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*OPINION REVIEW*

# Coronary artery disease and heart failure: Late-breaking trials presented at American Heart Association scientific session 2023

Avilash Mondal, Sashwath Srikanth, Sanjana Aggarwal, Naga R Alle, Olufemi Odugbemi, Ikechukwu Ogbu, Rupak Desai

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## Abstract

The late-breaking science presented at the 2023 scientific session of the American Heart Association paves the way for future pragmatic trials and provides meaningful information to guide management strategies in coronary artery disease and heart failure (HF). The dapagliflozin in patient with acute myocardial infarction (DAPA-MI) trial showed that dapagliflozin use among patients with acute MI without a history of diabetes mellitus or chronic HF has better cardiometabolic outcomes compared with placebo, with no difference in cardiovascular outcomes. The MINT trial showed that in patients with acute MI and anemia (Hgb < 10 g/dL), a liberal transfusion goal (Hgb ≥ 10 g/dL) was not superior to a restrictive strategy (Hgb 7-8 g/dL) with respect to 30-day all-cause death and recurrent MI. The ORBITA-2 trial showed that among patients with stable angina and coronary stenoses causing ischemia on little or no antianginal therapy, percutaneous coronary intervention results in greater improvements in anginal frequency and

exercise times compared with a sham procedure. The ARIES-HM3 trial showed that in patients with advanced HF who received a HeartMate 3 levitated left ventricular assist device and were anticoagulated with a vitamin K antagonist, placebo was noninferior to daily aspirin with respect to the composite endpoint of bleeding and thrombotic events at 1 year. The TEAMMATE trial showed that everolimus with low-dose tacrolimus is safe in children and young adults when given ≥ 6 months after cardiac transplantation. Providing patients being treated for HF with reduced ejection fraction (HFrEF) with specific out-of-pocket (OOP) costs for multiple medication options at the time of the clinical encounter may reduce 'contingency planning' and increase the extent to which patients are taking the medications decided upon. The primary outcome, which was cost-informed decision-making, defined as the clinician or patient mentioning costs of HFrEF medication, occurred in 49% of encounters with the checklist only control group compared with 68% of encounters in the OOP cost group.

**Key Words:** Heart failure; Coronary artery disease; Clinical trials; Myocardial infarction; Cardiovascular outcome; Percutaneous coronary intervention; Blood transfusion; Cardiac transplant



**Core Tip:** In this review paper, we discuss the late-breaking trials featured in the American Heart Association 2023, spanning various cardiac conditions and interventions. The review sheds light on treatment nuances and underscore the importance of evidence-based medicine.

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## INTRODUCTION

Cardiovascular research on heart failure (HF) and coronary artery disease, including always-evolving interventional techniques, continually shapes therapeutic approaches, elucidating optimal strategies and challenging established norms. In this review paper, we discuss the late-breaking trials featured in the American Heart Association 2023, held in Philadelphia, Pennsylvania, United States, in November 2023. Dapagliflozin in patient with acute myocardial infarction (DAPA-MI) investigated dapagliflozin's effect on post-MI without diabetes. MINT tried to elucidate transfusion thresholds in anemic MI patients, while ORBITA-2 assessed percutaneous coronary intervention (PCI)'s efficacy for angina relief. ARIES-HM3 scrutinized aspirin's role in levitated left ventricular assist device (LVAD)-treated HF. The TEAMMATE trial assessed everolimus in post-heart transplant care for children (Table 1).

Additionally, integrating cost data into shared decision-making for (HF with reduced ejection fraction) HFrEF treatments emerges as a patient-centered approach. These trials, spanning various cardiac conditions and interventions, shed light on treatment nuances and underscore the importance of evidence-based medicine. The findings contribute crucial insights into optimizing therapeutic strategies, enhancing patient outcomes, and guiding clinical decision-making. As these trials unravel, they offer novel perspectives and potential paradigm shifts in managing cardiovascular ailments, reshaping how we approach cardiac care and highlighting the evolving landscape of cardiovascular research and practice.

## CORONARY ARTERY DISEASE

### *DAPA-MI–A registry-based randomized trial of dapagliflozin in patient with acute myocardial infarction without diabetes*

**Study summary:** The DAPA-MI trial is a multicenter, parallel-group, registry-based, randomized, double-blind, placebo-controlled phase 3 trial integrating existing national clinical registries (SWEDEHEART and NICOR in Sweden and the United Kingdom, respectively) which aimed to assess the effect of dapagliflozin (10 mg daily) *vs* placebo in patients recently hospitalized for myocardial infarction without known diabetes or established HF[1].

**Clinical implications:** Patients with acute MI without diabetes mellitus or chronic HF have better cardiometabolic outcomes with dapagliflozin than placebo. Over two years, dapagliflozin patients lost 1.65 kg and were less likely to acquire diabetes.

Because the primary composite results were lower than predicted, the trial design was revised to focus on clinically important cardiometabolic outcomes using a hierarchical composite outcome method using the win ratio. However, with

**Table 1 Summary of coronary artery disease and heart failure trials from the late-breaking trials presented at the American Heart Association 3 scientific sessions**

| Trial name | Ref. | Type of study | Sample size | Follow-up duration | Inclusion criteria | Exclusion criteria | Study findings | Study highlights |
|---|---|---|---|---|---|---|---|---|
| DAPA-MI | James *et al*[1] | Randomized control Trial | 4017 | 24 months | NSTEMI or STEMI < 10 days, impaired LV systolic function or q-wave MI, hemodynamically stable | Type 1 or type 2 DM, chronic symptomatic HF with a prior HF hospitalization within the last year and known LVEF ≤ 40%, eGFR) < 20 mL/min/1.73 $m^2$ | The primary endpoint for dapagliflozin *vs* placebo was a win ratio of 1.34, 95%CI 1.20–1.50; $P < 0.001$[b] | The DAPA-MI trial indicated that for acute MI patients, without diabetes or chronic heart failure, the use of dapagliflozin results in improved cardiometabolic outcomes while it does not lead to any changes in cardiovascular outcomes |
| MINT trial | Carson *et al* [2] | Randomized control trial | 3504 | 30 days | Age ≥ 18 years, STEMI or NSTEMI, Hgb < 10 g/dL | Uncontrolled bleeding requiring blood transfusion, declined transfusion, anticipated cardiac surgery, palliative treatment intent | The primary outcome, composite of all-cause death or recurrent nonfatal MI, for restrictive *vs* liberal transfusion strategies at 30 days, was: 16.9% *vs* 14.5%; RR: 1.15, 95%CI: 0.99-1.34; $P = 0.07$ | The MINT trial showed that in patients with acute MI and Hgb < 10 g/dL, a liberal transfusion goal (Hgb ≥ 10 g/dL) was not superior to a restrictive strategy (Hgb 7-8 g/dL) with respect to 30-day all-cause death and recurrent MI |
| ORBITA-2 | Rajkumar *et al*[5] | Randomized control trial | 301 | 12 weeks | PCI eligible, had angina or angina equivalents, had anatomical evidence of at least one severe coronary stenosis that was identified on invasive diagnostic coronary angiography or CCTA, had evidence of ischemia on the basis of noninvasive imaging or invasive coronary physiological test | Age < 18 years and age > 85 years, recent ACS, Previous CABG, significant left main stem CAD, chronic total occlusion in the target vessel, contraindication to PCI or drug-eluting stent implantation, contraindication to antiplatelet therapy, severe valvular disease, severe LV dysfunction, severe respiratory disease, life expectancy < 2 years, pregnancy | The primary outcome, mean angina symptom score for PCI *vs* placebo, was: 2.9 *vs* 5.6, OR: 2.21, 95%CI: 1.41-3.47; $P < 0.001$[b]. Mean daily angina frequency: 0.3 *vs* 0.7 (OR: 3.44, 95%CI: 2.00-5.91) | The ORBITA-2 trial showed that among patients with stable angina on little or no antianginal therapy, PCI results in greater improvements in anginal frequency and exercise times compared with a sham procedure |
| ARIES-HM3 | Mehra *et al* [10] | Randomized control trial | 628 | 24 months | Age ≥ 18 years, first durable LVAD implantation with HM3 for an approved indication per local guidelines | Additional MCS in addition to HM3, alternative indication or contraindication for antiplatelet therapy, inability to take oral medications through day 7 postoperatively, aspirin allergy | The primary outcome, survival free from nonsurgical hemocompatibility-related adverse event (*i.e.*, stroke, pump thrombosis, major bleeding, or arterial thromboembolism > 14 days post-implant), for placebo *vs* aspirin at 1 year, was: 74.2 *vs* 68.1 events per 100 patient-years ($P$ for noninferiority < 0.0001[b]) | The ARIES-HM3 trial demonstrated that for patients with advanced heart failure treated with a HeartMate 3 LVAD and anticoagulated with a vitamin K antagonist, aspirin did not surpass placebo in terms of the combined incidence of bleeding and clotting events after one year |
| TEAMMATE | Almond *et al* [11] | Randomized control trial | 211 | 30 months | Cardiac transplantation at age ≤ 21 years, ≥ 6 months after heart transplantation, stable immunosuppression | Recurrent rejection/graft dysfunction, steroid dose > 0.1 mg/kg/day eGFR < 30 mL/min/1.73 $m^2$, active infection or wound healing problem, severe hyperlipidemia or proteinuria | The co-primary outcomes, median MATE-6 score at 30 months, was 1.96 in everolimus group *vs* 2.18 in tacrolimus group, median MATE-3 score at 30 months, was 0.93 in everolimus group *vs* 1.25 in tacrolimus group ($P$ = NS) | The TEAMMATE trial showed that everolimus + low-dose tacrolimus is safe in children and young adults when given ≥ 6 months after cardiac transplantation |
| POCKET-COST-HF | Montembeau *et al*[12] | Randomized control trial | 247 | - | LVEF ≤ 40% | | The primary outcome, which was cost-informed decision-making, defined as the clinician or patient mentioning costs | Providing detailed cost information had notable effect on discussions about costs during |

| | | | |
|---|---|---|---|
| | | of HFrEF medication, occurred in 49% of encounters with the checklist only control group compared with 68% of encounters in the OOP cost group ($P$ = 0.021[a]) | medical appointments for patients with HFrEF |

[a]$P < 0.05$.
[b]$P < 0.001$.
NSTEMI: Non-ST segment elevation myocardial infarction; STEMI: Segment elevation myocardial infarction; PCI: Percutaneous coronary intervention; CCTA: Coronary computed tomography angiography; ACS: Acute coronary syndrome; CABG: Coronary artery bypass graft; HF: Heart failure; LVEF: Left ventricular ejection fraction; eGFR: Estimated glomerular filtration rate; DM: Diabetes mellitus; MI: Myocardial infarction; LVAD: Left ventricular assist device; VKA: Vitamin K antagonist; MATE: Major adverse transplant event; HFrEF: Heart failure with reduced ejection fraction; OOP: Out-of-pocket; MCS: Mechanical circulatory support.

longer follow up we might be able to see favorable outcomes.

### *MINT: Restrictive vs liberal blood transfusion in patients with myocardial infarction and anemia: Results of the MINT trial*

**Study summary:** Several pivotal trials have attempted to delineate the optimal transfusion thresholds for acute myocardial infarction (AMI) patients[2-4], but none have been able to conclude a clear consensus. The theoretical benefit of preventing ischemic injury by improving oxygen delivery and reducing the risk of reinfarction or death needs to be weighed against the potential harm from fluid overload, transfusion-related infection, and thrombotic and inflammatory processes.

Of 3504 patients were included in the analysis. The primary outcome was defined as a 30-day composite of myocardial infarction or all-cause mortality which occurred in 16.9% of the restrictive-strategy group and 14.5% of the liberal-strategy group [RR: 1.15; 95% confidence interval (CI): 0.99-1.34, $P$ = 0.07]. Additionally, there were no significant differences in secondary outcomes like death (RR: 1.19; 95%CI: 0.96-1.47) or recurrent non-fatal MI (RR: 1.19; 95%CI: 0.94-1.49), combined death, myocardial infarction, ischemia-driven unscheduled coronary revascularization, or readmission to the hospital for an ischemic cardiac condition (RR: 1.13; 95%CI: 0.98-1.29), risk of HF (RR: 0.92; 95%CI: 0.71-1.20) at 30 days, pulmonary embolism, or deep venous thrombosis (RR: 0.77; 95%CI: 0.46-1.27) in the restrictive *vs* liberal strategy group. However, cardiac death was more frequent in the restrictive-strategy group (RR: 1.74; 95%CI: 1.26-2.40), while there was less risk of transfusion-associated cardiac overload events in the restrictive-strategy group than in the liberal-strategy group (RR: 0.35; 95%CI: 0.16-0.78). Subgroup analyses of primary outcome revealed trend favoring the liberal strategy for patients with type 1 myocardial infarction (RR: 1.32; 95%CI: 1.04-1.670 and in chronic or acute HF or reduced ejection fraction patients (RR: 1.25; 95%CI: 1.02-1.52).

**Clinical implications:** Despite not reaching statistical significance, the trial demonstrated an observed effect favoring the liberal strategy by approximately 15%, although the trial was powered to detect a 20% difference. This smaller-than-anticipated difference might be attributed to enrolling a diverse group of AMI patients, including a substantial proportion of type 2 MI patients.

Limitations included lack of masking of intervention, potential influence on healthcare decisions, unadjudicated outcomes, moderate adherence to the liberal strategy's hemoglobin threshold, and lack of adjustment for multiple comparisons in analyses.

### *ORBITA-2: PCI for stable angina: A randomized, placebo-controlled trial*

**Study summary:** Patients with stable coronary artery disease seek PCI[5], primarily for angina relief. Past unblinded trials show PCI's effect on symptoms, involving both physical changes and a placebo effect[6-9]. Understanding the actual physical impact after subtracting the placebo is crucial for informed clinical choices, especially for costly and risky procedures. Previous trials, like ORBITA mandated antianginal medications, found no significant PCI effect on exercise time. ORBITA-2, however, explores PCI's effect without these medications in stable angina patients.

The ORBITA-2 trial was a double-blind, randomized, placebo-controlled investigation across 14 sites in the United Kingdom. The study enrolled patients deemed suitable for PCI involving severe coronary stenosis and ischemic symptoms, evaluating the efficacy of PCI *vs* a placebo procedure.

Three hundred and one patients were subsequently randomly assigned to PCI (151 patients, mean age 65 ± 5 years) or placebo (150 patients, mean age 64 ± 9 years). Patients underwent an initial phase of symptom assessment and cessation of antianginal medications. They reported symptoms *via* a smartphone application and underwent assessments, including treadmill tests and stress echocardiography. Subsequently, patients were randomized to either PCI or a placebo procedure. Blinding was meticulously maintained throughout.

At the 12-week follow-up, the mean angina symptom score was 2.9 in the PCI group and 5.6 in the placebo group [odds ratio (OR): 2.21; 95%CI: 1.41-3.47; $P < 0.001$], the mean daily angina frequency was 0.3 episodes in the PCI group and 0.7 in the placebo group (OR: 3.44; 95%CI: 2.00-5.91), and the mean daily use of antianginal medication was 0.2 and 0.3 units in the PCI and placebo groups, respectively (OR: 1.21; 95%CI: 0.70-2.10). Secondary endpoints, including quality of life measures, treadmill exercise time, and physician-assessed angina severity, aligned with the primary outcome.

**Clinical implications:** The angina symptom score was considerably lower in the PCI group than the placebo group at 12 weeks. Angina frequency and antianginal drug usage favored PCI.

ORBITA-2 stressed the importance of double-blinded placebo-controlled studies for PCI evaluation. The experiment showed that PCI for angina relief is effective without baseline antianginal medication, contradicting the idea that PCI is best utilized in individuals with inadequate antianginal responses.

## HF

### *ARIES-HM3: Aspirin and hemocompatibility events with a left ventricular assist device in advanced HF, randomized clinical trial*

**Study summary:** ARIES-HM3 was an international, randomized, double-blind, placebo-controlled trial that aimed to investigate the safety of excluding aspirin from the antithrombotic regimen in patients with advanced HF utilizing LVADs, along with its potential to reduce bleeding incidents[10].

The primary endpoint, assessing survival without major hemocompatibility-related adverse events (such as stroke, pump thrombosis, significant nonsurgical bleeding, and arterial peripheral thromboembolism) at 12 months, was achieved for placebo *vs* aspirin at 1 year, was: 74.2 *vs* 68.1 events *per* 100 patient-years ($P$ for noninferiority < 0.0001). The trial met the noninferiority criterion (with a margin of -10%) showing a 6.0% absolute between-group difference (lower 1-sided 97.5%CI: -1.6%) with a significant $P$ value of less than 001.

Notably, the placebo group demonstrated a lower incidence of bleeding events (22.5% *vs* 28.2% in the aspirin group). Analyzing the time to the first event showed a lower occurrence of deaths or major hemocompatibility-related adverse events in the placebo group compared to the aspirin group over 24 months (36.9% *vs* 45.9%; HR: 0.73, 95%CI: 0.55-0.97, $P = 0.03$).

**Clinical implications:** The antithrombotic regimen for patients with advanced HF treated with a fully magnetically levitated LVAD without the use of aspirin is not inferior to that with the use of aspirin and shows reduced bleeding events.

### *The TEAMMATE trial: Everolimus to prevent rejections in children after cardiac transplantation*

**Study summary:** The TEAMMATE Trial evaluated the safety and efficacy of Everolimus and low-dose tacrolimus to prevent rejection, cardiac allograft vasculopathy[11], and renal dysfunction in children and young adults when introduced at 6 months post-heart transplant.

There was no significant difference in major adverse transplant events in the Everolimus group compared to the mycophenolate mofetil (MMF) group. The pre-specified safety criterion was met successfully by the Everolimus group. The cumulative burden of cardiac allograft vasculopathy, chronic kidney disease, and cellular rejection at 30 months was not different in the Everolimus group when compared to the MMF group. A higher glomerular filtration rate, a lower rate of anti-human leukocyte antigen antibody development, and less cytomegalovirus infection were seen in patients receiving Everolimus, but more hyperlipidemia and higher liver transaminases were also seen.

**Clinical implication:** Everolimus combined with low-dose tacrolimus is safe in children and young adults when initiated six months after transplant.

### *Integrating cost into shared decision-making for HFrEF: A trial providing out-of-pocket costs for HF medications during clinical encounters POCKET-COST-HF*

**Clinical implications:** Providing detailed cost information had a moderate but notable effect on discussions about costs during medical appointments for patients with HFrEF[12]. This preliminary evidence indicates that such cost disclosures might decrease the need for emergency planning and improve patient adherence to chosen medications.

To better understand the effects of detailed out-of-pocket (OOP) cost information on medication selection, prescribing habits, and patient adherence, larger studies with more participants and extended follow-up periods are necessary.

Additional research is required to explore effective methods for integrating cost information into clinical practice and to develop new tools that can be incorporated into Electronic Health Record systems.

## CONCLUSION

DAPA-MI investigated the effects of dapagliflozin after MI in individuals who do not have diabetes or HF. The study included a substantial sample of 4017 people and showed a trend in decrease in the combined mortality, hospitalization for HF, nonfatal myocardial infarction, atrial fibrillation/flutter, type 2 diabetes mellitus, and New York Heart Association class ($P < 0.001$) in the form of a win-ratio, which is being used by a number of newer trials. However, there are inherent limitations to using the win ratio for composite outcomes, such as overestimation of clinical benefits, flawed assessment of patient-reported outcomes, imbalance in the risk profiles of analyzed pairs, and the problematic dismissal of "ties" in treatment outcomes. These issues challenge the accuracy of the win ratio and clinical meaningfulness, suggesting a need for more reliable analytical methods in cardiovascular trials. However, this trial did have effects on the new diagnosis of diabetes and its effect on weight. Maybe with longer follow-up times, we might be able to see a reduction in hard endpoints. We also investigated transfusion thresholds in individuals with myocardial infarction. Prior randomized controlled trials did not offer a definitive consensus. The MINT trial compared restrictive and liberal transfusion strategies in patients with myocardial infarction and anemia[2]. It found no significant difference in 30-day myocardial infarction or death rates between strategies, suggesting that a liberal strategy might not reduce these risks more effectively than a restrictive approach. However, the liberal strategy slightly favored primary outcomes and death rates, indicating potential benefits. There was a 2013 pilot trial in 110 patients by the same author, which showed the liberal transfusion strategy was associated with a trend for fewer major cardiac events and deaths than a more restrictive strategy[2]. In comparison, other trials like REALITY, TRICS, and TITRe2 explored similar themes with varying findings. REALITY favored a restrictive transfusion strategy for patient's post-acute coronary syndrome, challenging the traditional 10/30 rule[4]. TRICS, involving patients undergoing cardiac surgery, found a restrictive strategy noninferior to a liberal one[13]. Contrarily, TITRe2 reported more deaths in the restrictive group[14]. MINT's strengths include its large sample size and practical approach, making its findings broadly applicable. However, the trial had limitations like non-blinding of interventions and moderate adherence to transfusion protocols. Future directions could involve confirming MINT's conclusions and exploring the implications of transfusion strategies in different patient subgroups, considering the nuanced results across various trials. Considering these data, the trend toward clinical benefit observed in MINT suggests that a liberal transfusion strategy in MI may be reasonable to consider without an appreciably increased risk of harm. The ORBITA-2 trial, a follow-up study of the original ORBITA study, enrolled 301 patients to evaluate PCI for stable angina in individuals who did not receive any antianginal medicines at the beginning of the study. At the 12-week mark, PCI demonstrated a substantial reduction in angina symptoms and frequency when compared to the administration of a placebo. Nevertheless, there was no discernible difference in the daily usage of antiangiogenic drugs. The results contradict those of the ORBITA study[15], which found no benefit of PCI in addition to appropriate medical treatment for the primary endpoint of treadmill exercise duration. This research aims to validate the antianginal advantage of PCI for stable coronary artery disease using a sham-controlled strategy, like the original ORBITA study. Patients were taken off anti-anginal medications. Limitations of the study include a brief 12-week period of monitoring and the relatively small size of the sample, which evaluates significant clinical outcomes. The trial's use of blinding emphasizes the notable placebo effect of PCI for angina. This questions the necessity of performing PCI in stable angina patients who are not taking baseline antianginal medications and emphasizes the importance of reevaluating the need for this procedure.

The ARIES-HM3 study examines aspirin use in patients with advanced HF using a fully magnetically LVAD[10]. This randomized, double-blind, placebo-controlled trial evaluated the necessity and impact of aspirin in combination with vitamin K antagonists. The study found that avoiding aspirin is not inferior to using it and is associated with a reduction in bleeding events without increasing thromboembolic risk. This finding challenges the traditional inclusion of aspirin in antithrombotic regimens for LVAD patients. The study suggests potential shifts in managing patients with advanced HF and LVADs, emphasizing personalized approaches to antithrombotic therapy. The TEAMMATE Trial explores the use of everolimus combined with low-dose tacrolimus in preventing transplant complications in pediatric heart transplant recipients[11]. This phase III open-label randomized clinical trial was conducted at 25 sites in the United States, with a primary endpoint focusing on major adverse transplant event. Strengths of the study include a robust sample size and the inclusion of a pediatric population, often underrepresented in clinical trials. Limitations include its open-label design and potential variations in standard care practices across multiple sites. This study opens pathways for future research in pediatric transplant immunosuppression, particularly regarding balancing efficacy and side effects in this vulnerable population. Finally, The POCKET-COST-HF study focuses on integrating OOP cost information into clinical decision-making for HFrEF treatments[12]. Key findings suggest that tailored cost disclosure modestly increases discussions about costs in clinical encounters. Limitations include a small sample size and potential biases in the stepped-wedge design.

This study paves the way for further research on implementing cost-disclosure strategies in clinical practice, highlighting the importance of cost considerations in patient care.

These studies together highlight the need for subtle and refined treatment techniques, question existing standards, and create opportunities for future research, influencing the changing field of cardiovascular care.

## FOOTNOTES

**Author contributions:** Mondal A and Desai R designed the methodology and performed analysis; Srikanth S, Aggarwal S, Alle NR, Odugbemi O and Ogbu I were involved with data curation, visualization, and interpretation, and writing of manuscript; Mondal A, Desai R, and Ogbu I performed reviewing and final editing; All authors have read and agreed to the published version of the manuscript.

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## REFERENCES

1 **James S**, Erlinge D, Storey RF, McGuire DK, de Belder M, Eriksson N, Andersen K, Austin D, Arefalk G, Carrick D, Hofmann R, Hoole SP, Jones DA, Lee K, Tygesen H, Johansson PA, Langkilde AM, Ridderstråle W, Parvaresh Rizi E, Deanfield J, Oldgren J. Dapagliflozin in Myocardial Infarction without Diabetes or Heart Failure. *NEJM Evid* 2024; **3**: EVIDoa2300286 [PMID: 38320489 DOI: 10.1056/EVIDoa2300286]

2 **Carson JL**, Brooks MM, Hébert PC, Goodman SG, Bertolet M, Glynn SA, Chaitman BR, Simon T, Lopes RD, Goldsweig AM, DeFilippis AP, Abbott JD, Potter BJ, Carrier FM, Rao SV, Cooper HA, Ghafghazi S, Fergusson DA, Kostis WJ, Noveck H, Kim S, Tessalee M, Ducrocq G, de Barros E Silva PGM, Triulzi DJ, Alsweiler C, Menegus MA, Neary JD, Uhl L, Strom JB, Fordyce CB, Ferrari E, Silvain J, Wood FO, Daneault B, Polonsky TS, Senaratne M, Puymirat E, Bouleti C, Lattuca B, White HD, Kelsey SF, Steg PG, Alexander JH; MINT Investigators. Restrictive or Liberal Transfusion Strategy in Myocardial Infarction and Anemia. *N Engl J Med* 2023; **389**: 2446-2456 [PMID: 37952133 DOI: 10.1056/NEJMoa2307983]

3 **Cooper HA**, Rao SV, Greenberg MD, Rumsey MP, McKenzie M, Alcorn KW, Panza JA. Conservative versus liberal red cell transfusion in acute myocardial infarction (the CRIT Randomized Pilot Study). *Am J Cardiol* 2011; **108**: 1108-1111 [PMID: 21791325 DOI: 10.1016/j.amjcard.2011.06.014]

4 **Ducrocq G**, Gonzalez-Juanatey JR, Puymirat E, Lemesle G, Cachanado M, Durand-Zaleski I, Arnaiz JA, Martínez-Sellés M, Silvain J, Ariza-Solé A, Ferrari E, Calvo G, Danchin N, Avendaño-Solá C, Frenkiel J, Rousseau A, Vicaut E, Simon T, Steg PG; REALITY Investigators. Effect of a Restrictive vs Liberal Blood Transfusion Strategy on Major Cardiovascular Events Among Patients With Acute Myocardial Infarction and Anemia: The REALITY Randomized Clinical Trial. *JAMA* 2021; **325**: 552-560 [PMID: 33560322 DOI: 10.1001/jama.2021.0135]

5 **Rajkumar CA**, Foley MJ, Ahmed-Jushuf F, Nowbar AN, Simader FA, Davies JR, O'Kane PD, Haworth P, Routledge H, Kotecha T, Gamma R, Clesham G, Williams R, Din J, Nijjer SS, Curzen N, Ruparelia N, Sinha M, Dungu JN, Ganesananthan S, Khamis R, Mughal L, Kinnaird T, Petraco R, Spratt JC, Sen S, Sehmi J, Collier DJ, Sohaib A, Keeble TR, Cole GD, Howard JP, Francis DP, Shun-Shin MJ, Al-Lamee RK; ORBITA-2 Investigators. A Placebo-Controlled Trial of Percutaneous Coronary Intervention for Stable Angina. *N Engl J Med* 2023; **389**: 2319-2330 [PMID: 38015442 DOI: 10.1056/NEJMoa2310610]

6 **Boden WE**, O'Rourke RA, Teo KK, Hartigan PM, Maron DJ, Kostuk WJ, Knudtson M, Dada M, Casperson P, Harris CL, Chaitman BR, Shaw L, Gosselin G, Nawaz S, Title LM, Gau G, Blaustein AS, Booth DC, Bates ER, Spertus JA, Berman DS, Mancini GB, Weintraub WS; COURAGE Trial Research Group. Optimal medical therapy with or without PCI for stable coronary disease. *N Engl J Med* 2007; **356**: 1503-1516 [PMID: 17387127 DOI: 10.1056/NEJMoa070829]

7 **De Bruyne B**, Pijls NH, Kalesan B, Barbato E, Tonino PA, Piroth Z, Jagic N, Möbius-Winkler S, Rioufol G, Witt N, Kala P, MacCarthy P, Engström T, Oldroyd KG, Mavromatis K, Manoharan G, Verlee P, Frobert O, Curzen N, Johnson JB, Jüni P, Fearon WF; FAME 2 Trial Investigators. Fractional flow reserve-guided PCI versus medical therapy in stable coronary disease. *N Engl J Med* 2012; **367**: 991-1001 [PMID: 22924638 DOI: 10.1056/NEJMoa1205361]

8 **Parisi AF**, Folland ED, Hartigan P. A comparison of angioplasty with medical therapy in the treatment of single-vessel coronary artery disease. Veterans Affairs ACME Investigators. *N Engl J Med* 1992; **326**: 10-16 [PMID: 1345754 DOI: 10.1056/NEJM199201023260102]

9 **Spertus JA**, Jones PG, Maron DJ, O'Brien SM, Reynolds HR, Rosenberg Y, Stone GW, Harrell FE Jr, Boden WE, Weintraub WS, Baloch K, Mavromatis K, Diaz A, Gosselin G, Newman JD, Mavromichalis S, Alexander KP, Cohen DJ, Bangalore S, Hochman JS, Mark DB;

ISCHEMIA Research Group. Health-Status Outcomes with Invasive or Conservative Care in Coronary Disease. *N Engl J Med* 2020; **382**: 1408-1419 [PMID: 32227753 DOI: 10.1056/NEJMoa1916370]

10 **Mehra MR**, Netuka I, Uriel N, Katz JN, Pagani FD, Jorde UP, Gustafsson F, Connors JM, Ivak P, Cowger J, Ransom J, Bansal A, Takeda K, Agarwal R, Byku M, Givertz MM, Bitar A, Hall S, Zimpfer D, Vega JD, Kanwar MK, Saeed O, Goldstein DJ, Cogswell R, Sheikh FH, Danter M, Pya Y, Phancao A, Henderson J, Crandall DL, Sundareswaran K, Soltesz E, Estep JD; ARIES-HM3 Investigators. Aspirin and Hemocompatibility Events With a Left Ventricular Assist Device in Advanced Heart Failure: The ARIES-HM3 Randomized Clinical Trial. *JAMA* 2023; **330**: 2171-2181 [PMID: 37950897 DOI: 10.1001/jama.2023.23204]

11 **Almond CS**, Sleeper LA, Rossano JW, Bock MJ, Pahl E, Auerbach S, Lal A, Hollander SA, Miyamoto SD, Castleberry C, Lee J, Barkoff LM, Gonzales S, Klein G, Daly KP. The teammate trial: Study design and rationale tacrolimus and everolimus against tacrolimus and MMF in pediatric heart transplantation using the major adverse transplant event (MATE) score. *Am Heart J* 2023; **260**: 100-112 [PMID: 36828201 DOI: 10.1016/j.ahj.2023.02.002]

12 **Montembeau SC**, Rao BR, Mitchell AR, Speight CD, Allen LA, Halpern SD, Ko YA, Matlock DD, Moore MA, Morris AA, Scherer LD, Ubel P, Dickert NW. Integrating Cost into Shared Decision-Making for Heart Failure with Reduced Ejection Fraction (POCKET-COST-HF): A Trial Providing Out-of-Pocket Costs for Heart Failure Medications during Clinical Encounters. *Am Heart J* 2024; **269**: 84-93 [PMID: 38096946 DOI: 10.1016/j.ahj.2023.11.013]

13 **Mazer CD**, Whitlock RP, Fergusson DA, Hall J, Belley-Cote E, Connolly K, Khanykin B, Gregory AJ, de Médicis É, McGuinness S, Royse A, Carrier FM, Young PJ, Villar JC, Grocott HP, Seeberger MD, Fremes S, Lellouche F, Syed S, Byrne K, Bagshaw SM, Hwang NC, Mehta C, Painter TW, Royse C, Verma S, Hare GMT, Cohen A, Thorpe KE, Jüni P, Shehata N; TRICS Investigators and Perioperative Anesthesia Clinical Trials Group. Restrictive or Liberal Red-Cell Transfusion for Cardiac Surgery. *N Engl J Med* 2017; **377**: 2133-2144 [PMID: 29130845 DOI: 10.1056/NEJMoa1711818]

14 **Murphy GJ**, Pike K, Rogers CA, Wordsworth S, Stokes EA, Angelini GD, Reeves BC; TITRe2 Investigators. Liberal or restrictive transfusion after cardiac surgery. *N Engl J Med* 2015; **372**: 997-1008 [PMID: 25760354 DOI: 10.1056/NEJMoa1403612]

15 **Al-Lamee R**, Thompson D, Dehbi HM, Sen S, Tang K, Davies J, Keeble T, Mielewczik M, Kaprielian R, Malik IS, Nijjer SS, Petraco R, Cook C, Ahmad Y, Howard J, Baker C, Sharp A, Gerber R, Talwar S, Assomull R, Mayet J, Wensel R, Collier D, Shun-Shin M, Thom SA, Davies JE, Francis DP; ORBITA investigators. Percutaneous coronary intervention in stable angina (ORBITA): a double-blind, randomised controlled trial. *Lancet* 2018; **391**: 31-40 [PMID: 29103656 DOI: 10.1016/S0140-6736(17)32714-9]

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