

Meta-Analysis Comparing the Safety and Efficacy of Single vs Dual Antiplatelet Therapy in Post Transcatheter Aortic Valve Implantation Patients



Waqas Ullah, MD^a, Mohamed Zghouzi, MD^b, Bachar Ahmad^b, Suman Biswas, MD^c, Nathan Zaher, MD^b, Yasar Sattar, MD^d, Homam Moussa Pacha, MD^e, Andrew M. Goldsweig, MDMS^f, Poonam Velagapudi, MD^f, David L. Fichman, MD^g, Anand Prasad, MD^h, and M. Chadi Alraies, MD^{b,*}

The relative safety and efficacy of aspirin versus dual antiplatelet therapy (DAPT; aspirin +clopidogrel) in patients who underwent transcatheter aortic valve implantation (TAVI) and did not have a long-term indication for oral anticoagulation remains controversial. Digital databases were searched to identify relevant articles. The major safety end point was bleeding, while the efficacy end points included after-TAVI ischemic and thrombotic events. Data were analyzed using a random effect model to calculate the pooled unadjusted odds ratio (OR) for dichotomous outcomes. Eleven studies comprising 4805 patients (aspirin 2258, DAPT 2547) were included in the quantitative analysis. Patients receiving aspirin-alone had significantly lower odds of all cause bleeding (OR 0.41, 95% CI 0.29 to .057, $p < 0.00001$), major vascular bleeding (OR 0.51, 95% CI 0.34 to 0.77, $p = 0.001$), Valve Academic Research Consortium 2 (VARC-2) major bleeding (OR 0.50, 95% CI 0.30 to 0.83 $p = 0.008$), VARC-2 minor bleeding (OR 0.55, 95% CI 0.31 to 0.97, $p = 0.04$), transfusion requirement (OR 0.39, 95% CI 0.15 to 0.98, $p = 0.05$) and major vascular complications (OR 0.41, 95% CI 0.26 to 0.66, $p = 0.0002$) compared with after-TAVI patients receiving both aspirin and clopidogrel. There was no significant difference in the odds of VARC-2 life threatening bleeding (OR 0.52, 95% CI 0.25 to 1.07, $p = 0.08$), prosthetic valve thrombosis (OR 1.17, 95% CI 0.22 to 6.30, $p = 0.85$), cardiac tamponade (OR 0.77, 95% CI 0.20 to 2.98, $p = 0.70$), conversion to open procedure (OR 1.99, 95% CI 0.42 to 9.44, $p = 0.39$), MI (OR 0.79 95% CI 0.38 to 1.64, $p = 0.52$), transient ischemic attack (TIA) (OR 0.89, 95% CI 0.12 to 6.44, $p = 0.91$), major stroke (OR 0.68 95% CI 0.43 to 1.08, $p = 0.10$), disabling stroke (OR 1.01, 95% CI 0.41 to 2.48, $p = 0.99$), cardiovascular mortality (OR 0.81 95% CI 0.38 to 1.74, $p = 0.59$) and all-cause mortality (OR 0.86, 95% CI 0.63 to 1.16, $p = 0.31$) between the 2 groups. In conclusion, after-TAVI patients who received aspirin alone had lower bleeding events with no significant differences in mortality and stroke rate compared with those who received DAPT. © 2021 Elsevier Inc. All rights reserved. (Am J Cardiol 2021;145:111–118)

Transcatheter aortic valve implantation (TAVI) has recently emerged as a safe and effective alternative to open surgical valve implantation (SAVR) for the management of patients with severe symptomatic aortic stenosis.¹ Current recommendations for oral anticoagulation (OAC) following bioprosthetic SAVR valves include aspirin and vitamin K antagonist for the first three months in the absence of other risk factors. For patients with compelling indications for OAC, the use of vitamin K antagonist reduces the risk of

valvular thrombosis and after-TAVI stroke in the absence of other risk factors. The optimal antithrombotic therapy following TAVI in patients with no indication for OAC has not been well defined. The current American College of Cardiology guidelines recommend dual antiplatelet therapy (DAPT), aspirin plus clopidogrel for the first 6 months followed by lifelong low dose aspirin in after-TAVI patients.² The European Society of Cardiology also recommend aspirin along with a thienopyridine in the early after-TAVI period and aspirin or thienopyridine alone indefinitely.³ These recommendations, based mostly on expert opinion have not been widely adopted. With the release of recent POPular TAVI (Antiplatelet Therapy for Patients Undergoing Transcatheter Aortic Valve Implantation) data pointing towards the better safety and equal efficacy of aspirin-only therapy, antithrombotic therapy following TAVI needs to be reevaluated.⁴ We reviewed the safety and efficacy of aspirin versus aspirin and clopidogrel in after-TAVI patients with no other indication for long term anticoagulation in this meta-analysis which may help guide antiplatelet strategy in this group of patients.

^aAbington Jefferson Health, Abington, Pennsylvania; ^bDetroit Medical Center, Heart Hospital, Detroit, Michigan; ^cRochester Regional Health, Rochester, New York; ^dIcahn school of medicine at Mount Sinai Elmhurst Hospital New York, New York; ^eUniversity of Texas Health Science Center, Houston, Texas; ^fUniversity of Nebraska Medical Center, Omaha, Nebraska; ^gThomas Jefferson University Hospital, Philadelphia; and ^hUniversity of Texas Health San Antonio Texas, Texas. Manuscript received November 1, 2020; revised manuscript received and accepted December 29, 2020.

Disclosure: none
Funding: none

*Corresponding author. Tel: 1 (216) 255-0008

E-mail address: alraies@hotmail.com (M.C. Alraies).

Methods

A comprehensive literature search of digital databases, including PubMed, Embase and Cochrane up to October 4, 2020, was performed. Medical subject headings (MeSH) and keywords were systematically identified from previous sources and the PubMed database. Using the boolean operators, the MESH terms for TAVI such as “transcatheter aortic valve implantation,” “TAVI,” “TAVI,” were combined with a list of MeSH terms for medications including “aspirin,” “DAPT,” “clopidogrel,” “antiplatelet,” “aspirin +clopidogrel,” and “dual antiplatelet agents.”. The results from all possible combinations were screened by 4 authors for relevance. Based on our clinical research question, studies from the reference lists were also screened by an independent author (backward snowballing). (Supplementary Appendix) All randomized control trials (RCTs) and observational cohort studies (OCS) including patients age>18 years and comparing the merits of aspirin against DAPT in patients with TAVI and having no indication for OAC therapy were included. (Supplementary Table 1) The primary safety end point was major bleeding. Other safety and efficacy outcomes included a risk of MI, valve thrombosis and stroke.

The statistical analysis was performed using the DerSimonian Laird test on a random-effects model to compute

the pooled unadjusted odds ratio (OR) for dichotomous data. To assess the effect of potential confounders on the pooled effect size, data were stratified based on matched definitions of standard outcomes. To avoid the imputation of data by the larger potentially influential studies, a sensitivity analysis based on the study weight was also performed. Higgins I-squared (I²) statistic model was used to evaluate heterogeneity and variations in outcomes of the included studies. I²>50% corresponded to low to moderate, and >75% indicated high heterogeneity. The publication bias was assessed using Egger’s regression test and illustrated graphically with funnel plotting. The methodological quality of observational studies was reported using a risk of bias tool-2 (ROB-2) for RCTs and the NewCastle Ottawa Scale (NOS) for OCS. All point estimates were reported along with a 95% confidence interval (CI). An alpha criterion of p-value less than 0.05 was considered statistically significant. The statistical analysis was performed using the Cochrane Review Manager version 5.4.1.

The overall quality of the included RCTs and OCS was high. (Figure 1) Most RCTs except the SAT-TAVI trial were open labels violating the “allocation concealment,” however, all RCTs were randomized reducing the overall risk of selection bias. The risk of reporting and detection

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Brouwer (POPULAR TAVI) 2020	+	-	+	+	+	+	
Rodes-Cabau (ARTE) 2017	+	-	+	+	+	+	
Stabile (SAT TAVI) 2014	+	+	+	+	+	+	
Ussia 2011	+	-	+	+	+	+	

Figure 1. Summary and detailed graphs of methodological bias of the included RCTs.

bias was also minimal due to adequate outcomes reporting and blinding of assessment, respectively. (Supplementary Figure 1) The “intention to treat” model in most RCTs reduced the risk of attrition bias. The risk of bias across OCS was also low on NOS as shown in the supplementary appendix. (S. Table 2)

Results

Our initial comprehensive search identified a total of 2,407 articles. After exclusion of duplicate (1,042) and irrelevant (1,297) studies, 68 were reviewed in the full-text form. (Figure 2) A prespecified inclusion criterion was used to select articles. After a detailed group discussion, eleven articles qualified for the quantitative analysis. Four studies were randomized controlled trials (RCTs) and seven articles were observational cohort studies (OCS) (6 retrospective, 1 prospective). The detailed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram is given in Figure 2.

A total of 4,805 patients; 2,258 in the aspirin and 2,547 in the DAPT group were included in this analysis. There were no differences in the baseline characteristics between the 2 comparison groups. The overall mean age was 82 years; 81.9 years in aspirin-alone and 81.6 years in the DAPT group. 55% of the patients were female. Baseline co-morbidities included hypertension (78.6% vs 78.4%),

diabetes mellitus (22.6% vs 22.3%) and prior history of coronary artery bypass graft (CABG) (14.9% vs 16.2%) in aspirin-alone and DAPT groups, respectively. It is important to note that most trials including the ARTE and SAT-TAVI trials excluded patients with recent PCI within the last 12 and 6 months of enrollment. The follow-up duration ranged from 30-days to 1-year with a median follow-up duration of 12-months. The detailed characteristics, definitions of outcomes and the selection criteria of the included studies are presented in supplementary tables. (Supplementary Table 1.)

The use of aspirin-alone was associated with significantly lower odds of all cause bleeding (OR 0.41, 95% CI 0.29 to .057, $p < 0.00001$), major vascular bleeding (OR 0.51, 95% CI 0.34 to 0.77, $p = 0.001$), VARC-2 major bleeding (OR 0.50, 95% CI 0.30 to 0.83 $p = 0.008$), VARC-2 minor bleeding (OR 0.55, 95% CI 0.31 to 0.97, $p = 0.04$), transfusion requirement (OR 0.39, 95%CI 0.15 to 0.0.98, $p = 0.05$) and major vascular complications (OR0.41, 95% CI 0.26 to 0.66, $p = 0.0002$) compared with patients receiving both aspirin and clopidogrel. There was no significant difference in the odds of VARC-2 life threatening bleeding (OR 0.52, 95% CI 0.25 to 1.07, $p = 0.08$), valve thrombosis (OR 1.17, 95% CI 0.22 to 6.30, $p = 0.85$), cardiac tamponade (OR 0.77, 95% CI 0.20 to 2.98, $p = 0.70$), and conversion of TAVI to SAVR (OR 1.99, 95 % CI 0.42 to 9.44, $p = 0.39$) between the two groups. (Figure 3, Supplementary Figure 2-6)

The major efficacy end point including MI (OR 0.79 95% CI 0.38 to 1.64, $p = 0.52$), transient ischemic attack (TIA) (OR 0.89, 95% CI 0.12 to 6.44, $p = 0.91$), minor stroke (OR 0.79 95% CI 0.38 to 1.66, $p = 0.53$), stroke (OR 0.68 95 % CI 0.43 to 1.08, $p = 0.10$), disabling stroke (OR 1.01, 95% CI 0.41 to 2.48, $p = 0.99$), cardiovascular mortality (OR 0.81 95% CI 0.38- to 1.74, $p = 0.59$), and all-cause mortality (OR 0.86, 95% CI 0.63 to 1.16, $p = 0.31$) also remained identical in patients on aspirin compared with DAPT after-TAVI. There was minimal to moderate heterogeneity in the outcomes of the included studies with few exceptions as shown in the Figures 4,5.

A subgroup analysis based on study design (RCT vs OCS) and follow up duration (<6 vs >6months) closely mirrored the findings of pooled analysis with a few exceptions. Contrary to OCS and overall results, there was no significant difference in the rate of major (OR 0.69, 95% CI 0.30 to 1.55, $p = 0.53$) and minor vascular complications (OR 0.63, 95% CI 0.20 to 2.00, $p = 0.90$). The odds of VARC-2 major bleeding were identical between the 2 groups across OCS (OR 0.52, 95% CI 0.22 to 1.26, $p = 0.05$) while it was lower in the aspirin-alone arm in RCTs and pooled analysis. The rate of VARC minor and major bleeding and cardiovascular and all-cause mortality was significantly lower in the aspirin-alone arm at <6 months, while it was identical at 6 or greater than 6 months follow-up duration. (S. Figure 7-39)

On visual assessment, our funnel plot was symmetrical with an equal amount of studies on each side of the vertical axis. There was no publication bias demonstrated. The limited scatter on the graph was due to sampling variation. Egger’s equation for the measure of publication bias was nonsignificant (2-tailed $p = 0.75$). (Figure 6)

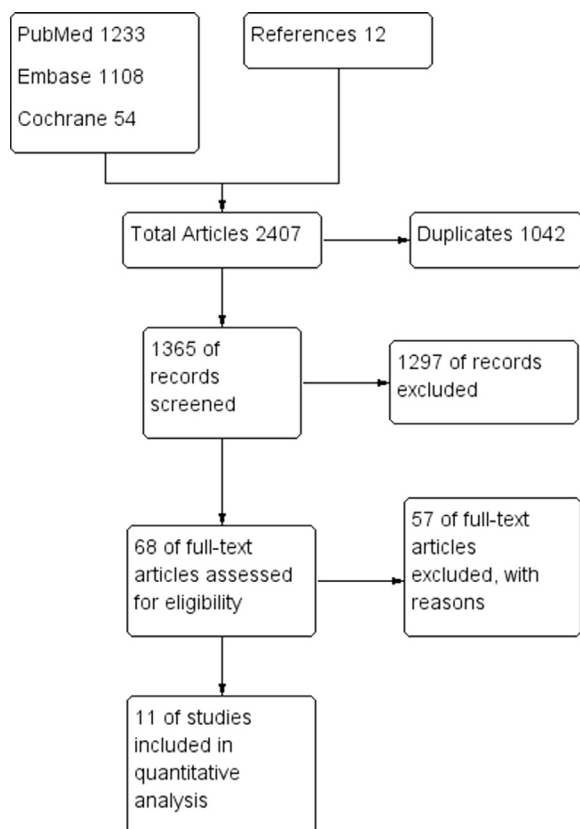
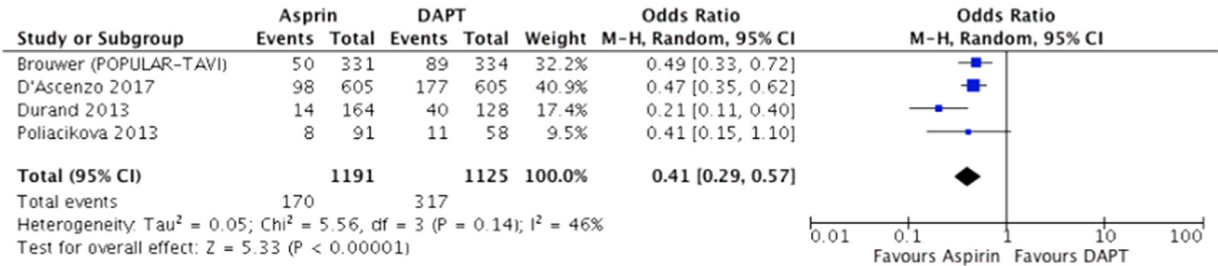
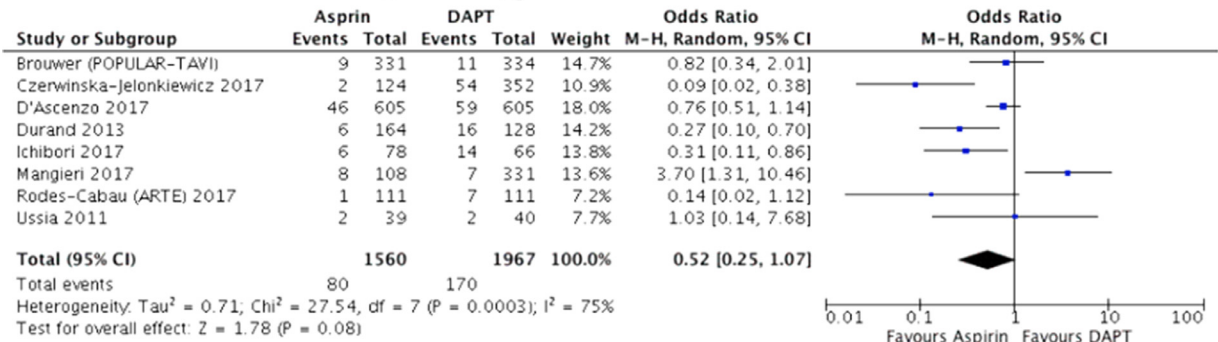


Figure 2. PRISMA flow diagram showing the included studies and reasons of exclusion.

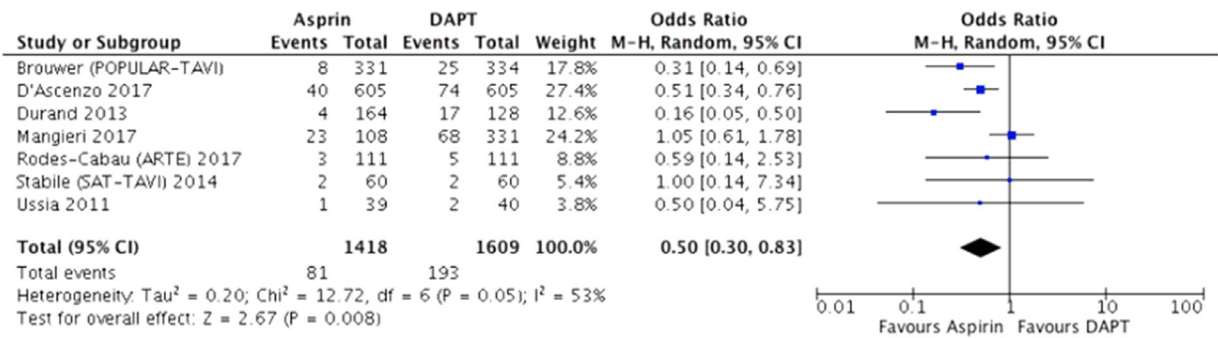
A. All cause major bleeding



B. VARC-2 life threatening bleeding



C. VARC-2 major bleeding



D. VARC-2 minor bleeding

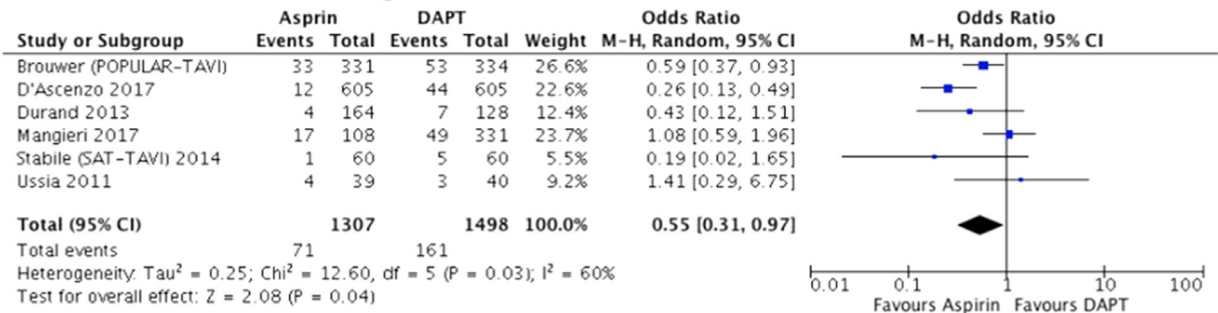


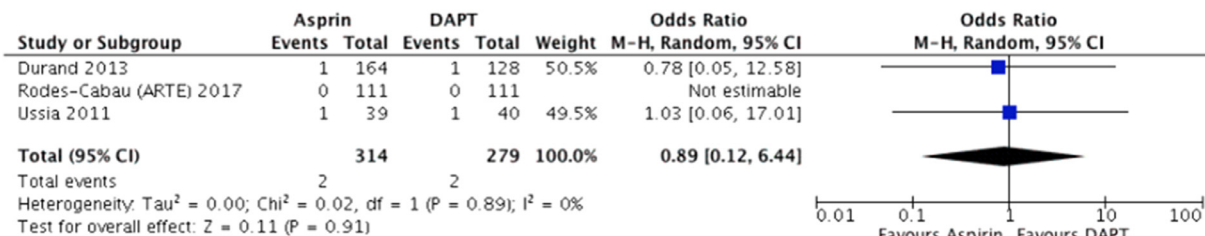
Figure 3. Forest plot showing the odds of major bleeding events between the 2 groups.

Discussion

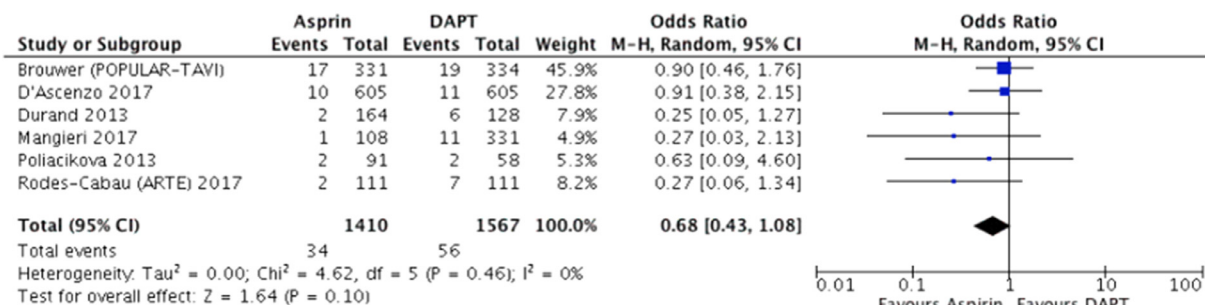
Our meta-analysis is the largest and most contemporary evidence available on the safety and efficacy of aspirin-alone compared with DAPT in patients with severe AS who underwent TAVI and no other indication for anticoagulation therapy. Our findings revealed that aspirin-only significantly reduced the odds of all types of bleeding events, minor and

major vascular complications by 61%, 49%, and 59%, respectively. Similarly, the VARC minor, major and VARC life threatening were lowered by 55%, 50% and 48% in the corresponding aspirin group compared with DAPT. The resultant transfusion requirements were substantially decreased by 61% in the former group. The major efficacy end point, valvular thrombosis was identical between the

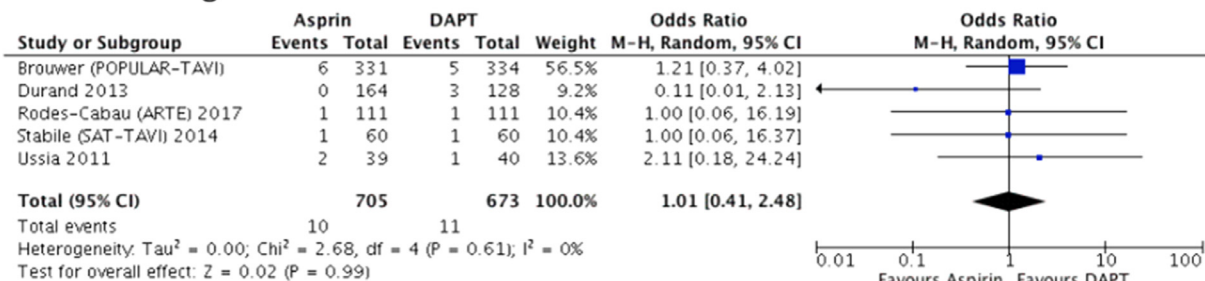
A. TIA



B. All stroke



C. Disabling stroke



D. Minor stroke

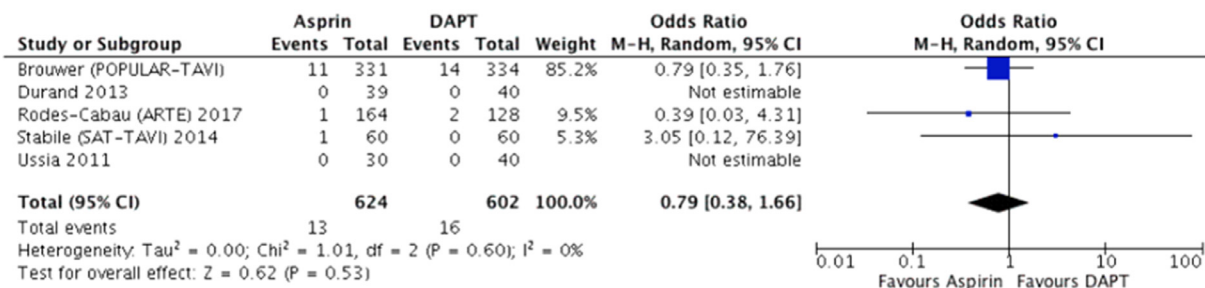


Figure 4. Forest plot showing the odds of stroke events between the 2 groups.

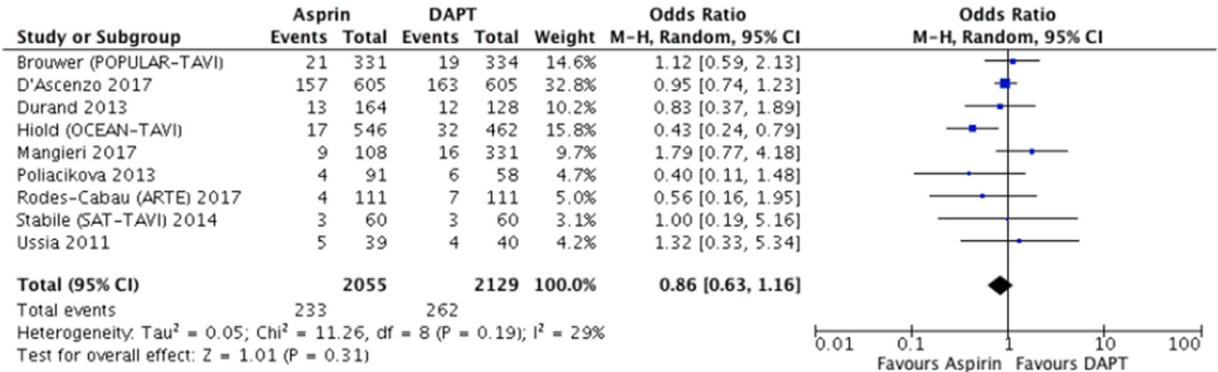
two groups. The after-TAVI in-hospital rate of MI, cardiovascular and all-cause mortality were numerically lower by 21%, 19%, and 14% in the aspirin monotherapy group.

Of the included studies, Ussia et al. were the first to compare the utility of aspirin against DAPT. They found no differences in the composite end point between participants treated with aspirin and those treated with 3 months of DAPT followed by aspirin alone at 30 days and 6 months.⁴ This trial was limited by its small sample size. Poliacikova et al. revealed that aspirin-alone is superior to DAPT due to a lower incidence of composite end point, including all-cause mortality, stroke, major bleeding, and coronary events.⁵ This benefit was primarily driven by a lower risk of

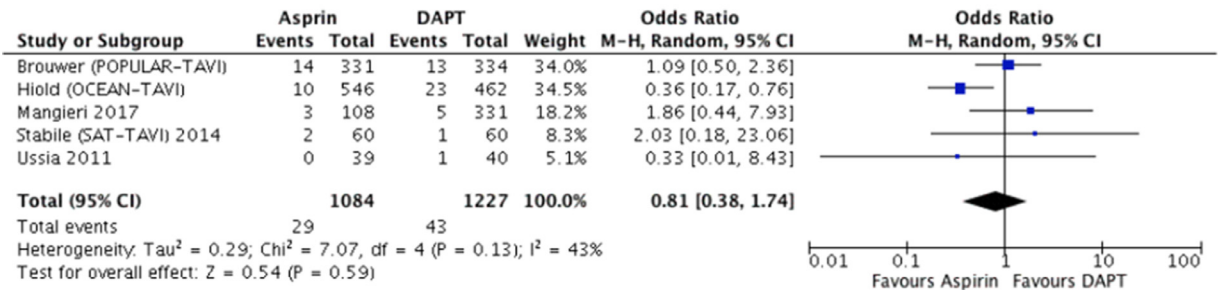
major bleeding with no difference in the 30-day rate of cardiovascular and thromboembolic events. This study was notable for being nonrandomized, where the allocation of treatment was based on hospital policy regarding antiplatelet treatment following TAVI. The impact of cross over between experimental and control regimens during the study period could not be accounted for, introducing a potential risk of detection bias.

Although smaller by design, these observational studies by Durand et al. and Czerwińska-Jelonkiewicz et al. validated the findings of these studies, demonstrating lower risk of major and life-threatening bleeding with aspirin-alone. The authors of the former study compensated the risk of

A. All-cause mortality



B. Cardiovascular mortality



C. MI

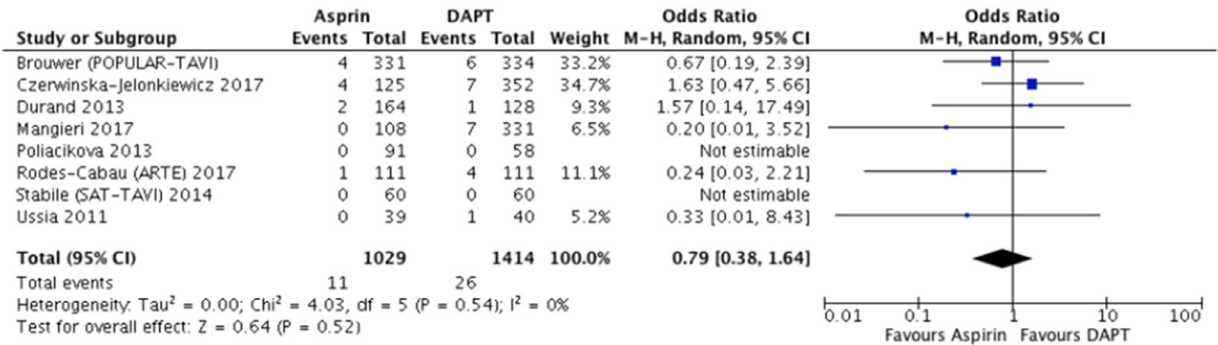


Figure 5. Forest plot showing the odds of mortality and MI events between the 2 groups.

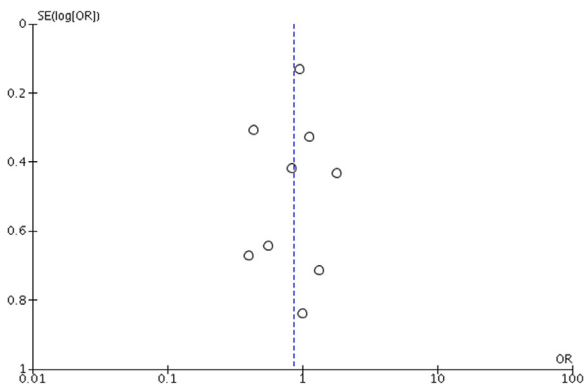


Figure 6. Funnel plot showing minimal publication Bias.

selection bias by calculating propensity scores using a matched group of participants to support their findings. The later study used the POL-TAVI registry, showing that patients on aspirin-monotherapy had lower vascular complication along with lower major bleeding events.^{6,7} Using the TAVI database (Milan, Italy) Mangieri et al demonstrated an increased risk of life threatening bleeding in the aspirin group, with no difference in all cause mortality, cerebrovascular events, valve thrombosis between the 2 groups.⁸ Later, the SAT-TAVI trial also favored aspirin monotherapy due to lower vascular complications.⁹ Unfortunately, despite being a double-blinded controlled trial the study was not powered for individual clinical outcomes.

Contrary to the previous cited studies, D'Ascenzo et al, Ichibori et al. and the ARTE trial demonstrated a significant reduction in mortality and/or ischemic events with aspirin

only therapy.^{10,11} However, the findings should be interpreted with similar caveates, due to small sample size and being underpowered to assess the hard clinical outcomes. Recently, the OCEAN-TAVI investigators revealed that switching from DAPT to single APT was associated with lower cardiovascular mortality at >1-year of TAVI procedure.¹⁴ The findings of this study were subject to selection and recall bias due to the retrospective nature of the study. POPular TAVI, the most recent clinical trial on the subject, hurdled these limitations by randomizing 326 patients with exclusion criteria of any patient who received DES within 3 months or BMS within a month of enrollment, to further eliminate any possible confounders.⁴ The primary end point (all bleeding events) was significantly lower in the monotherapy group at 1-year. Both secondary composite end points were also significantly lower in the aspirin alone arm. Aspirin was superior due to a significantly lower incidence of first composite that included nonprocedural bleed, all-cause stroke, MI and cardiovascular mortality. Aspirin monotherapy was non-inferior, but not superior when the bleeding events were excluded from the secondary composite end point. The major limitations of this trial were being an open label trial and underpowered to assess the individual components of composite outcomes. Also, the POPular TAVI designated procedural bleeding as BARC type 4 events and the possibility of subclinical valve thrombosis could not be excluded as the trial was not designed to perform computed tomographic (CT) imaging.⁴

On review, we found 12 prior meta-analyses, reporting conflicting findings on the merits of aspirin-alone compared with DAPT. However, in light of recent evidence, the applicability of their results is limited. All of these meta-analyses were published before the completion of POPULAR-TAVI and were subject to major methodological limitations. The follow-up duration was short, methodological quality assessment was mostly neglected and some of the observational data was missing. Some studies inappropriately used a fixed effect model on a heterogeneous set of data, overestimating the pooled effect size. Together, these limitations question the widespread applicability of their results. The detailed description of previous meta-analyses are presented in Supplementary Table 1. The present study represents the most comprehensive meta-analysis seeking to address the limitations of individual studies and previous meta-analyses on after-TAVI patients.

Our study is constrained by the limitations of the included studies. Patient-level data were missing to determine the impact of procedure technique on TAVI related outcomes. We could not account for the impact of unmeasured confounding factors (operator's skill and compliance to medications) on overall outcomes. Due to scarce data, we could not perform a stratified subgroup analysis based on follow up duration, baseline bleeding tendency of the included population, study design and varying inclusion criterias of the included studies. Large scale randomized controlled trials are needed to validate our findings.

After-TAVI patients on aspirin-only therapy have a lower rate of major and minor bleeding events compared with patients receiving both aspirin and clopidogrel. The rate of stroke, mortality and valve thrombosis remained similar between the two groups. [Table 1](#)

Table 1
Selected baseline characteristics of randomized trials [15]

Author/Year	ASA/DAPT	Mean Age (Years)	Women (%)	HTN (%)	DM (%)	Logistic Euro Score	Previous PCI (%)	NYHA III/IV (%)	Previous CABG (%)
Brouwer and Nijenhuis et al ⁴	331/334	80.4/79.5	164 (49.5%)	160 (47%)	78 (23.6%)	-	-	212 (64%)	61 (18.4%)
Ussia et al ⁵	39/40	81/80	23 (58.9%)	20 (50%)	8 (20.5%)	21/23	9 (23.1%)	23 (59%)	4 (10.3%)
Stabile et al ¹⁰	60/60	81.1/80.2	36 (60%)	44 (73.3%)	17 (28.3%)	25.1/23.4	-	53 (88.3%)	-
Policikova et al ⁶	91/58	82/81.6	42 (46.1%)	26 (44%)	16 (17.6%)	-	-	-	19 (20.9%)
Rodés-Cabau et al ¹⁴	111/111	79/79	52 (46.8%)	41 (36%)	36 (32.4%)	-	20 (22%)	-	42 (37.8%)
Durand et al ⁷	164/128	82.7/84	74 (45.1%)	78 (65%)	40 (24.4%)	20/20.2	-	131 (79.9%)	30 (18.3%)
Mangieri et al ⁹	108/331	84.3/82.9	62 (57.4%)	214 (64%)	19 (17.6%)	21.3/19.4	26 (24.1%)	53 (49.1%)	20 (18.5%)
D'Ascenzo et al ¹¹	605/605	81/81	349 (57.6%)	336 (55%)	495 (81.8%)	19/21	-	-	-
Hioeki et al ¹³	546/462	85/84	395 (72.3%)	315 (68%)	425 (77.8%)	-	88 (16.1%)	-	33 (6%)
Ichihori et al ¹²	78/66	83/84	50 (64.1%)	42 (63%)	24 (30.8%)	24.2/25.5	11 (14.1%)	37 (47.4%)	10 (12.8%)

All data is presented in the format of ASA/DAPT format. ASA=Aspirin monotherapy, DAPT=Dual Antiplatelet Therapy i.e. Aspirin plus Clopidogrel (%). HTN= Hypertension, DM= Diabetes Mellitus, Euro Score: European System for Cardiac Operative Risk Evaluation.

Credit Author Statement

Waqas Ullah MD: Conceptualization, Methodology, Formal Analysis, Writing - Review & Editing; Mohamed Zghouzi, MD: Writing, Data collection and Revision; Bachar Ahmad: Data collection and Writing; Suman Biswas: References, Data Extraction; Nathan Zaher: Introduction, Data Mining; Yasar Sattar: Figures and Data validation; Homam Moussa Pacha: Data Validation; Andrew M. Goldsweig: Critical Review and Edits; Poonam Velagapudi: Critical Review and Edits; David L. Fichman: Critical Review and Edits and Supervision; Anand Prasad: Critical Review and Edits; M. Chadi Alriaes: Resources, Supervision.

Declaration of Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary materials

Supplementary material associated with this article can be found in the online version at <https://doi.org/10.1016/j.amjcard.2020.12.087>.

- Ullah W, Gowda SN, Khan MS, Sattar Y, Al-Khadra Y, Rashid M, Mohamed MO, Alkhouli M, Kapadia S, Bagur R. Early intervention or watchful waiting for asymptomatic severe aortic valve stenosis: a systematic review and meta-analysis. *J Cardiovasc Med* 2020;21:897–904.
- Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, Iung B, Lancellotti P, Lansac E, Rodríguez Muñoz D, Rosenhek R, Sjögren J, Tornos Mas P, Vahanian A, Walther T, Wendler O, Windecker S, Zamorano JL, ESC Scientific Document Group. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J* 2017;38:2739–2791.
- Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP, Fleisher LA, Jneid H, Mack MJ, McLeod CJ, O’Gara PT, Rigolin VH, Sundt TM, Thompson A. 2014 AHA/ACC Focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines. *Circulation* 2017;135:e1159–e1195.
- Brouwer J, Nijenhuis VJ, Delewi R, Hermanides RS, Holvoet W, Dubois CLF, Frambach P, De Bruyne B, Houwelingen GK van, Van Der Heyden JAS, Toušek P, Kley F van der, Buyschaert I, Schotborgh CE, Ferdinande B, Harst P van der, Roosen J, Peper J, Thielen FWF, Veenstra L, Chan Pin Yin DRPP, Swaans MJ, Rensing BJWM, Hof AWJ van ’t, Timmers L, Kelder JC, Stella PR, Baan J, Berg JM ten. Aspirin with or without clopidogrel after transcatheter aortic-valve implantation. *N Engl J Med* 2020;383:1447–1457.
- Ussia GP, Scarabelli M, Mulè M, Barbanti M, Sarkar K, Cammalleri V, Immè S, Aruta P, Pistrutto AM, Gulino S, Deste W. Dual antiplatelet therapy versus aspirin alone in patients undergoing transcatheter aortic valve implantation. *Am J Cardiol* 2011;112:1772–1776.
- Poliacikova P, Cockburn J, Adam de Belder MD, Trivedi U, Hildick-Smith D. Antiplatelet and antithrombotic treatment after transcatheter aortic valve implantation - comparison of regimes. *J Invasive Cardiol* 2013;25:544–548.
- Durand E, Blanchard D, Chassaing S, Gilard M, Laskar M, Borz B, Lafont A, Barbey C, Godin M, Tron C, Zegdi R, Chatel D, Le Page O, Litzler P-Y, Bessou J-P, Danchin N, Cribier A, Eltchaninoff H. Comparison of two antiplatelet therapy strategies in patients undergoing transcatheter aortic valve implantation. *Am J Cardiol* 2014;113:355–360.
- Czerwińska-Jelonkiewicz K, Zembala M, Dąbrowski M, Witkowski A, Ochała A, Kochman J, Dudek D, Kübler P, Jagielak D, Stępińska J. Can TAVI patients receive aspirin monotherapy as patients after surgical aortic bioprosthesis implantation? Data from the polish registry - POL-TAVI. *Int J Cardiol* 2017;227:305–311.
- Mangieri A, Jabbour RJ, Montalto C, Pagnesi M, Regazzoli D, Ancona MB, Giannini F, Tanaka A, Bertoldi L, Monaco F, Agricola E, Giglio M, Mattioli R, Ferri L, Montorfano M, Chieffo A, Alfieri O, Colombo A, Latib A. Single-antiplatelet therapy in patients with contraindication to dual-antiplatelet therapy after transcatheter aortic valve implantation. *Am J Cardiol* 2017;119:1088–1093.
- Stabile E, Pucciarelli A, Cota L, Sorropago G, Tesorio T, Salemme L, Popusoi G, Ambrosini V, Cioppa A, Agrusta M, Catapano D, MoscarIELLO C, Trimarco B, Esposito G, Rubino P. SAT-TAVI (single antiplatelet therapy for TAVI) study: a pilot randomized study comparing double to single antiplatelet therapy for transcatheter aortic valve implantation. *Int J Cardiol* 2014;174:624–627.
- D’Ascenzo F, Benedetto U, Bianco M, Conrotto F, Moretti C, D’Onofrio A, Agrifoglio M, Colombo A, Ribichini F, Tarantini G, D’Amico M, Salizzoni S, Rinaldi M. Which is the best antiaggregant or anticoagulant therapy after TAVI? A propensity-matched analysis from the ITER registry. The management of DAPT after TAVI. *Euro-Intervention* 2017;13:e1392–e1400.
- Ichibori Y, Mizote I, MaeIchibori Y, Mizote I, Maeda K, Onishi T, Ohtani T, Yamaguchi O, Torikai K, Kuratani T, Sawa Y, Nakatani S, Sakata Y. Clinical outcomes and bioprosthetic valve function after transcatheter aortic valve implantation under dual antiplatelet therapy vs. aspirin alone. *Circ J* 2017;81:397–404.
- Hioki H, Watanabe Y, Kozuma K, Kataoka A, Yashima F, Naganuma T, Araki M, Tada N, Shirai S, Yamanaka F, Mizutani K, Tabata M, Takagi K, Ueno H, Yamamoto M, Hayashida K, OCEAN-TAVI Investigators. Short-term dual anti-platelet therapy decreases long-term cardiovascular mortality after transcatheter aortic valve replacement. *Heart Vessels* 2020;1–8.
- Rodés-Cabau J, Masson J-B, Welsh RC, Garcia Del Blanco B, Pelletier M, Webb JG, Al-Qoofi F, Génereux P, Maluenda G, Thoenes M, Paradis J-M, Chamandi C, Serra V, Dumont E, Côté M. Aspirin versus aspirin plus clopidogrel as antithrombotic treatment following transcatheter aortic valve replacement with a balloon-expandable valve: the ARTE (aspirin versus aspirin + clopidogrel following transcatheter aortic valve implantation) randomized clinical trial. *JACC Cardiovasc Interv* 2017;10:1357–1365.