Differences between men and women in short-term outcomes after CABG: a meta-analysis

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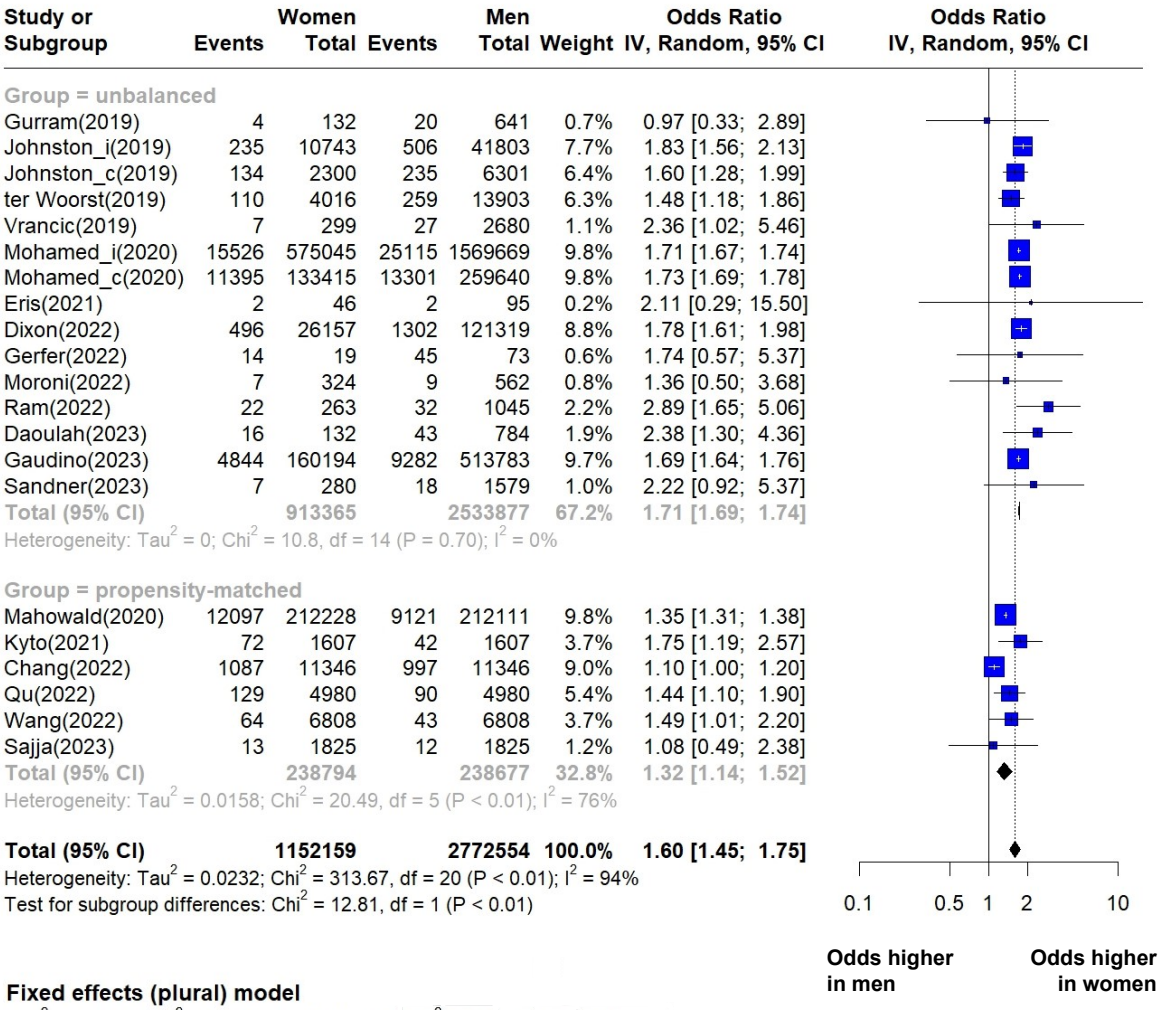
Figure S1: Forest plots showing pooled odds ratios (OR) for short-term mortality and test for group differences. When within individual studies outcomes were calculated separately by procedure: "_i" designates isolated CABG, and "_c" designates CABG concomitant with valve repair.



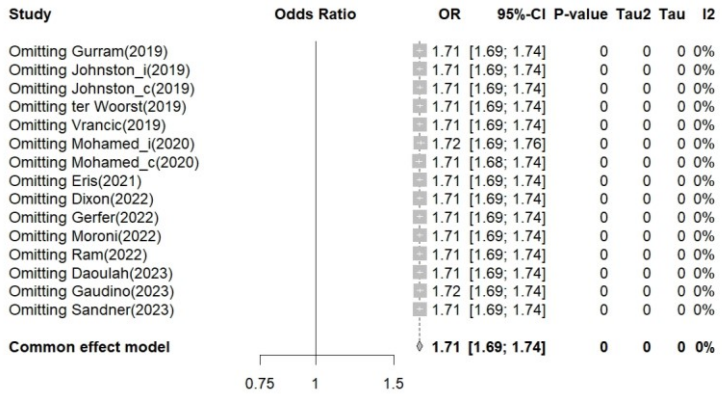
Fixed effects (plural) model

$Tau^2 = 0.0232$; $Chi^2 = 12.81$, df = 1 ($P < 0.01$); $I^2 = 94\%$ [92%; 95%]

Test for subgroup differences: $P < 0.01$

Figure S2: Sensitivity analysis for short-term mortality

Group= unbalanced



Group= propensity-matched

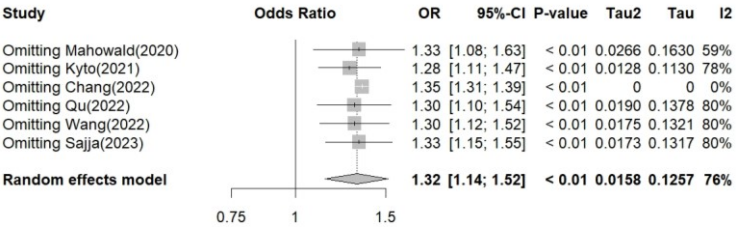
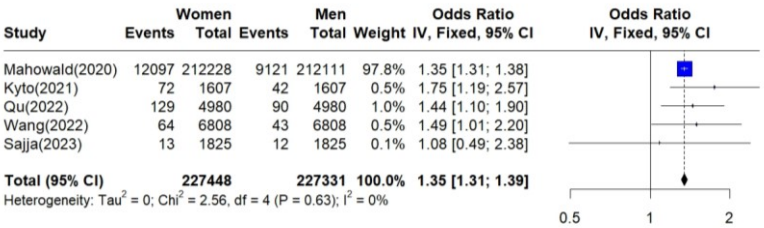


Figure S3: pooled effects and sensitivity analysis for short-term mortality in the propensity-matched group, after omitting Chang (2022)

Group= propensity-matched, after omitting Chang (2022)



Group= propensity-matched, after omitting Chang (2022)

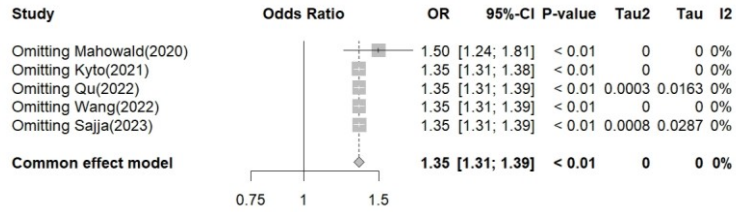
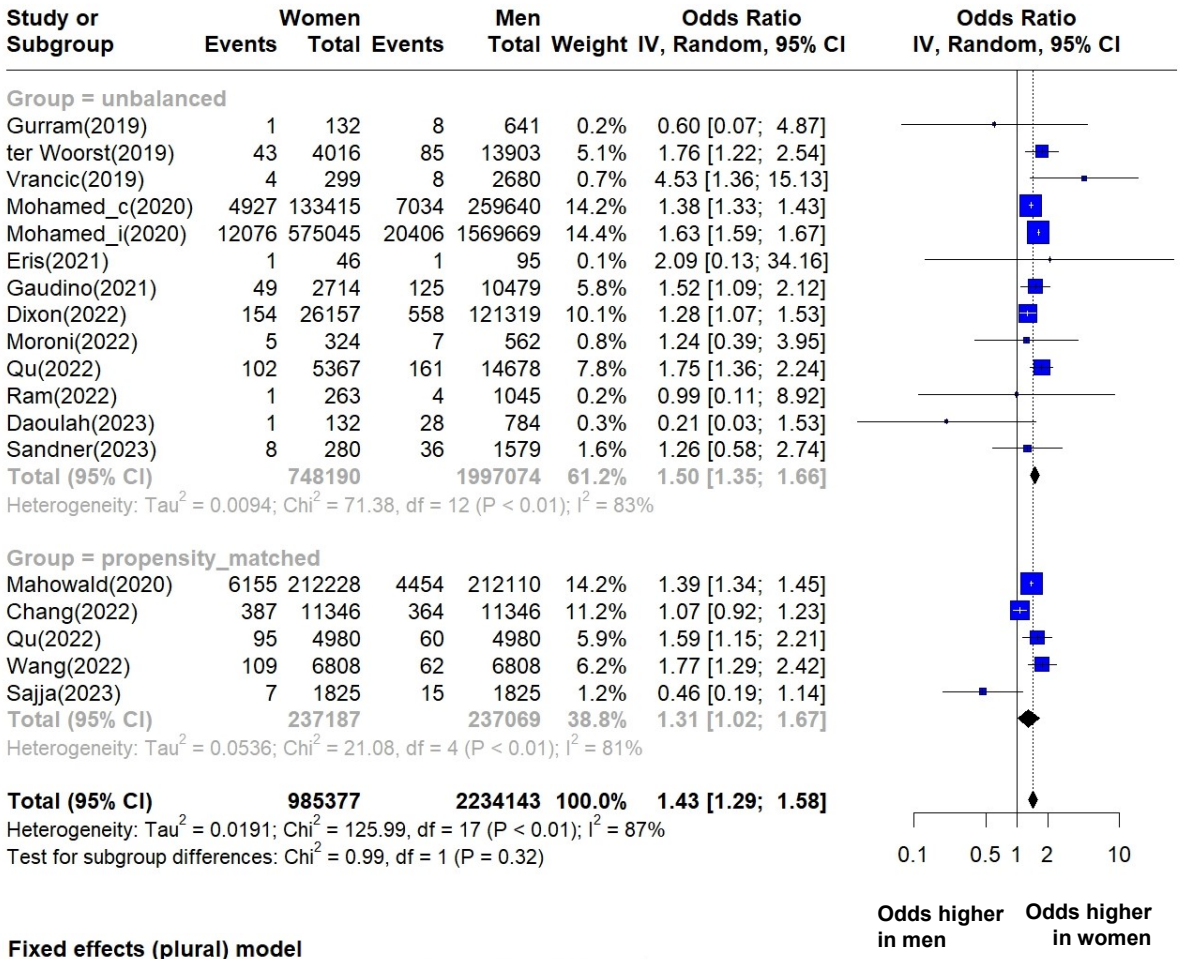


Figure S4: Forest plots showing pooled odds ratios (OR) for postoperative stroke and test for group differences. When within individual studies outcomes were calculated separately by procedure: "_i" designates isolated CABG, and "_c" designates CABG concomitant with valve repair.



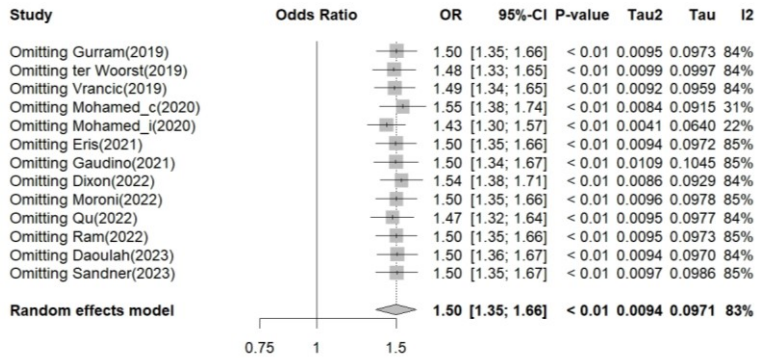
Fixed effects (plural) model

Tau^2 = 0.0191; Chi^2 = 0.99, df = 1 (P = 0.32); I^2 = 87% [80%; 91%]

Test for subgroup differences: P = 0.32

Figure S5: Sensitivity analysis for postoperative stroke

Group= unbalanced



Group= propensity-matched

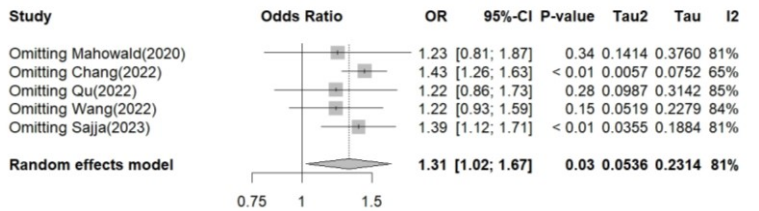
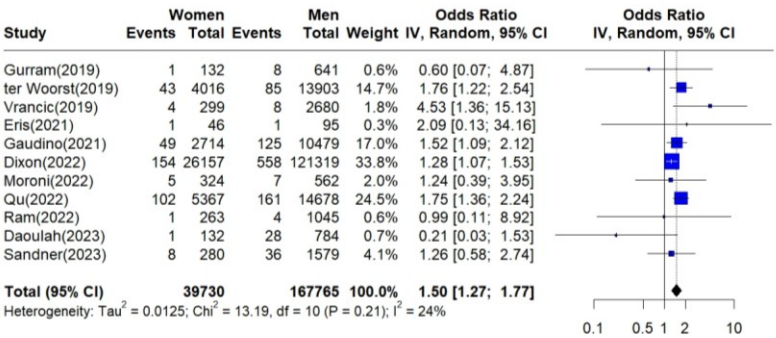


Figure S6: pooled effects and sensitivity analysis for postoperative stroke in the unbalanced group, after omitting Mohamed (2020)

Group=unbalanced, after omitting Mohamed (2020)



Group= unbalanced, after omitting Mohamed (2020)

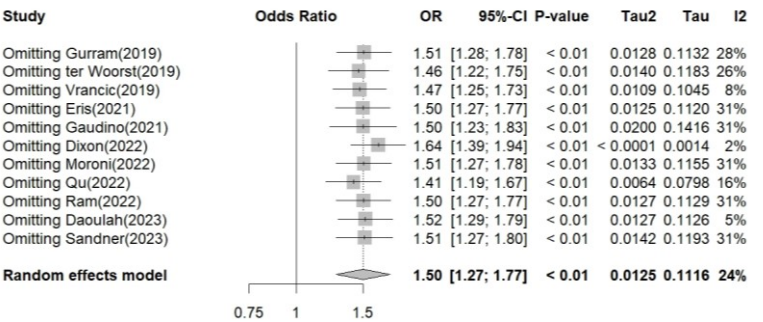
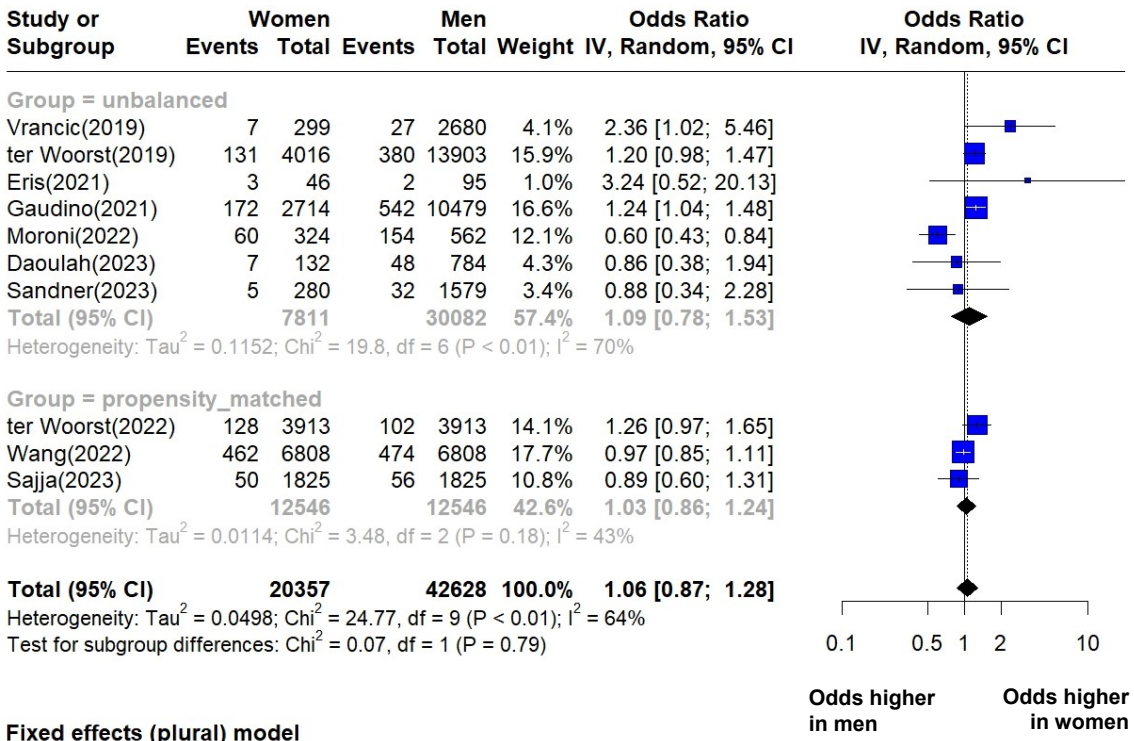


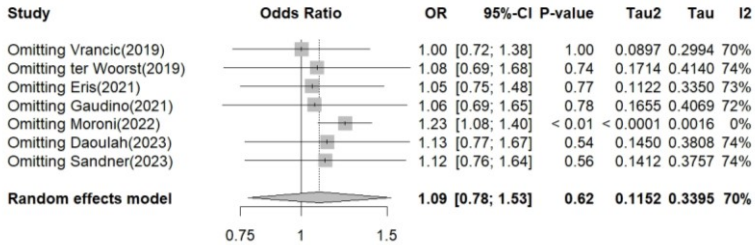
Figure S7: Forest plots showing pooled odds ratios (OR) for myocardial infarction and test for group differences. When within individual studies outcomes were calculated separately by procedure: "_i" designates isolated CABG, and "_c" designates CABG concomitant with valve repair.



Fixed effects (plural) model
$Tau^2 = 0.0498$; $Chi^2 = 0.07$, df = 1 (P = 0.79); $I^2 = 64\%$ [28%; 82%]
Test for subgroup differences: P = 0.79

Figure S8: Sensitivity analysis for postoperative myocardial infarction

Group= unbalanced



Group= propensity-matched

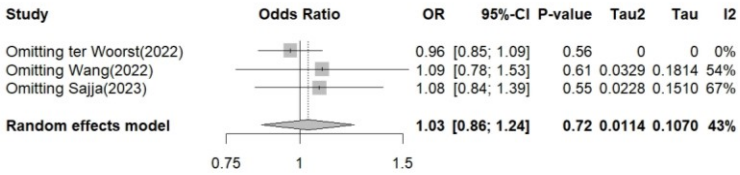


Figure S9: Sensitivity analysis for postoperative atrial fibrillation

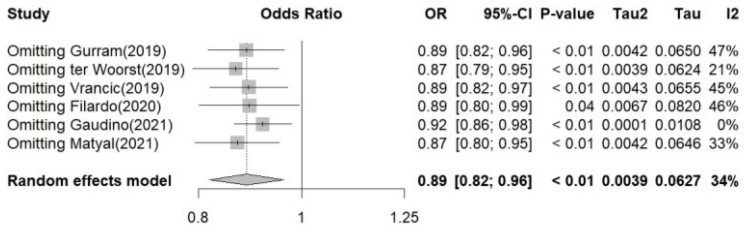


Figure S10: Postoperative atrial fibrillation summary of effects (unadjusted effect in individual studies) after excluding studies in which there was no significant differences in age between men and women (Gurram (2019), Matyal (2021)).

A

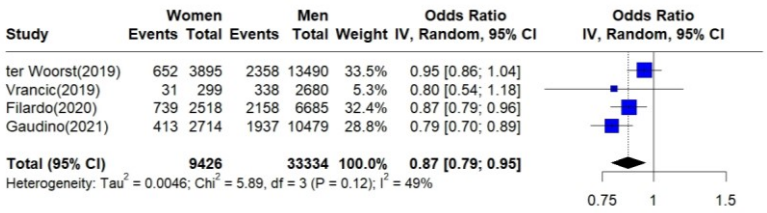


Figure S11: Funnel plots for identification of publication bias, for each of the outcomes: A – postoperative mortality; B- stroke; C – myocardial infarction; D – new onset atrial fibrillation.

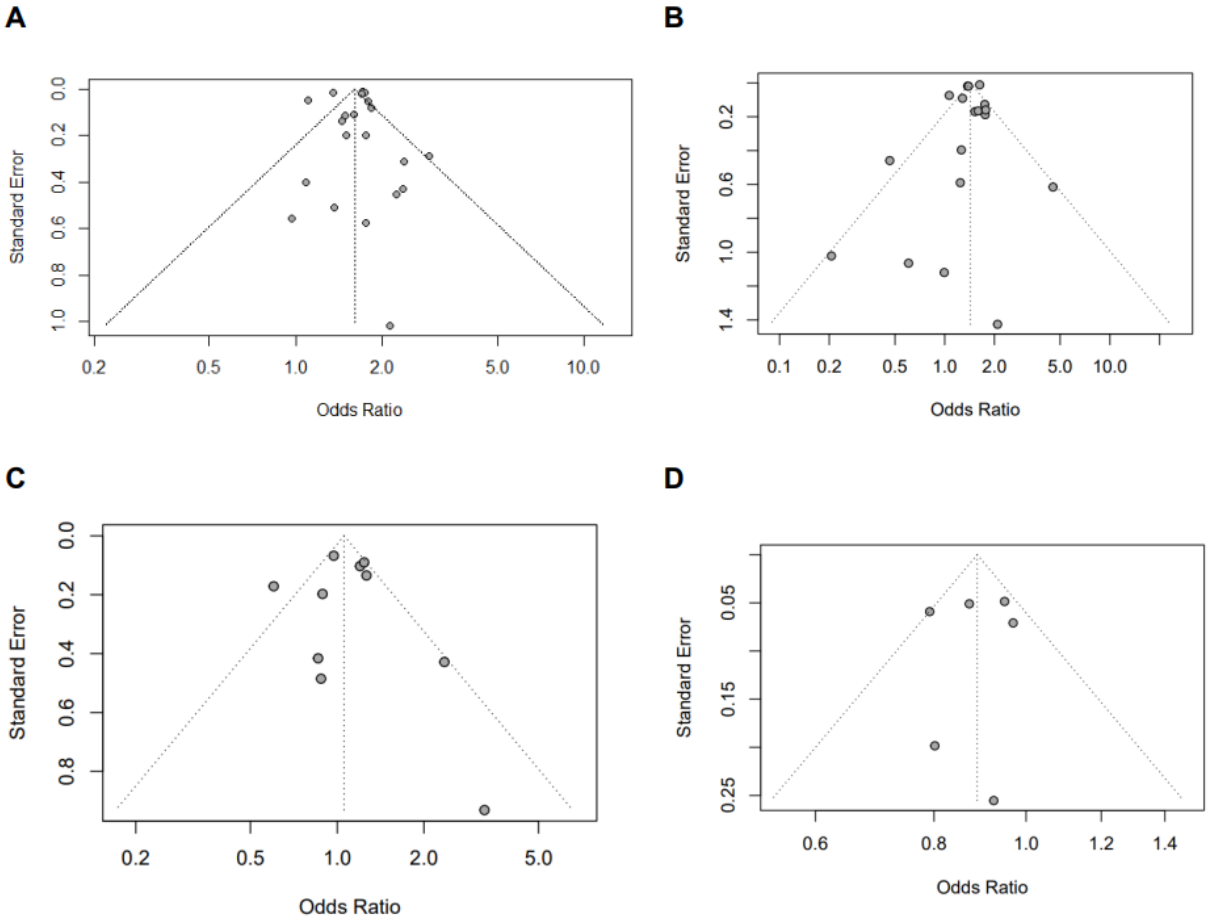


Table S1 : Newcastle-Ottawa assessment of studies included in the meta-analysis

Author, year	Postoperative outcomes of interest	Selection				Comparability	Outcome		
		Representativeness of the exposed cohort (CABG patients)	Selection of the non exposed (men/women)	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	study controls for In hospital /30-day outcome (*) and propensity matched (*)	Assessment of outcome	Adequacy of follow-up period	Adequacy of follow up of cohorts
Gurram, 2019 [1]	mortality	*	*	*	*	*	*	*	*
	stroke	*	*	*	*	*	*	*	*
Johnston, 2019 [2]	mortality	*	*	*	*	*	*	*	*
ter Woorst, 2019 [3]	mortality	*	*	*	*	*	*	*	*
	stroke	*	*	*	*	*	-	*	*
	myocardial infarction	*	*	*	*	*	-	*	*
	atrial fibrillation	*	*	*	*	*	-	*	*
Vrancic, 2019 [4]	mortality	*	*	*	*	*	*	*	*
	stroke	*	*	*	*	*	-	*	*
	myocardial infarction	*	*	*	*	*	-	*	*
	atrial fibrillation	*	*	*	-	*	-	*	*
Filardo, 2020 [5]	atrial fibrillation	*	*	*	*	*	*	*	*
Mahowald, 2020 [6]	mortality	*	*	*	*	* *	*	*	*
	stroke	*	*	*	*	* *	-	*	*
Mohamed, 2020 [7]	mortality	*	*	*	*	*	*	*	*
	stroke	*	*	*	*	*	-	*	*

Eris, 2021 [8]	mortality	*	*	*	*	*	*	*	*
	stroke	*	*	*	*	*	-	*	*
	myocardial infarction	*	*	*	*	*	-	*	*
Gaudino, 2021 [9]	mortality	*	*	*	*	*	*	*	*
	stroke	*	*	*	*	*	-	*	*
	myocardial infarction	*	*	*	*	*	*	*	*
	atrial fibrillation	*	*	*	*	*	-	*	*
Kytö, 2021 [10]	mortality	*	*	*	*	* *	*	*	*
Matyal, 2021 [11]	atrial fibrillation	*	*	*	*	*	-	*	*
Chang, 2022 [12]	mortality	*	*	*	*	* *	*	*	*
	stroke	*	*	*	*	* *	-	*	*
Dixon, 2022 [13]	mortality	*	*	*	*	*	*	*	*
	stroke	*	*	*	*	*	-	*	*
Gerfer, 2022 [14]	mortality	*	*	*	*	*	*	*	*
Moroni, 2022 [15]	mortality	*	*	*	*	*	*	*	*
	stroke	*	*	*	*	*	-	*	*
	myocardial infarction	*	*	*	*	*	*	*	*
Qu, 2022 [16]	mortality	*	*	*	*	* *	*	*	*
	stroke	*	*	*	*	* *	-	*	*
Ram, 2022 [17]	mortality	*	*	*	*	*	*	*	*
	stroke	*	*	*	*	*	-	*	*
Ter Woorst, 2022 [18]	myocardial infarction	*	*	*	*	*	-	*	*

Wang, 2022 [19]	mortality	*	*	*	*	* *	*	*	*
	stroke	*	*	*	*	* *	-	*	*
	myocardial infarction	*	*	*	*	* *	*	*	*
Daoulah, 2023 [20]	mortality	*	*	*	*	*	*	*	*
	stroke	*	*	*	*	*	-	*	*
	myocardial infarction	*	*	*	*	*	*	*	*
Gaudino, 2023 [21]	mortality	*	*	*	*	*	*	*	*
Sajja, 2023 [22]	mortality	*	*	*	*	* *	*	*	*
	stroke	*	*	*	*	* *	-	*	*
	myocardial infarction	*	*	*	*	* *	*	*	*
Sandner, 2023 [23]	mortality	*	*	*	*	*	*	*	*
	stroke	*	*	*	*	*	-	*	*
	myocardial infarction	*	*	*	*	*	*	*	*
Gupta, 2020 [24] (excluded for overlapping with Gaudino 2023)	mortality	*	*	*	*	*	*	*	*
Lin, 2022 [25](excluded for overlapping with Chang, 2022)	mortality	*	*	*	*	*	*	*	*
O'Shaughnessy, 2022 [26] (excluded for overlapping with Gaudino 2023)	mortality	*	*	*	*	*	*	*	*
Safdar, 2022 [27] (excluded for overlapping	mortality	*	*	*	*	*	*	*	*

with Gaudino 2023)									

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Table S2: Criteria for myocardial infarction in the studies included in the analysis

Article	Definition of myocardial infarction (MI)
Ter Woorst 2022 [1]	Perioperative MI – definition not provided
Wang 2022 [2]	Perioperative myocardial infarction: is diagnosed by an Isolated elevation of CK-MB to ≥10×99th percentile upper reference limit (URL) or cTn (I or T) to ≥70×URL during the first 48 h following CABG surgery with or without ECG or imaging changes of MI
Sajja 2023 [3]	Post-operative MI was defined as electrocardiographic (ECG) changes consistent with infarction (new significant Q waves in two contiguous leads in the absence of previous left ventricular hypertrophy (LVH), or conduction abnormalities) or evolving ST segment to T wave changes in two contiguous leads, or new left bundle branch block, or ST segment elevation requiring thrombolysis or percutaneous coronary intervention (PCI), and cardiac markers (troponins or creatinine kinase myocardial band (CK-MB)) in the necrosis range.
Vrancic 2019 [4]	Early (30-days) MI - No definition provided
Ter Woorst 2019 [5]	Perioperative infarction - definition not provided
Eris 2021[6]	Perioperative myocardial infarction was defined as the formation of a new Q wave in ≥2 consecutive leads on the electrocardiogram and a TnI value >10 times the 99th percentile upper reference value within the first 48 hours after surgery.
Gaudino 2021 [7]	In hospital myocardial infarction: ART trial: MI within 72 hours of CABG MI post-CABG defined as: - elevation of cardiac markers to at least 5 x the upper limit of normal or - development of new pathological Q waves in at least two contiguous leads. CORONARY trial: MI perioperative (within 72 hours of surgery): MI is defined by any of the following three criteria: - a CK-MB measurement ≥5 x 99th percentile upper reference limit (URL) without new pathological Q waves or new LBBB (non-Q wave MI) or with new pathological Q waves or new LBBB (Q wave MI); - angiographic evidence of new graft or native. MI non-perioperative (later than 72 hours after surgery): Detection of rise and/or fall of cardiac biomarkers with at least one value above the 99th percentile of the URL together with evidence of myocardial ischaemia with at least one of the following: - symptoms of ischaemia; - ECG changes indicative of new ischaemia [new ST-T changes or new LBBB]; - development of pathological Q waves in the ECG; or - imaging evidence of new loss of viable myocardium or new regional wall motion abnormality. GOPCABE Trial: MI within 72 hours after surgery is defined by the observation of at least one of the following three criteria: - measured CK-MB ≥ 5 x 99th percentile upper reference limit; or - angiographic evidence of new graft or native coronary artery occlusion; or - imaging evidence of new loss of viable myocardium. MI later than 72 hours after surgery was defined as a rise of cardiac biomarkers with at least one value above the 99th percentile of the upper reference limit in conjunction with evidence of myocardial ischemia with at least one of the following: - symptoms of ischemia; or - ECG changes indicative of new ischemia (new ST-T changes or new LBBB); or - development of pathological Q waves in the ECG; or - imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.

	PREVENT IV Trial: Perioperative MI was defined as a creatine kinase-MB (CK-MB) fraction of greater than 10 times the URL or greater than 5 times the URL with new Q waves longer than 30 ms in 2 contiguous leads or, if postoperative CK-MB samples were not available, new Q waves longer than 30 ms in 2 contiguous leads. Perioperative MI was diagnosed if CK-MB was elevated within 24 hours of surgery when there was not an interval clinical event and when the elevation was not attributable to a preoperative MI. Postoperative MI was defined as either spontaneous (CK-MB >2 times the URL or new Q waves >30 ms in 2 contiguous leads), after percutaneous coronary intervention (CK-MB >3 times the URL or new Q waves >30 ms in 2 contiguous leads), or after CABG surgery (CK-MB >10 times the URL or > times the URL with new Q waves >30 ms in 2 contiguous leads). For patients for whom CK-MB samples and electrocardiograms were not available, MI could be defined by the presence of "myocardial infarction," "heart attack," or similar term in the medical record documenting that an MI had occurred after the initial CABG procedure.
Moroni 2022 [8]	In hospital myocardial infarction: In- hospital non– Q- wave MI was defined as the elevation of the serum creatine kinase isoenzyme myocardial band that was 5x the upper limit of normal in the CABG group, in the absence of new pathological Q waves. In this analysis were included as cumulative MI all Q- wave MI that occurred during hospital stay … Q- wave MI was defined as the development of new pathological Q waves in 2 or more contiguous leads with or without creatine kinase or creatine kinase- myocardial band levels elevated above normal.
Daoulah 2023	Hospital MI : Coronary artery bypass grafting (CABG) related MI is termed type 5 MI. Coronary procedure-related MI #48 hours after the index procedure is arbitrarily defined by an elevation of cTn values >10 times for type 5 MI of the 99th percentile URL in patients with normal baseline values. Patients with elevated pre-procedural cTn values, in whom the preprocedural cTn level are stable (#20% variation) or falling, must meet the criteria for a >10 fold increase and manifest a change from the baseline value of >20%. In addition with at least one of the following: - Development of new pathological Q waves; - Imaging evidence of loss of viable myocardium that is presumed to be new and in a pattern consistent with an ischaemic aetiology; - Angiographic findings consistent with a procedural flow-limiting complication such as coronary dissection, occlusion of a major epicardial artery or graft, side-branch occlusion-thrombus, disruption of collateral flow or distal embolization. Isolated development of new pathological Q waves meets the type 5 MI criteria if cTn values are elevated and rising but less than the pre-specified thresholds for CABG.
Sandner 2023 [9]	30-days MI : CABG-related myocardial infarction (MI) is arbitrarily defined as elevation of cardiac biomarker values (>10 x 99th percentile upper reference limit, URL) in patients with normal baseline cTn values (≤99th percentile URL). In addition, either (i) new pathological Q waves or new LBBB, or (ii) angiographically documented new graft or new native coronary artery occlusion, or (iii) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality. The term acute MI should be used when there is evidence of myocardial necrosis in a clinical setting consistent with

	acute myocardial ischemia. Under these conditions any one of the following criteria meets the diagnosis for MI: • Detection of a rise and/or fall of cardiac biomarker values [preferably cardiac troponin (cTn)] with at least one value above the 99th percentile URL and with at least one of the following: Symptoms of ischemia. New or presumed new significant ST-segment–T wave (ST–T) changes or new left bundle branch block (LBBB). Development of pathological Q waves in the ECG. Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality. Identification of an intracoronary thrombus by angiography or autopsy. • Cardiac death with symptoms suggestive of myocardial ischemia and presumed new ischemic ECG changes or new LBBB, but with death occurring before cardiac biomarkers were obtained, or before cardiac biomarker values would be increased.

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Table S3: terminology and definition of postoperative atrial fibrillation in the studies included in the analysis, and preoperative data

Article	Terminology and definition of postoperative atrial fibrillation (PoAF)	Preoperative data:
Gurram 2019 [1]	PoAF : no definition provided	No statistically significant difference between men and women in preoperative sinus rhythm: Females 132 out of 132 (100%), Males 637out of 641 (99.37%); p = 0.363
Ter Woorst 2019 [2]	Postoperative new-onset AF: no definition provided	No statistically significant difference between men and women regarding preoperative AF (Women 121 out of 4016 (3.0%), Men 413 out of 13903 (3.0%), p=0.878)
Vrancic 2019 [3]	Early (30-day) AF: no definition provided	Data not provided (baseline characteristics description does not provide data on preoperative AF)
Filardo 2020 [4]	Post-CABG new-onset AF: new-onset in-hospital post-CABG AF, defined as any episode detected via continuous electrocardiogram/telemetry monitoring for the duration of the hospital stay and documented by a physician in the chart, regardless of duration or need for treatment	Included consecutive patients without a history of AF, no data on preoperative AF available for patients excluded from the study
Gaudino 2021 [5]	Postoperative atrial fibrillation: no definition provided	Data not provided
Matyal 2021 [6]	In-hospital post-operative AF : no definition provided	Preoperatively, a significantly larger proportion of women had a history of heart failure, but there was no statistically significant difference between men and women regarding pre-operative arrythmia

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