

Appendix 5 Risk of bias of included case-control studies

Author (year)	Ascertainment of type 2 diabetes	Is case definition adequate	Selection of controls	Definition of controls	Ascertainment of exposure to incretin agents	Ascertainment of other confounding variables	Same method of ascertainment for exposure to DPP-4 inhibitors agents	Comparability of study controls for important factors	Completeness of data within database
Studies reporting heart failure									
Eurich (2014) ¹¹²	Diabetes subjects identified by ICD-9 CM codes	Yes, cases were patients who developed incident heart failure within 30 days of admission to hospital for acute coronary syndrome	Cases were matched (using risk set sampling) by age and sex with up to 10 controls with no heart failure prior to the index date for their given case	Patients with no heart failure	Statement not explicit; likely from the data of pharmacy claims	NR	Yes, both cases and controls who had been prescribed incretins identified with claims database	Conditional logistic regression was used to control for demographics, clinical and laboratory data, pharmacy claims, health care utilization and propensity scores (conditional probability of being treated with metformin or sulfonylurea or insulin or sitagliptin).	Authors did not mention the completeness of data in the database
Studies reporting hospital admission for heart failure									
Weir (2014) ¹⁶	Statement not explicit; likely from identifying the clinical diagnoses according to the ICD-9-CM codes	Yes, cases were patients with the outcome of hospitalization for heart failure	Up to 10 controls were selected by matching on age (quartiles) and sex with no hospital admission, and all controls were alive on the same index date for their given case using conventional risk set sampling (i.e., incident density sampling)	Patients with no hospital admission	Statement not explicit; likely from the data of pharmacy claims	NR	Statement not explicit; likely from the data of pharmacy claims	Conditional logistic regression was used to control for demographics (age, sex, and socioeconomic status), most recent clinical laboratory data (HbA1c; low- and high-density lipoprotein cholesterol; triglycerides; estimated glomerular filtration rate; albuminuria; and hemoglobin concentrations), history of cardiovascular disease, and prescription drug use	Authors did not mention the completeness of data in the database
Yu (2015) ¹⁷	Statement not explicit; likely from identifying patients newly treated with noninsulin antidiabetic drugs	Yes, case subjects were defined by hospitalization for congestive heart failure	Up to 20 control subjects per case were randomly selected using risk set sampling, matched on duration	Statement not explicit; likely patients with no hospitalization for congestive heart failure	Statement not explicit; likely from the medical records	Statement not explicit; confounding variables were likely ascertained by identifying the	Statement not explicit; likely from the medical records	In addition to conditioning on the matching variables (i.e., duration of follow-up, age, duration of treated diabetes, and calendar year of cohort entry) , conditional logistic	Completeness of data in the database not mentioned, however, the

(metformin, sulfonylureas, thiazolidinediones, α -glucosidase inhibitors, guar gum, meglitinides, and incretin-based drugs)

of follow up, age, duration of treated diabetes, and calendar year of study cohort entry

medical records

regression was used to control for sex, BMI, excessive alcohol use, smoking status, HbA1c level, comorbidities such as neuropathy, renal disease, retinopathy, atrial fibrillation, cancer, chronic obstructive pulmonary disease, coronary artery disease, dyslipidemia, hypertension, previous myocardial infarction, peripheral arteriopathy, previous coronary revascularization, peripheral vascular disease, and previous stroke, all measured at any time prior to cohort entry

database has been shown to be valid and of high quality

ICD-9-CM= International Classification of Diseases, Ninth Revision, Clinical Modification; NR= not reported.