus	Rosiglitazone and metformin versus.sulfonylurea and metformin	1 year	2/294	1/301	Not stated. Baseline characteristics not given.
GSK 049653 334[6]	Double-blind, adequate allocation concealment	Insulin resistance syndrome and Type 2 diabetes	Rosiglitazone versus placebo	1 year	0/277	3/278	"Adverse events, laboratory findings and vital signs were closely monitored." Baseline characteristics were similar between both groups for disease duration, HbA_{1c} and BMI.

GSK 049653 351[7]	Double-blind, unclear allocation concealment	Type 2 diabetes mellitus with co-existing vascular disease or hypertension	Rosiglitazone versus placebo	1 year	0/30	1/30	Not stated
Jain 2006[8]	Double-blind, unclear allocation concealment	Type 2 diabetes mellitus	Pioglitazone versus glibenclamide	1 year	0/251	2/251	"Adverse events, serious adverse events, and hypoglycemic events were recorded at each visit. Any untoward medical event concurrent with the use of the study drugs was considered an adverse event." Baseline characteristics were similar between both groups for ethnicity, disease duration, HbA_{1c} and BMI.
Nissen 2008 (PERISCOPE)[9]	Double-blind, adequate allocation concealment	Type 2 diabetes mellitus	Pioglitazone versus glimepiride	18 months	Women: 6/84 Men: 2/186	Women: 0/93 Men: 0/180	Investigators reported listed adverse events, including hypoglycemia, angina pectoris, peripheral edema, hypertension and bone fractures. Baseline characteristics were similar between both groups for ethnicity, disease duration, HbA_{1c} and BMI.
DeFronzo 2008 (ACTNow)[10]	Double-blind, unclear allocation concealment	Impaired glucose tolerance	Pioglitazone versus placebo	2.5 years	8/303	8/299	Adverse events were collected as secondary outcomes. Baseline characteristics not given.
Seufert (a) 2008[11]	Double-blind, adequate allocation concealment	Type 2 diabetes mellitus	Pioglitazone plus metformin versus gliclazide plus metformin	2 years	Women: 1/156 Men: 0/161	Women: 1/159 Men: 0/154	Tolerability and safety assessed by monitoring adverse events, physical examination and vital signs and standard clinical laboratory tests. Baseline characteristics were similar between both groups for ethnicity, disease duration, HbA_{1c} and BMI.
Seufert (b) 2008[11]	Double-blind, adequate allocation concealment	Type 2 diabetes mellitus	Pioglitazone plus sulfonylurea versus metformin plus sulfonylurea	2 years	Women: 0/148 Men: 0/171	Women: 1/145 Men: 1/175	Tolerability and safety assessed by monitoring adverse events, physical examination and vital signs and standard clinical laboratory tests. Baseline characteristics were similar between both groups for ethnicity, disease duration, HbA_{1c} and BMI.

*We extracted fracture data from the manufacturer's product information for the PROactive study, as the data on fractures remain unpublished. [3]

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