Trials

REVIEW

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Assessing the uptake of the core outcome set in randomized controlled trials for coronary artery disease: a trial registry analysis

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Abstract

Background Coronary artery disease (CAD) is a global health crisis, responsible for nearly 20 million deaths annually worldwide and 12.6% of all deaths in the United States. Randomized controlled trials (RCTs) are critical for developing evidence-based clinical guidelines, but inconsistent outcome reporting across RCTs hinders evidence synthesis and comparability. In 2015, McNamara et al. introduced a CAD core outcome set (COS) to promote standardization in CAD trial outcomes. This study evaluates the uptake of the CAD COS in RCTs registered at ClinicalTrials.gov since its publication.

Methods This trial registry analysis evaluated the uptake of the CAD COS in phase III/IV RCTs registered on ClinicalTrials.gov from May 2010 to June 2023. Trials were included if they assessed CAD interventions and excluded if the trials were non-randomized, focused on diagnostic tests, or were categorized as "not applicable" (e.g., behavioral interventions). COS adherence was measured as the proportion of reported outcomes among the 23 defined in the CAD COS. We analyzed changes in adherence over time, including pre- and post-COS publication periods, with secondary analyses examining continent, sponsor type, recruitment status, and enrollment number.

Results Among 433 trials, procedural interventions (45.0%) and all-cause mortality (40.9%) were the most reported outcomes, while acute renal failure (2.1%) and dyspnea (2.8%) were the least. Pre-2015, trials reported an average of 11.5% of the COS-defined outcomes. Post-2015, trials initiated after the CAD COS publication reported a slightly higher proportion of COS-defined outcomes compared to earlier trials, reflecting a modest increase in the number of items reported. However, this increase was not statistically significant ($p = 0.012$). Recruitment status significantly influenced adherence ($p < 0.001$), while continent and sponsor type did not. A weak positive correlation was observed between enrollment number and adherence ($r = 0.27$, $p < 0.001$).

Conclusions Despite its publication in 2015, CAD COS uptake remains limited, with no significant changes in adherence over time. Barriers such as limited dissemination, lack of trialist awareness, and preferences for custom outcomes likely contribute to these findings. Greater emphasis on education, patient-centered outcomes, and COS tailored to specific CAD indications is needed to enhance uptake and comparability in CAD trials.

Keywords Coronary artery disease, Clinical trials, Outcome assessment

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Introduction

Coronary artery disease (CAD) is a global health crisis, responsible for nearly 20 million deaths annually worldwide [1], including 12.6% of all deaths in the United States [2, 3]. Modifiable and non-modifiable risk factors, such as smoking, hyperlipidemia, diabetes, and previous familial history, contribute to the prevalence of CAD [4]. The escalating incidence of obesity and other risk factors [5] underscores the urgent need for evidence-based interventions to mitigate the burden of CAD.

Evidence-based medicine (EBM) relies on high-quality data from randomized clinical trials (RCTs) and other study designs to develop clinical guidelines and inform decision-making [6]. Inconsistent outcome reporting across RCTs complicates evidence synthesis, reduces the comparability of results, and limits the ability to draw meaningful conclusions [7]. This variability undermines systematic reviews and meta-analyses and increases the risk of selective reporting bias [7]. To promote consistency, core outcome sets (COS) were developed with input from patients, physicians, and researchers [8, 9].

In 2015, McNamara et al. published the Standardized Outcome Measurement for Patients With Coronary Artery Disease: Consensus From the International Consortium for Health Outcomes Measurement (ICHOM) [10]. This COS aims to improve the comparability and quality of RCTs by standardizing outcome measures in CAD trials. The COS encompasses longitudinal outcomes (e.g., all-cause mortality, admissions, acute renal failure), patient-reported health status (e.g., angina, dyspnea, depression), acute complications of treatment (coronary artery bypass grafting and percutaneous coronary intervention), major surgery complications (coronary artery bypass grafting only), and interventional cardiology complications (percutaneous coronary intervention only). Developed by international stakeholders, the COS serves as a benchmark for standardizing CAD trial outcomes.

Evaluating the uptake of the CAD COS in clinical trials is essential to understanding its influence on CAD research and identifying barriers to its implementation. This study assesses the use of the CAD COS in RCTs registered at ClinicalTrials.gov. Findings aim to guide future efforts to improve outcome standardization and enhance the comparability of CAD trials.

Methods

Eligibility criteria

The inclusion criteria required RCTs to (1) assess patients with CAD; (2) be registered between May 19, 2010 (5 years prior to the CAD COS publication) and June 26, 2023; and (3) evaluate the effectiveness, efficacy, or safety of interventions. Trials were excluded if they (1) did not focus exclusively on CAD; (2) were non-randomized; (3) evaluated diagnostic test accuracy; (4) focused on drug pharmacokinetics/pharmacodynamics; or (5) were categorized as "not applicable" (e.g., behavioral interventions), as these trials are outside the scope of regulated products and the CAD COS.

Information sources

This trial registry analysis evaluated the reporting and uptake of the CAD COS in clinical trials registered on ClinicalTrials.gov. Our methodology, based on Kirkham et al. [11], was made publicly available on Open Science Framework (OSF) [12]. The Institutional Review Board determined that this study did not involve human subject research.

Search strategy

Using the Core Outcome Measures in Effectiveness Trials (COMET) Initiative database, the CAD COS published by McNamara et al. in 2015 was identified for uptake analysis [10]. The COMET Initiative provides guidance to COS developers and hosts a freely accessible database to support collaboration among patients, clinicians, researchers, and other stakeholders in COS development [13]. ClinicalTrials.gov, an electronic clinical trial registry, was searched for phase III/IV CAD RCTs. Filters applied included "conditions: coronary artery disease," "study type: interventional studies," "phase: 3 and 4 (applicable to regulated products)," and "date: 05/19/2010 to 06/26/2023," with no restrictions regarding recruitment status. Comprehensive search terms used on ClinicalTrials.gov are detailed in Supplemental File A.

Although earlier-phase trials also assess interventional therapies, this study focused on phase III/IV trials, as these later stages evaluate efficacy and safety in larger populations, aligning with the clinical outcomes targeted by the CAD COS [10]. The CAD COS does not mandate its use in earlier-phase trials, further supporting this focus. We examined trial registry entries up to 5 years before COS publication to establish a baseline for outcome measurement.

Selection process

Before screening and data extraction, all authors underwent training on COS methodology using the COMET handbook [13, 14], video tutorials, presentations from the COMET Initiative, and group discussions led by the senior investigator (MV). Identified RCTs were compiled into a Google sheet for screening. Two authors (SB, SS) independently screened trials in a masked, duplicate manner. Discrepancies in eligibility decisions were

resolved through discussion, with a third-party adjudicator (TM) consulted if consensus could not be reached.

Data collection process

Data on general trial characteristics and COS uptake were collected using a pilot-tested Google Form. Two investigators (SB, SS) independently extracted data from the first five RCTs to calibrate the process, resolving discrepancies through discussion, with a third investigator (TM) available for arbitration. The same investigators then completed masked, duplicate data extraction for the remaining trials. After data extraction, data reconciliation was performed, and unresolved discrepancies were addressed by the third investigator.

Data items

General characteristics recorded for each RCT included year of trial start date, National Clinical Trial (NCT) number, trial continent affiliation(s), phase of trial, recruitment status, sponsor type, enrollment number, trial duration, and type of intervention. The Google Form also captured data on specific outcomes defined in the CAD COS, which includes 23 outcomes across five domains: (1) longitudinal (e.g., all-cause mortality, admissions, procedural interventions, acute renal failure); (2) patient-reported (e.g., angina, dyspnea, depression, functional status, health-related quality of life); (3) acute complications (e.g., mortality post-procedure, place of death, stroke and stroke type, acute renal failure, total length of stay, post-procedure length of stay); (4) major surgery (e.g., prolonged ventilation, deep sternal wound infection, reoperation required); (5) interventional (e.g., significant dissection, perforation, emergent CABG for failed PCI, vascular complications requiring intervention, bleeding event within 72 h). These outcomes are detailed in Supplemental File B.

To assess CAD COS uptake, the authors evaluated whether registered trials planned to measure the CAD COS outcomes, based on the trial registry entry [11]. The method and timing of outcome collection were also documented. If an established screening instrument (e.g., Seattle Angina Questionnaire [SAQ-7]) was used, referenced scales were reviewed to confirm inclusion of core outcomes.

Synthesis methods

To evaluate CAD COS uptake, we measured the percentage of registered trials that intended to report COS outcomes based on trial registry entries. Descriptive statistics (number and percentage of trials) were used to summarize trial characteristics. We investigated changes in the proportion of CAD COS outcomes reported over time, using the total 23 defined outcomes as the denominator, and applied the Newey-West method [15] for standard error estimation. A 1-year grace period post-COS publication was excluded to account for potential delays in adoption.

For each trial, adherence was calculated as the percentage of COS outcomes listed in the registry entry out of the total 23 outcomes. Average monthly adherence percentages were calculated to evaluate changes in adherence over time. Secondary analyses examined the effects of "continent," "sponsor type," and "recruitment status" on mean COS adherence percentages, as well as the Pearson correlation between "enrollment number" and COS adherence. Statistical analyses were performed using

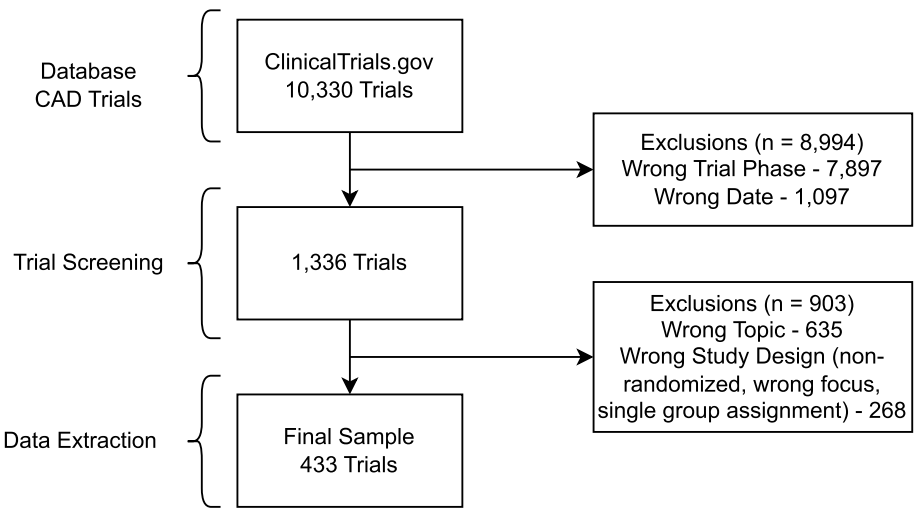

Fig. 1 Study selection flowchart

Stata/BE 17.0 (StataCorp, LLC, College Station, TX), R (version 4.2.1), and RStudio. All data, reconciled data, and statistical analysis scripts are available on OSF [12].

Results

Clinical trial inclusions

The ClinicalTrials.gov database initially contained 10,330 CAD trials. After filtering by registration date and trial phase, 1336 trials were eligible for screening. Of these, 903 trials were excluded, resulting in a final sample of 433 trials included for data extraction. The study selection process is detailed in Fig. 1.

Trial characteristics

Of the 433 included trials, 28.2% (122/433) were phase 3 trials, and 71.8% (311/433) were phase 4 trials. The median enrollment was 243 participants, with a median trial duration of 32 months. Most trials (68.4%, 296/433) evaluated pharmacologic interventions, followed by percutaneous interventions (13.2%, 57/433), multiple interventions (10.6%, 46/433), and other interventions (7.9%, 34/433). Trial status included 37.2% (161/433) completed, 16.2% (70/433) recruiting, and 6.7% (29/433) terminated. Additional trial characteristics are detailed in Table 1.

Analysis of COS uptake

In June 2010, CAD clinical trials reported an average of 11.5% of the outcomes specified in the COS. Using a statistical approach with the Newey-West method, we analyzed changes in the proportion of COS-define outcomes reported before and after the CAD COS publication. Before the publication in May 2015, trials reported an average of 11.5% of the COS-defined outcomes. Trials initiated after the COS publication in 2015 reported a slightly higher proportion of COS-defined outcomes, reflecting a modest increase in the number of items reported compared to earlier trials, as shown in Fig. 2. However, the increase in the mean percentage of COS-defined outcomes over time (0.1% per month) was not statistically significant ($p=0.12$, 95% CI = [−0.02, 0.16]). Figure 2 illustrates these findings, incorporating a 1-year grace period for COS uptake to account for implementation delays, while Fig. 3 shows the average percentage of outcomes reported annually.

Among the outcomes specified in the CAD COS, procedural interventions (45.0%, 195/433) and all-cause mortality (40.9%, 177/433) were the most frequently measured. In contrast, the least measured outcomes were acute renal failure (2.1%, 9/433) and patient-reported dyspnea (2.8%, 12/433). Detailed frequency data for COS uptake are summarized in Table 2, with a comprehensive comparison of trial outcomes and CAD COS alignment provided in Supplemental File C.

Table 1 Trial characteristics

Characteristic	*N* = 433
Year, *n* (%)	
2011	55 (12.7)
2012	45 (10.4)
2015	42 (9.7)
2014	41 (9.5)
2013	34 (7.9)
2021	34 (7.9)
2010	31 (7.2)
2018	30 (6.9)
2019	25 (5.8)
2022	25 (5.8)
2017	24 (5.5)
2016	19 (4.4)
2020	16 (3.7)
2023	12 (2.8)
Phase, *n* (%)	
4	311 (71.8)
3	122 (28.2)
Continent, *n* (%)	
Asia	215 (49.7)
Europe	138 (31.9)
North America	35 (8.1)
Multiple	23 (5.3)
South America	14 (3.2)
Africa	7 (1.6)
Australia	1 (0.2)
Recruitment status, *n* (%)	
Completed	161 (37.2)
Unknown	134 (30.9)
Recruiting	70 (16.2)
Terminated	29 (6.7)
Not yet recruiting	12 (2.8)
Withdrawn	12 (2.8)
Enrolling by invitation	2 (0.5)
Funding type, *n* (%)	
Hospital	144 (33.3)
University	71 (16.4)
Multiple with industry	57 (13.2)
Multiple without industry	56 (12.9)
Private	51 (11.8)
Industry	46 (10.6)
Government	8 (1.8)
Enrollment number, median (IQR)	243 (100–951)
Trial duration in months, median (IQR)	32 (21–50)
Type of intervention, *n* (%)	
Pharmacologics	296 (68.4)
PCI	57 (13.2)
Multiple	46 (10.6)

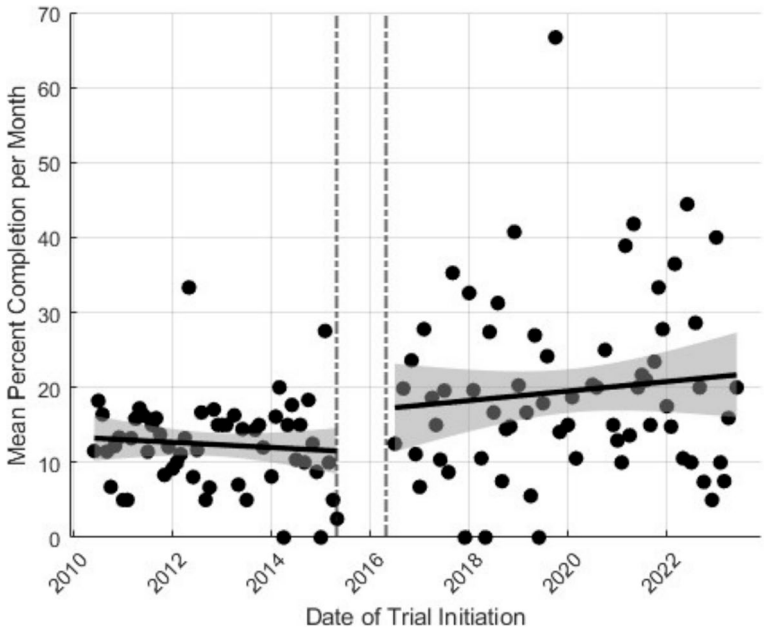

Fig. 2 Analysis of changes in the proportion of coronary artery disease core outcome set outcomes reported by year of trial initiation (actual start date). This figure illustrates the mean percentage of coronary artery disease core outcome set-defined outcomes reported by randomized controlled trials over time, stratified by trial initiation year. The solid line represents the overall trend in the proportion of core outcome set-defined outcomes reported, with a 1-year grace period excluded following the 2015 publication of the coronary artery disease core outcome set to account for adoption delays. The shaded area represents the 95% confidence intervals, indicating the range of uncertainty around the mean trend. Dashed vertical lines mark the publication of the coronary artery disease core outcome set in May 2015 and the end of the grace period. Each data point corresponds to the mean percentage of core outcome set-defined outcomes reported by trials initiated in a given month

Relationship between trial characteristics and outcome measures

Our analysis showed a non-significant relationship between mean COS adherence percentages for both "continent" ($F=0.57$, $p=0.76$, $\eta^2=0.01$) and "sponsor type" ($F=1.35$, $p=0.23$, $\eta^2=0.02$). However, a statistically significant relationship was found for "recruitment status" ($F=5.21$, $p<0.001$, $\eta^2=0.08$), with 8.0% of variation attributed to this factor, compared to 2.0% for "sponsor type" and 1.0% for "continent."

A Pearson correlation analysis revealed a statistically significant but weakly positive correlation between "enrollment number" and COS adherence ($r=0.27$, $t=5.91$, $p<0.001$). Although significant, the small effect size suggests limited practical implications. Table 3 summarizes the results of statistical analyses, including ANOVAs and a Pearson correlation analysis, that evaluated the relationships between trial characteristics (continent, sponsor type, and recruitment status) and CAD COS adherence percentages. These analyses aimed to identify factors influencing CAD COS adherence.

Discussion

Our study found no significant change in the uptake of the CAD COS since its publication in 2015, with adherence levels remaining low throughout the study periods. Nearly a decade later, a lack of standardization persists among outcomes in CAD clinical trials. This may reflect limited dissemination of the COS, low awareness among trialists, or challenges in integrating the COS into trial designs. Of the 23 items in the CAD COS, only 4 were reported in at least 20.0% of trials, and no trial reported all applicable items. While the average percentage of reported outcomes has increased since 2015, it remains below 25.0%. These results underscore the need for improved COS dissemination and targeted education to enhance uptake in CAD trials.

Although the CAD COS aligns with broader efforts to standardize clinical trial outcomes [16–18], our findings suggest persistent barriers for trialists. One potential barrier is the broad definition of CAD within the International Consortium for Health Outcomes Measurement's (ICHOM) COS, which encompasses diverse patient populations, including those with angina, myocardial infarction, and patients undergoing PCI or CABG [10]. This heterogeneity likely contributes to the variability in outcome reporting observed in our study. To enhance the comparability of RCT results, trial outcomes should be as specific and relevant as possible [7].

For example, Kirkham et al. reported over 80.0% uptake of a rheumatoid arthritis COS in 273 trials [11], which may reflect the specificity of focusing solely on

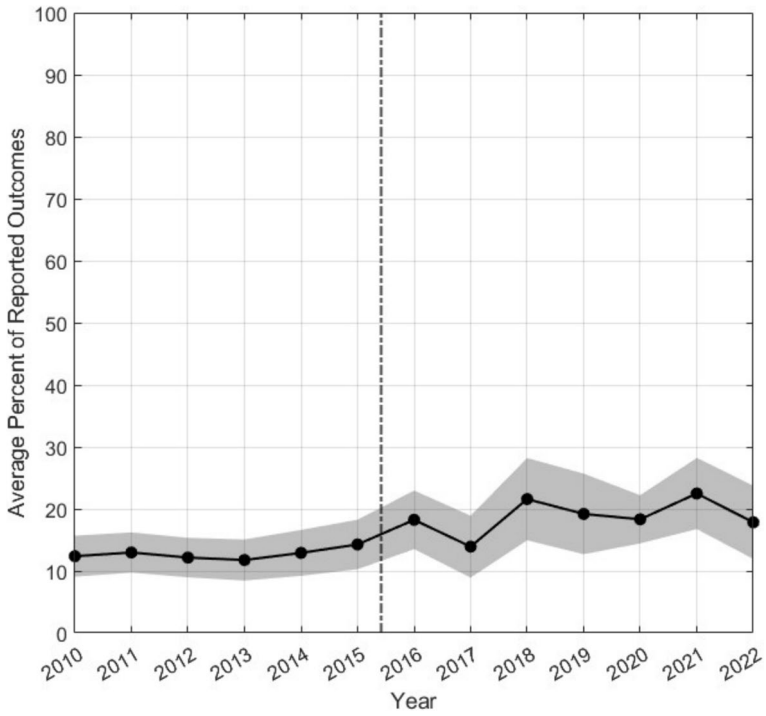

Fig. 3 Annual reporting of coronary artery disease core outcome set outcomes in randomized controlled trials. This figure illustrates the average percentage of coronary artery disease core outcome set-defined outcomes reported annually by randomized controlled trials, stratified by the year of trial initiation. The solid line represents the mean proportion of core outcome set-defined outcomes reported each year. The shaded area represents the 95% confidence intervals, highlighting the range of uncertainty around the annual mean percentages. Data points reflect the mean percentage of reported core outcome set-defined outcomes for all trials initiated within a given year. The figure demonstrates trends in adherence to the coronary artery disease core outcome set over the study period

rheumatoid arthritis, a condition with fewer variations than CAD [19]. Future efforts should prioritize improved dissemination of the CAD COS while encouraging the development of COS tailored to specific CAD subgroups. For instance, Benstoem et al. proposed a COS for adult cardiac surgery trials, which could provide more precise outcomes for patients undergoing CABG surgeries for CAD [20]. Similarly, COS developed for traditional Chinese medicine interventions, such as Zhang et al.'s [21], may better suit trials evaluating these therapies. While specificity may partly explain the limited uptake of the CAD COS, other barriers likely exist.

Our results indicate that patient-reported outcomes were underrepresented, with none of the five patient-reported outcomes in the CAD COS being reported in more than 15.0% of trials. Despite the growing emphasis on patient-centered care, trialists may encounter challenges in incorporating these outcomes into trial designs. The CAD COS's scope, with its 23 outcomes, may be difficult for trialists to adopt comprehensively. A review of the COS could help determine whether all included outcomes are truly "core," or if a streamlined set of outcomes would enhance its practical utility. Refining the COS to focus on the most essential outcomes may facilitate integration into trials and improve uptake.

Additionally, a 2020 survey by Bellucci et al. identified trialists' preferences for their own outcomes and insufficient awareness of the COS as key barriers to adoption [8]. To improve uptake, we recommend targeted educational initiatives and promotional efforts to highlight the value of COS within the clinical trial landscape. Enhancing COS adoption in CAD trials could address patient concerns, improve care, and support better-informed clinical decisions by patients and physicians [22].

Strengths and limitations

Our study has several strengths. First, transparency and reproducibility were prioritized by pre-registering our study protocol on OSF [12] and subsequently uploading our data extraction forms, data, and analysis scripts. Second, we evaluated all CAD clinical trials registered on ClinicalTrials.gov, a widely recognized and reputable registry [23] that facilitates efficient evaluation of clinical trials [11]. Third, data screening and extraction were

Table 2 Frequency of outcome set uptake

Domain	Outcome set item	Before COS publication	After COS publication	*N* = 433
Longitudinal outcomes (all)	All-cause mortality, *n* (%)			
	No	137 (53.5)	119 (46.5)	256 (59.1)
	Yes	70 (39.5)	107 (60.5)	177 (40.9)
	Admissions (for AMI, hemorrhagic stroke, ischemic stroke, or heart failure), *n* (%)			
	No	178 (51.3)	169 (48.7)	347 (80.1)
	Yes	29 (33.7)	57 (66.3)	86 (19.9)
	Procedural interventions, *n* (%)			
	No	113 (47.5)	125 (52.5)	238 (55.0)
	Yes	94 (48.2)	101 (51.8)	195 (45.0)
	Acute renal failure, *n* (%)			
	No	203 (47.9)	221 (52.1)	424 (97.9)
	Yes	4 (44.4)	5 (55.6)	9 (2.1)
Patient-reported health status (all)	Angina, *n* (%)			
	No	179 (48.9)	187 (51.1)	366 (84.5)
	Yes	28 (41.8)	39 (58.2)	67 (15.5)
	Dyspnea, *n* (%)			
	No	205 (48.7)	216 (51.3)	421 (97.2)
	Yes	2 (16.7)	10 (83.3)	12 (2.8)
	Depression, *n* (%)			
	No	205 (49.3)	211 (50.7)	416 (96.1)
	Yes	2 (11.8)	15 (88.2)	17 (3.9)
	Functional status, *n* (%)			
	No	188 (49.9)	189 (50.1)	377 (87.1)
	Yes	19 (33.9)	37 (66.1)	56 (12.9)
	Health-related QOL, *n* (%)			
	No	196 (49.9)	197 (50.1)	393 (90.8)
	Yes	11 (27.5)	29 (72.5)	40 (9.2)
Acute complications of treatment (PCI and CABG)	Mortality post-procedure, *n* (%)			
	No	131 (53.9)	112 (46.1)	243 (81.3)
	Yes	22 (39.3)	34 (60.7)	56 (18.7)
	Not applicable	54	80	134
	Place of death, *n* (%)			
	No	150 (50.8)	145 (49.2)	295 (98.7)
	Yes	3 (75.0)	1 (25.0)	4 (1.3)
	Not applicable	54	80	134
	Stroke and stroke type, *n* (%)			
	No	95 (59.7)	64 (40.3)	159 (53.2)
	Yes	58 (41.4)	82 (58.6)	140 (46.8)
	Not applicable	54	80	134
	Acute renal failure, *n* (%)			
	No	149 (51.2)	142 (48.8)	291 (97.7)
	Yes	3 (42.9)	4 (57.1)	7 (2.3)
	Not applicable	55	80	135
	Total length of stay, *n* (%)			
	No	148 (51.6)	139 (48.4)	287 (96.3)
	Yes	4 (36.4)	7 (63.6)	11 (3.7)
	Not applicable	55	80	135
	Post-procedure length of stay, *n* (%)			
	No	150 (51.9)	139 (48.1)	289 (97.0)
	Yes	2 (22.2)	7 (77.8)	9 (3.0)
	Not applicable	55	80	135

Table 2 (continued)

Domain	Outcome set item	Before COS publication	After COS publication	*N* = 433
Major surgery complications (CABG only)	Prolonged ventilation (> 24 h post-surgery), *n* (%)			
	No	10 (37.0)	17 (63.0)	27 (93.1)
	Yes	0 (0.0)	2 (100.0)	2 (6.9)
	Not applicable	197	207	404
	Deep sternal wound infection, *n* (%)			
	No	9 (32.1)	19 (67.9)	28 (96.6)
	Yes	1 (100.0)	0 (0.0)	1 (3.4)
	Not applicable	197	207	404
	Reoperation required, *n* (%)			
	No	8 (33.3)	16 (66.7)	24 (82.8)
	Yes	2 (40.0)	3 (60.0)	5 (17.2)
	Not applicable	197	207	404
Interventional cardiology complications (PCI only)	Significant dissection, *n* (%)			
	No	140 (52.0)	129 (48.0)	269 (98.5)
	Yes	4 (100.0)	0 (0.0)	4 (1.5)
	Not applicable	63	97	160
	Perforation, *n* (%)			
	No	142 (52.2)	130 (47.8)	272 (99.3)
	Yes	2 (100.0)	0 (0.0)	2 (0.7)
	Not applicable	63	96	159
	Emergent CABG for failed PCI, *n* (%)			
	No	131 (55.7)	104 (44.3)	235 (85.8)
	Yes	13 (33.3)	26 (66.7)	39 (14.2)
	Not applicable	63	96	159
	Vascular complications requiring intervention, *n* (%)			
	No	140 (52.0)	129 (48.0)	269 (98.2)
	Yes	4 (80.0)	1 (20.0)	5 (1.8)
	Not applicable	63	96	159
	Bleeding event within 72 h, *n* (%)			
	No	91 (56.5)	70 (43.5)	161 (59.0)
	Yes	53 (47.3)	59 (52.7)	112 (41.0)
	Not applicable	63	97	160

The table summarizes the frequency of outcome set uptake before and after COS publication. Percentages for "Before COS publication" and "After COS publication" are calculated relative to the total population (*N* = 433). Percentages for the "Total" column reflect cumulative reporting across both time periods.

Abbreviations: *AMI* acute myocardial infarction, *PCI* percutaneous coronary intervention, *CABG* coronary artery bypass grafting, *QOL* quality of life

performed in a masked, duplicate manner following the Cochrane Handbook's guidelines [24].

Our study is not without limitations. We implemented a rigorous data extraction process, including masked, duplicate screening and reconciliation of discrepancies, to minimize the risk of incorrect outcome matching. However, not all outcomes may have been reported in the registry, as updates may not fully reflect changes made or additional outcomes added during the trial. Additionally, we excluded "not applicable" trials, such as behavioral interventions, to focus on phase III/IV trials involving regulated products. Despite this limitation, ClinicalTrials.gov is recommended by the International Committee of Medical Journal Editors (ICMJE) and remains a valuable tool to mitigate selective reporting bias [25].

Conclusion

Our study evaluated the uptake of the CAD COS in clinical trials and identified persistent challenges in outcome standardization. Despite its publication in 2015, COS uptake has increased only marginally, with more than half of trials in our sample failing to report any COS-defined outcomes and patient-reported outcomes being rarely included. Barriers such as limited dissemination, lack of trialist awareness, and preferences for custom outcomes likely contribute to these findings.

Table 3 Statistical analysis of trial characteristics and CAD COS adherence

Characteristic	$N = 433$[a]	F-statistic[b]	p value[b]	(η^2)[b]
Continent		0.57	0.76	0.01
Africa	8.65 (13.58)			
Asia	15.06 (12.31)			
Australia	22.22 (NA)			
Europe	15.72 (15.61)			
Multiple	16.79 (9.90)			
North America	17.62 (15.27)			
South America	16.55 (12.63)			
Sponsor type		1.35	0.23	0.02
Government	15.69 (9.89)			
Hospital	16.15 (14.92)			
Industry	13.60 (12.12)			
Multiple with industry	16.02 (12.08)			
Multiple without industry	18.96 (15.02)			
Private	15.22 (11.21)			
University	12.65 (13.21)			
Recruitment status		5.21	< 0.001	0.08
Active, but no recruiting	28.68 (19.82)			
Completed	14.14 (12.48)			
Enrolling by invitation	12.50 (10.61)			
Not yet recruiting	20.48 (14.29)			
Recruiting	21.43 (17.50)			
Terminated	12.65 (8.28)			
Unknown	13.35 (11.01)			
Withdrawn	12.55 (14.14)			
Characteristic		**t-statistic**[c]	**p value**[c]	**(r)**[c]
Enrollment number		5.91	< 0.001	0.27

ANOVA analyses evaluated the effects of continent, sponsor type, and recruitment status on CAD COS adherence percentages, while Pearson correlation analysis examined the relationship between enrollment number and adherence

[a] Mean (SD)

[b] One-way ANOVA, η^2

[c] Pearson correlation coefficient

To address these issues, we recommend developing more specific COS tailored to distinct CAD indications, prioritizing educational initiatives to emphasize the importance of COS, and encouraging greater incorporation of patient-centered outcomes. These efforts are essential to improving the standardization and comparability of outcomes in CAD clinical trials, ultimately supporting better evidence-based care.

Abbreviations

CAD	Coronary artery disease
RCTs	Randomized controlled trials
COS	Core outcome set(s)
EBM	Evidence-based medicine
SRs	Systematic reviews
OSF	Open Science Framework
CABG	Coronary artery bypass grafting
PCI	Percutaneous interventions

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13063-025-08765-2.

Additional file 1.

Additional file 2.

Additional file 3.

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Authors' contributions
All authors contributed equally to the intellectual development of this manuscript. All authors performed the drafting and preliminary research needed to formulate this manuscript. Author MV provided oversight and critical appraisal of this manuscript. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Data availability
The datasets generated and/or analyzed during the current study are available in the Open Science Framework repository, https://osf.io/s8zxw/.

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Not applicable.

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Not applicable.

Competing interests
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