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# Abbreviated Antiplatelet Therapy in Patients at High Bleeding Risk With or Without Oral Anticoagulant Therapy After Coronary Stenting: An Open-Label, Randomized, Controlled Trial

**Running Title**: *Smits, et al.; DAPT Duration in High Bleeding Risk PCI Patients*

Pieter C. Smits, MD, PhD[1]; Enrico Frigoli, MD[2]; Jan Tijssen, PhD[3]; Peter Jüni, MD[4]; Pascal Vranckx, MD, PhD[5,6]; Yukio Ozaki, MD, PhD[7]; Marie-Claude Morice, MD[8]; Bernard Chevalier, MD[9]; Yoshinobu Onuma, MD, PhD[10]; Stephan Windecker, MD[11]; Pim A.L. Tonino, MD[12]; Marco Roffi, MD[13]; Maciej Lesiak, MD[14]; Felix Mahfoud, MD[15]; Jozef Bartunek, MD, PhD[16]; David Hildick-Smith, MD[17]; Antonio Colombo, MD[18]; Goran Stankovic, MD, PhD[19]; Andrés Iñiguez, MD, PhD[20]; Carl Schultz, MD, PhD[21]; Ran Kornowski, MD[22]; Paul J.L. Ong, MD, PhD[23]; Mirvat Alasnag, MD, PhD[24]; Alfredo E. Rodriguez, MD, PhD[25]; Aris Moschovitis, MD[26]; Peep Laanmets, MD[27]; Dik Heg, PhD[2]; Marco Valgimigli, MD, PhD[28]; on behalf of the MASTER DAPT investigators*

[1]Department of Cardiology, Maasstad Hospital, Rotterdam, the Netherlands; [2]Clinical Trial Unit, University of Bern, Bern, Switzerland; [3]Amsterdam University Medical Centers, Department of Cardiology, Amsterdam, and ECRI, Rotterdam, the Netherlands; [4]University of Toronto, Applied Health Research Centre, Li Ka Shing Knowledge Institute, St Michael's Hospital, Toronto, Ontario, Canada; [5]Department of Cardiology and Critical Care Medicine, Hartcentrum Hasselt, Jessa Ziekenhuis, Hasselt, Belgium; [6]Faculty of Medicine and Life Sciences, Hasselt University, Hasselt, Belgium; [7]Department of Cardiology, School of Medicine, Fujita Health University, Toyoake, Aichi, Japan; [8]Cardiovascular European Research Center (CERC), Massy, France; [9]Ramsay Générale de Santé, Interventional Cardiology Department, Institut Cardiovasculaire Paris Sud, Massy, France; [10]National University of Ireland, Galway, Ireland; [11]Department of Cardiology, Bern University Hospital, Bern, Switzerland; [12]Department of Cardiology, Catharina Hospital, Eindhoven, the Netherlands; [13]Division of Cardiology, Geneva University Hospitals, Geneva, Switzerland; [14]1st Department of Cardiology, University of Medical Sciences, Poznan, Poland;

[15]Department of Cardiology, Angiology, Intensive Care Medicine, Saarland University, Homburg, Germany; [16]Cardiovascular Center, OLV Hospital, Aalst, Belgium; [17]Brighton and Sussex University Hospitals NHS Trust, Brighton, United Kingdom; [18]Unit of Cardiovascular Interventions, IRCCS San Raffaele Scientific Institute, Milan, Italy; [19]Department of Cardiology, Clinical Center of Serbia, and Faculty of medicine, University of Belgrade, Belgrade, Serbia; [20]Hospital Alvaro Cunqueiro, Vigo, Spain; [21]Department of Cardiology, Royal Perth Hospital Campus, University of Western Australia, Perth, Australia; [22]Rabin Medical Center, Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel; [23]Tan Tock Seng Hospital, Singapore, Singapore; [24]Department of Cardiology, King Fahad Armed Forces Hospital, Jeddah, Saudi Arabia; [25]Cardiac Unit Otamendi Hospital, Buenos Aires School of Medicine Cardiovascular Research Center (CECI) Buenos Aires, Argentina; [26]HerzZentrum, Hirslanden, Zürich, Switzerland; [27]North-Estonia Medical Centre Foundation, Tallinn, Estonia; [28]Cardiocentro Ticino Institute, Ente Ospedaliero Cantonale, Università della Svizzera Italiana (USI), CH- 6900 Lugano, Switzerland

* A complete list of the MASTER DAPT investigators is provided in Data Supplement I.





**Address for Correspondence:**
Pieter C. Smits, MD, PhD
Department of Cardiology
Maasstad Ziekenhuis, Maasstadweg 21
3079 DZ Rotterdam
The Netherlands.
Tel: +31-10-2913322
Email SmitsP@maasstadziekenhuis.nl

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## Abstract

**Background:** The optimal duration of antiplatelet therapy (APT) in patients at high bleeding risk with or without oral anticoagulation (OAC) after coronary stenting remains unclear.
**Methods:** In the investigator-initiated, randomized, open-label MASTER DAPT trial, 4579 patients at high bleeding risk were randomized after 1-month dual APT (DAPT) to abbreviated or nonabbreviated APT strategies. Randomization was stratified by concomitant OAC indication. In this subgroup analysis we report outcomes of populations with or without an OAC indication. In the population with an indication, patients changed immediately to single APT (SAPT) for 5 months (abbreviated regimen) or continued ≥2 months of DAPT and SAPT thereafter (nonabbreviated regimen). Patients without an OAC indication changed to SAPT for 11 months (abbreviated regimen) or continued ≥5 months of DAPT and SAPT thereafter (nonabbreviated regimen). Coprimary outcomes at 335 days after randomization were: net adverse clinical outcomes (NACE; composite of all-cause death, myocardial infarction, stroke, and Bleeding Academic Research Consortium [BARC] 3 or 5 bleeding events); major adverse cardiac and cerebral events (MACCE; all-cause death, myocardial infarction, and stroke); and type 2, 3, or 5 BARC bleeding.
**Results:** NACE or MACE did not differ with abbreviated versus nonabbreviated APT regimens in patients with OAC indication (n=1666; HR, 0.83; 95% CI, 0.60 to 1.15, HR, 0.88; 95% CI, 0.60 to 1.30; respectively) or without OAC indication (n=2913; HR, 1.01; 95% CI, 0.77 to 1.33; HR, 1.06; 95% CI, 0.79 to 1.44; $P_{interaction}$=0.35 and 0.45, respectively). BARC 2, 3 or 5 bleeding did not significantly differ in patients with OAC indication (HR, 0.83; 95% CI, 0.62 to 1.12) but was lower with abbreviated APT in patients without OAC indication (HR, 0.55; 95% CI, 0.41 to 0.74; $P_{interaction}$=0.057). The difference in bleeding in patients without OAC indication was driven mainly by a reduction in BARC 2 bleedings (HR, 0.48; 95% CI 0.33 to 0.69; $P_{interaction}$=0.021).
**Conclusions:** Rates of NACE and MACCE did not differ with abbreviated APT in high bleeding risk patients with or without an OAC indication and resulted in lower bleeding rates in patients without an OAC indication.
**Clinical Trial Registration:** URL: https://www.clinicaltrials.gov Unique identifier: NCT03023020


**Key Words:** Antiplatelet therapy; percutaneous coronary intervention; dual antiplatelet therapy

**Non-standard Abbreviations and Nonstandard Acronyms**
APT, antiplatelet therapy
BARC, Bleeding Academic Research Consortium
CI, confidence interval
DAPT, dual antiplatelet therapy
HR, hazard ratio
MACCE, major adverse cardiac and cerebral events
MASTER DAPT, Management of High Bleeding Risk Patients Post Bioresorbable Polymer Coated Stent Implantation With an Abbreviated Versus Standard DAPT Regimen
NACE, net adverse clinical outcomes
NARC, nonadherence Academic Research Consortium
NOAC, nonvitamin K antagonist oral anticoagulant
NSAID, nonsteroidal anti-inflammatory drug

OAC, oral anticoagulation
SAPT, single antiplatelet therapy
VKA, vitamin K antagonist

## Clinical Perspective

### What is new?

- The MASTER DAPT trial investigated an abbreviated (1 month) versus nonabbreviated (3−12 month) dual antiplatelet therapy (DAPT) and a stopping of antiplatelet therapy (APT) at 6 months strategy after coronary stenting in an all-comer population at high-bleeding risk.
- This prespecified subgroup analysis reports on the outcome of patients with or without an oral anticoagulation (OAC) indication.
- At 12-month follow-up, ischemic and net risk did not differ with abbreviated versus nonabbreviated ATP regimens in both subgroups, although significantly fewer clinically relevant bleeding events occurred in the group without an OAC indication, whereas only numerically fewer bleeding events occurred in the group with an OAC indication.

### What are the clinical implications?

- This subgroup analysis from the MASTER DAPT trial adds additional evidence that DAPT beyond 1 month in patients with or without an indication for OAC has no benefit and only increases bleeding risk.
- The strategy of stopping APT after 6 months in patients with an OAC indication needs to be explored further.

## Introduction

Patients undergoing coronary stenting for obstructive coronary artery disease require dual antiplatelet therapy (DAPT), comprising aspirin and a P2Y12 receptor blocker, for a certain period to reduce the risk of ischemic events such as stent thrombosis. The optimal duration of antiplatelet therapy (APT) after implantation of drug-eluting coronary stents remains a matter of debate, especially in patients at high risk for bleeding, which is associated with a three- to fivefold increased risk of death.[1, 2] Approximately 10% of patients undergoing coronary stent implantation have an indication for oral anticoagulation (OAC), mainly because of concomitant atrial fibrillation.[3] These patients present with a clinical dilemma because of the need to combine APT with OAC therapy. OAC therapy *per se* is associated with increased risk of bleeding and adding APT further amplifies that risk.[4] Patients without OAC therapy but aged ≥75 years and/or with renal insufficiency, active cancer, blood disorders, bleeding history, need for surgery, chronic use of nonsteroidal anti-inflammatory drugs (NSAIDs) or steroids, and cerebral infarcts constitute another large group at high risk of bleeding post coronary stenting.[5]

Little evidence exists on the optimal combination and duration of APT in patients at high bleeding risk with and without OAC therapy after coronary artery stenting. Only two relatively small-sized, randomized, controlled trials have investigated the combination of a vitamin K antagonist (VKA) and APT, with discordant results.[6, 7] With the advent of more potent P2Y12 inhibitors and nonvitamin K antagonist oral anticoagulants (NOACs), finding the optimal antithrombotic therapy post coronary stenting has become more complex. Four randomized trials with different NOACs in patients with atrial fibrillation undergoing coronary stenting or treatment for acute coronary syndrome focused primarily on dual therapy with a NOAC and a P2Y12 inhibitor (mainly clopidogrel) versus triple therapy with VKA and DAPT.[8-11] Meta-

analyses of these four trials show that dual therapy, after up to 1 week of triple therapy, significantly reduced the risk of bleeding compared with prolonged (i.e. mainly 6 months or more) triple therapy, at the cost of a significant increase in stent thrombosis and a borderline higher risk of myocardial infarction.[12-14] Therefore, the optimal duration of APT remains to be determined.

The Management of High Bleeding Risk Patients Post Bioresorbable Polymer Coated Stent Implantation With an Abbreviated Versus Standard DAPT Regimen (MASTER DAPT) trial was designed to investigate the safety of abbreviated versus nonabbreviated APT in high-bleeding risk patients undergoing coronary stenting. The trial protocol provided differential APT recommendations for patients at high bleeding risk with or without an indication for OAC therapy and stratified randomization accordingly. In this prespecified analysis, we assessed the treatment effects of abbreviated versus nonabbreviated APT regimens in patients with or without a concomitant indication for OAC.





## Methods

The data, analytic methods, and study materials will not be made available to other researchers for the purposes of reproducing the results or replicating the procedure.

### Study design

The MASTER DAPT trial (ClinicalTrials.gov number, NCT03023020) was an investigator-initiated, randomized, open-label, noninferiority trial with sequential superiority testing in largely unselected patients at high bleeding risk who underwent implantation with a biodegradable polymer-coated Ultimaster™ (Terumo Corporation, Tokyo, Japan) sirolimus-eluting stent.[15] The trial was performed at 140 sites in 30 countries across Europe, South

America, the Middle East, Asia, and Australia. The study protocol was approved in each country and center. All patients gave written informed consent. An independent data safety monitoring board regularly reviewed the conduct of the trial and the safety of the patients. Trial organization and participating sites are mentioned in Data Supplement I .

**Patients**

Patients at high risk for bleeding who underwent treatment of all planned coronary artery stenoses with Ultimaster stent implantation for acute or chronic coronary syndromes were eligible if they remained event-free until the time of randomization at 1 month after the index procedure. Patients were considered at high bleeding risk if at least one of the following criteria applied: OAC (VKA or NOAC) therapy for at least 12 months, recent (<12 months) nonaccess site bleeding episode(s) that required medical attention, previous bleeding episode(s) that required hospitalization if the underlying cause had not been definitively treated, age ≥75 years, systemic conditions associated with an increased bleeding risk (e.g. hematological disorders or any known coagulation disorder associated with increased bleeding risk), documented anemia (defined as repeated hemoglobin levels <11 g/dL or transfusion within 4 weeks before randomization), need for chronic treatment with steroids or NSAIDs, diagnosed malignancy (other than skin), stroke at any time or transient ischemic attack in the previous 6 months, or PRECISE DAPT score ≥25.[16] Exclusion criteria were minimal and limited to implantation of a nonstudy stent within the previous 6 months or a bioresorbable scaffold at any time before the index procedure, or if they underwent treatment because of an in-stent restenosis or stent thrombosis. Detailed inclusion and exclusion criteria are provided in the Data Supplement II.

**Randomization, masking, and procedures**

Patients were centrally randomized (1:1 ratio) to an open-label abbreviated or nonabbreviated APT regimen 30 to 44 days after the index procedure. Randomization was concealed using a web-based system; randomization sequences were computer generated, blocked, with randomly selected block sizes of 2, 4, or 6, and were stratified by site, history of acute myocardial infarction within 12 months, and indication for at least 12 months of OAC therapy. In this subgroup analysis we report the outcomes of the populations with or without an OAC indication.

Figure 1 shows the trial design and the specific subgroups of this analysis. Patients with an indication for OAC therapy who were randomly allocated to receive abbreviated treatment immediately discontinued DAPT and continued single APT (SAPT) for 6 months after the index procedure, and continued thereafter with OAC monotherapy only. Patients on OAC therapy who were randomly allocated to receive nonabbreviated treatment continued DAPT until at least 3 months after the index stent procedure (i.e. at least 2 months after randomization) and continued thereafter with SAPT until 12 months after the index procedure. Patients without an indication for OAC who were randomly allocated to the abbreviated group immediately discontinued DAPT and continued with SAPT until 12 months after the index procedure. Patients without an indication for OAC who were randomly allocated to the nonabbreviated group continued DAPT for at least 6 months post index procedure (i.e. ≥5 months after randomization), after which SAPT with aspirin was continued. All antiplatelet and OAC treatment options were dosed according to the corresponding authorization for use and locally approved regimens. Table I in the online-only Data Supplement shows the APT regimen(s) allowed after each type of event according to the presence of absence of a clinical indication for OAC.

Follow-up visits occurred at 60±14 and 150±14 days after randomization, preferably as on-site visits, and at 335±14 days after randomization, exclusively as an on-site visit. Two independent clinical research organizations (CERC, Massy, France and Cardialysis, Rotterdam, the Netherlands) performed on-site and remote monitoring visits, verified the source documents, and collected source material for event adjudication. All events were adjudicated by an independent adjudication committee that was unaware of the treatment allocations. All data was stored at a central database (CTU, Bern, Switzerland). Nonadherence to the allocated treatment regimen was evaluated according to the Non-adherence Academic Research Consortium (NARC) classification (Table II in the online-only Data Supplement).[17]

**Outcomes**

Coprimary outcomes were net adverse clinical outcomes (NACE), defined as the composite of all-cause death, myocardial infarction, stroke, and Bleeding Academic Research Consortium (BARC) 3 or 5 bleeding events[18]; major adverse cardiac and cerebral events (MACCE), expressed as a composite of all-cause death, myocardial infarction, and stroke; and major or clinically relevant nonmajor bleeding, defined as a composite of type 2, 3, or 5 BARC bleeding events.

The secondary outcomes include the individual components of the three coprimary outcomes; the composite of cardiovascular death, myocardial infarction, and stroke; the composite of cardiovascular death, myocardial infarction, definite or probable stent thrombosis, and any revascularization; the composite of stroke and transient ischemic attack; and all bleeding events, adjudicated according to the BARC classifications.[18] All outcomes were prespecified.[15] All analyses evaluated the occurrence of the adjudicated outcomes between randomization and 335 days.

**Statistical analysis**

The data were analyzed according to the intention-to-treat principle. Outcomes were assessed separately for patients with and without indication for OAC therapy by calculating hazard ratios (HR) with 95% confidence intervals (CI). The Com-Nougue method[19] was used to analyze time to event and calculate event rates and *P* values. We report cause-specific estimates throughout the paper. For patients with a primary outcome, time-to-event was calculated as the difference between the date of occurrence of the outcome event and the date of randomization plus 1. For patients with an outcome event and complete follow-up until the end of day 335, time to censoring was calculated as 335 days. For patients with incomplete clinical follow-up, time to censoring was defined as the difference between the dates of last known clinical status and randomization plus 1. For the third coprimary end point, the occurrence of death was defined as a competing risk event, and follow-up was censored at the time of the occurrence of death. Kaplan−Meier curves were created for the first two (time-to-event) coprimary outcomes, and cause-specific Kaplan−Meier curves for the third coprimary end point (with censoring at the time of the competing risk event of unrelated death). Kaplan−Meier calculations included all (first) adjudicated outcome events that occurred between randomization and 335 days thereafter according to the randomized treatment assignment, irrespective of the dual antiplatelet regimen received at the time of the outcome event. Cause-specific hazard ratios and 95% confidence intervals were generated for primary and secondary end points with the use of Cox proportional hazards regression analysis with censoring at end of study and at the time of the competing risk event of unrelated death as defined above.

P values for testing homogeneity of the hazard ratio in subgroups of patients were derived in Cox proportional hazards models with interaction terms for treatment group and subgroup

membership. The 95% confidence intervals and P values for interaction were not adjusted for multiplicity and should not be used to infer definitive treatment effects.

**Role of the funding source**

The study was sponsored by the European Cardiovascular Research Institute (ECRI), a nonprofit organization, and received grant support from Terumo. The sponsor and funder had no role in the study design, data collection, data monitoring, analysis, interpretation, or writing of the report.

**Results**

From 28 February 2017 to 5 December 2019, 5204 patients were screened and 4579 (88.1%) were randomized a median of 34 days (interquartile range, 32 to 39) post stenting, of which 1666 (36.4%) patients had an indication for OAC and 2913 (63.6%) had no indication for OAC. Of the 1666 patients with OAC therapy, 848 were assigned to the abbreviated APT group and 818 to the nonabbreviated APT group (Figure 2). Of the 2913 patients without OAC, 1447 were assigned to the abbreviated APT group and 1466 to the nonabbreviated APT group. Complete follow-up in the OAC subgroup was 99.3% for the abbreviated APT arm and 98.8% for the nonabbreviated APT arm, and 99.4% and 99.5%, respectively, in the subgroup without OAC.

Baseline and procedural characteristics are described in Tables 1 and 2 and Table III in the online-only Data Supplement. The overall mean±SD age was 76.0±8.7 years. On average, 33.6% of patients received treatment for diabetes. The indication for coronary stenting was acute coronary syndrome for 48.3% of patients. Atrial fibrillation was present in 84.2% of patients in the OAC group.

In the OAC group, 64.9% of the patients received a NOAC and 33.5% a VKA (Table IV in the online-only Data Supplement), largely in combination with clopidogrel (98.8%) in the

abbreviated group or aspirin plus clopidogrel (97.4%) in the nonabbreviated group. In the non-OAC group, aspirin plus clopidogrel (67.8%) was the most frequently implemented regimen, followed by aspirin and ticagrelor (28.4%) (Table V in the online-only Data Supplement). Median durations of DAPT since coronary stenting were 33 days (IQR, 30 to 39) in patients with OAC and 34 days (IQR, 31 to 40) in patients without OAC in the abbreviated arm; and 96 days (IQR, 90 to 114) and 364 days (IQR, 190 to 369), respectively, in the nonabbreviated group. Detailed information on antiplatelet use is shown in Figure 3.

Adherence to the allocated antiplatelet regimen decreased over time and was lower in the abbreviated versus nonabbreviated group at 12 months in the OAC subgroup (82.7% vs 95.8%; *P*<0.001, respectively). Detailed information on adherence is depicted in Figure I and Tables V and VI in the online-only Data Supplement, with 16.1% of the patients with an OAC indication who still used APT at the 11 months visit post randomization in the abbreviated arm.

**Outcomes among patients with OAC indication**

Clinical outcomes at 12 months in OAC patients are shown in Table 3. NACE occurred in 68 (8.0%) patients in the abbreviated arm versus 78 (9.6%) patients in the nonabbreviated arm (HR, 0.83; 95% CI, 0.60 to 1.15; *P*=0.26) (Figure 4A). MACCE did not differ, occurring in 50 (5.9%) patients in the abbreviated arm versus 54 (6.7%) patients in the nonabbreviated arm (HR, 0.88; 95% CI, 0.60 to 1.30; *P*=0.53) (Figure 4B). BARC 2, 3, or 5 bleeding occurred in 83 (9.9%) patients in the abbreviated arm versus 94 (11.7%) patients in the nonabbreviated arm (HR, 0.83; 95% CI, 0.62 to 1.12; *P*=0.25) (Figure 4C). Fewer cerebrovascular events occurred in the abbreviated arm (HR, 0.22; 95% CI, 0.06 to 0.77; *P*=0.01). Other outcomes did not differ between groups.

Landmark analyses at 150 days after randomization showed consistent treatment effects for the coprimary and secondary endpoints with respect to time among patients with an indication for OAC (Table 4). Numerically, fewer BARC 3 or 5 bleeding events occurred in the first 150 days in the abbreviated arm compared to the nonabbreviated arm. No differences in ischemic and bleeding events were noted between 150 and 335 days when APT was stopped in the abbreviated arm.

**Outcomes among patients without an OAC indication**

Clinical outcomes at 12 months in patients without an OAC indication are shown in Table 3. NACE did not differ between the abbreviated and nonabbreviated APT groups (104 [7.2%] vs 104 [7.1%], respectively; HR, 1.01; 95% CI, 0.77 to 1.33; *P*=0.91) (Figure 4A). MACCE also did not differ between the treatment groups (88 [6.1%] vs 84 [5.7%]; HR, 1.06; 95% CI, 0.79 to 1.44; *P*=0.67) (Figure 4B). BARC 2, 3, and 5 bleeding occurred less frequently in the abbreviated arm (65 [4.6%] vs 117 [8.1%]; HR, 0.55; 95% CI, 0.41 to 0.74; *P*<0.001) (Figure 4C). Fewer BARC 1 and BARC 2 bleedings occurred in the abbreviated APT arm (*P*=0.001 and *P*<0.001, respectively).

Landmark analyses at 150 days after randomization showed consistent treatment effects with respect to time for the coprimary and secondary endpoints among patients without an indication for OAC (Table 4).

**Consistency of treatment effects between OAC and non-OAC patients**

The treatment effects between abbreviated and nonabbreviated APT were consistent in patients with or without an OAC indication, except for the coprimary endpoint of BARC 2, 3, or 5 bleeding and the secondary endpoint of BARC 2 bleeding. Both HRs were lower in patients with

an OAC indication, with a borderline ($P_{interaction}$=0.057) and significant ($P_{interaction}$=0.021) interaction test, respectively.

The coprimary endpoint of BARC 2, 3, or 5 bleedings was twofold higher in the OAC versus non-OAC therapy subgroup, whereas rates of first ischemic events did not differ in both subgroups (Figures 4B and 4C).

**Per-protocol population**

The coprimary findings remained unchanged in the per-protocol population (Table VII and VIII in the online-only Data Supplement). An overview of protocol violations used to define the per-protocol population are summarized in Table IX in the online-only Data Supplement.

## Discussion

The main findings of this subgroup analysis from the MASTER DAPT trial are threefold. First, in an abbreviated APT strategy, stopping DAPT at 1 month post coronary stenting with a biodegradable polymer coated sirolimus-eluting stent, the occurrence of ischemic and net events did not differ in patients with or without OAC therapy. Second, stopping DAPT at 1 month and continuing with SAPT reduces clinically relevant bleeding risk significantly in high bleeding risk patients without an indication for OAC and numerically in patients with an indication for OAC. Third, stopping SAPT 6 months after coronary stenting demonstrated no effect on ischemic events, or in prevention of bleeding events in patients with an indication for OAC, although a significant proportion of patients were nonadherent to the allocated abbreviated APT regimen and did not stop APT 6 months after coronary stenting. These findings have the following implications: our results show that it is safe and beneficial to stop DAPT after 1 month in

patients at high bleeding risk with or without an indication for OAC, and that the effect of stopping all APT after 6 months in patients on OAC needs to be explored further.

Patients at high bleeding risk constitute a considerable proportion of those undergoing coronary stenting.[20] This high-bleeding-risk population comprises a heterogenous group in which two large subgroups can be identified based on the need, or not, for concomitant OAC therapy. The need for APT in combination with OAC therapy increases bleeding risk,[3, 21] whereas OAC therapy alone post stenting is insufficient in preventing ischemic complications such as stent thrombosis.[22, 23] Therefore, guidelines[24-27] recommend different APT strategies for patients at high bleeding risk after coronary stenting depending on whether they receive APT or OAC therapy. Based on these recommendations, the MASTER DAPT trial was designed as an all-comer high-bleeding-risk trial with two APT strategies for each stratified subgroup. Patients without an indication for OAC who were allocated to the nonabbreviated APT regimen received DAPT for a minimum of 6 months, consistent with the guidelines. Patients allocated to the experimental abbreviated APT therapy arm received 1 month of DAPT, similar to other recent high-bleeding-risk trials investigating an abbreviated DAPT regimen.[20, 28, 29] However, in the OAC subgroup, the duration of therapy in the nonabbreviated APT arm (with a minimum of 3 months of DAPT) is longer than recommended in the current North-American guidelines[24, 27] and European non−ST-segment elevation myocardial infarction[25] and atrial fibrillation guidelines,[26] which recommend DAPT for 1 week to 1 month in patients on OAC. No previous trial has investigated the value of 1 month versus 3 months of DAPT in the OAC population. The ISAR-TRIPLE compared 6 weeks of clopidogrel with 6 months of clopidogrel in 614 patients receiving aspirin and OAC after drug-eluting stent implantation; the authors found no difference between treatment strategies for the composite of death, myocardial infarction, stroke, stent thrombosis,

or major bleeding.[6] Therefore, the recommendation of a very short (i.e. 1 week) duration of DAPT in OAC patients after percutaneous coronary intervention or an acute coronary syndrome in the current NOAC era is supported by the findings of four studies.[8-11] Three of these studies[8, 9, 11] tested a very short duration of triple therapy consisting of aspirin, NOAC, and a $P2Y_{12}$ inhibitor, followed by continuation of the latter two drugs, versus a very long duration of triple therapy comprising aspirin, VKA, and a $P2Y_{12}$ inhibitor for mainly 6 months or longer. The AUGUSTUS trial is the largest among the four and the only study that disentangled the effect of OAC type from duration of aspirin treatment.[8] When data from these studies are pooled, they show a major reduction in bleeding events with a very short duration of triple therapy. However, they also show higher rates of stent thrombosis, likely clustered in the first few weeks after aspirin discontinuation,[30] which are consistently observed in patients with or without an acute coronary syndrome.[12] Our findings are in concert with observational data,[31] showing no rebound of ischemic events after 1 month of DAPT in OAC patients.

Although North-American and European guidelines[25-27] recommend stopping APT after 6 months in an OAC population (level of evidence C), no previous trial has actually investigated the value of no APT versus SAPT after 6 months. Our present study failed to show a clear benefit of stopping APT after 6 months, high likely because of the lack of power in this subgroup analysis and the fact that a considerable proportion of patients were nonadherent to the abbreviated allocated treatment regimen and continued using SAPT after 6 months. Whether the absence of an increase in ischemic events and a decrease in bleeding events relates to this nonadherence remains to be explored.

In our trial of an all-comer population at high bleeding risk, we observed a twofold higher bleeding rate in the OAC subgroup compared with the non-OAC subgroup. This can be

explained in part by the relative long DAPT regimens in the nonabbreviated APT arm of this subgroup but not for the abbreviated APT arm. Furthermore, most patients on OAC were treated with a NOAC (64.9%) and no outcome differences were noted between patients on VKA or NOAC medications (data not shown). The increased bleeding risk of patients on OAC versus not on OAC emphasizes the importance of defining the optimal APT duration and combination in this subgroup who are already categorized as at high bleeding risk. A numerically lower rate of BARC 3 or 5 bleedings was noted in the first 150 days post randomization in the abbreviated arm of patients on OAC, whereas this was less apparent in the abbreviated APT arm of the population without an OAC indication. In contrast, patients at high bleeding risk without an OAC indication in the abbreviated arm had significantly fewer BARC 2 bleedings, whereas this was less apparent in the OAC population. This different signal of bleeding severity between both subgroups is likely related to the higher bleeding risk of OAC patients and differences in baseline characteristics between subgroups.

Another interesting finding is the reduced risk of ischemic stroke in the abbreviated APT arm of the OAC subgroup ($P$=0.03). A similar observation was noted in the WOEST trial ($P$=0.056).[7] Whether this paradoxical finding relates to lower dosing of VKA or NOAC in the nonabbreviated DAPT arm or is a result of chance of this low frequent event remains to be determined.

Every randomized trial has its strengths and weaknesses. The fact that randomization was done at 1 month could indicate that patients at lower ischemic risk were selected, as patients with an ischemic event before 1 month were excluded from randomization. However, allowing patients entering the trial only after 30 days of uneventful follow-up mimics clinical practice and prevents inclusion of patients in whom the clinical equipoise between DAPT continuation or

discontinuation is questionable and perhaps unethical. On the other hand, patients experiencing a manageable bleeding event post PCI but who were stable 1 week before randomization could be included as they were *de facto* high bleeding risk. In our trial, randomization at 1 month is the preferred strategy, because at that timepoint the comparison of the allocated treatment strategies started and events that happened before randomization while both subgroups were on DAPT did not interfere with the outcome of this trial.

Nonadherence often occurs in randomized trials and can have important implications for the results. In general, nonadherence of <20% is considerate acceptable; however, the cut-off of 20% is arbitrary and encompasses several reasons as to why nonadherence occurred. In the MASTER DAPT trial, nonadherence was carefully monitored and classified.[17] In our trial, we observed a significant drop in adherence in the abbreviated APT arm of the OAC subgroup. A considerable number of patients continued APT after 6 months, whereas the protocol stipulated stopping at 6 months. During the trial monitoring process, we noticed this phenomenon and tried to make all investigators aware of this protocol violation. Unfortunately, despite many communications during the trial to the principal investigators in each country and to local investigators, the NARC 2 (temporary) and NARC 3 (permanent discontinuation) nonadherence patterns remained prevalent at around 30% in the abbreviated arm of the OAC subgroup. Local physicians and patients were reluctant to stop APT at 6 months.

**Limitations**

Several limitations must be acknowledged. This was a subgroup analysis (albeit the investigated subgroups were prespecified and stratified at randomization). The subgroups were not powered for the coprimary outcomes and individual endpoints, such as myocardial infarction and stent thrombosis, therefore the results should therefore be interpreted with caution. Treatment

allocation was open label, which reflects a treatment-strategy trial and the impossibility of masking treatment for three oral $P2Y_{12}$ inhibitors and aspirin. Nonadherence to the allocated APT regimen occurred more often in the abbreviated DAPT arm of the OAC subgroup. Our trial included patients at high risk for bleeding who underwent biodegradable polymer sirolimus-eluting stent implantation; consequently, our results may not extend to patients who are not at high bleeding risk or received other stent types.

**Conclusions**

In an all-comer high bleeding risk population with minimal angiographic restrictions, stopping DAPT 1 month after coronary stenting was associated with lower bleeding risk without additional ischemic risk in patients with or without OAC. Stopping APT after 6 months in patients on OAC needs to be explored further.







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| **Principal investigator** | **Affiliation** |
|---|---|
| Dr Juan Mieres | Otamendi Hospital, Buenos Aires, Argentina |
| Dr Fernando Cura | Institutio Cardiovascular de Buenos Aires, Buenos Aires, Argentina |
| Dr Carlos Fernandez-Pereira | Clinica IMA, Buenos Aires, Argentina |
| Dr Astin Lee | Wollongon Hospital, Wollongong, Australia |
| Dr Nigel Jepson | Prince of Wales Hospital, Sydney, Australia |

| | |
|---|---|
| Prof. Robert Whitbourn | St Vincent Hospital, Fitzroy, Australia |
| Dr Owen Christopher Raffel | The Prince Charles Hospital, Chermside, Australia |
| Prof. Kurt Huber | Wilhelminenspital, Vienna, Austria |
| Prof. Franz Weidinger | Rudolfstiftung Hospital, Vienna, Austria |
| Prof. Fazila-Tun-Nesa Malik | National Heart Foundation Hospital & Research Institute, Dhaka, Bangladesh |
| Dr Willem Dewilde | Imelda Ziekenhuis, Bonheiden, Belgium |
| Dr Adel Aminian | CHU de Charleroi – Hôpital Civil Marie Curie, Charleroi, Belgium |
| Prof. Emanuele Barbato | OLV Ziekenhuis, Aalst, Belgium |
| Dr Suzanne Pourbaix | CHR La Citadelle, Liege, Belgium |
| Dr Panagiotis Xaplanteris | CHU St. Pierre UMC St. Pieter, Brussels, Belgium |
| Dr Vasil Velchev | UMHAT St. Anna, Sofia, Bulgaria |
| Dr Dimitar Karageorgiev | MHAT "Sveta Karidad" Plovdiv, Plovdiv, Bulgaria |
| Dr Hristo Mateev | National Heart Hospital, Sofia, Bulgaria |
| Prof. Valeri Gelev | Tokuda Hospital, Sofia, Bulgaria |
| Prof. Petr Kala | University Hospital Brno, Brno, Czech Republic |
| Dr Martin Mates | Na Homolce Hospital, Praha, Czech Republic |
| Dr Henning Kelbæk | Roskilde Hospital Kogevej Roskilde, Denmark |
| Dr Thomas Hovasse | Hopital Prive Jacques Cartier, Massy, France |
| Dr Laurent Delorme | Clinique du Pont de Chaume, Montauban, France |
| Prof. Thomas Cuisset | CHU La Timone Marseille, France |
| Dr Loïc Belle | Centre Hospitalier Annecy Genvois, Annecy, France |
| Prof. Farzin Beygui | Centre Hospitalier regional universitaire de Caen, Caen, France |

| | |
|---|---|
| Dr Ashok Tirouvanziam | Hôpital Prive le Confluent, Nantes, France |
| Prof. Christophe Piot | Clinique du Millenaire, Montpellier, France |
| Dr Jean François Morelle | Hopital Prive Saint Martin, Caen, France |
| Dr Rene Koning | Clinique Saint-Hilaire Rouen,, France |
| Dr Mathieu Valla | Hopital de Mercy, Metz, France |
| Dr Philippe Brunel | GCIDB – Hopital Prive Dijon Bourgogne, Dijon, France |
| Dr Guillaume Cayla | CHU Caremeau, Nimes, France |
| Prof. Emmanuel Teiger | Centre Hospitalier Universitaire Henri-Mondor, Creteil, France |
| Prof. Gilles Montalescot | Hôpital Universitaire Pitié-Salpêtrière, Paris, France |
| Prof. Christian Spaulding | Hôpital Europeen Georges-Pompidou, Paris, France |
| Dr Phillipe Guyon | Centre Cardiologique du Nord, Saint-Denis, France |
| Prof. Felix Mahfoud | Saarland University, Homburg, Germany |
| Dr Pyxaras, Stylianos | Landshut-Archdorf Krankenhaus, Landshut, Germany |
| Prof. Béla Merkely | Semmelweis University Heart and Vascular Center, Budapest, Hungary |
| Dr Imre Ungi | Invasive Cardiology Unit University of Szeged, Szeged, Hungary |
| Dr Rajpal K Abhaichand | G Kuppuswamy Naidu Memorial Hospital, Coimbatore, India |
| Dr Atul Damodar Abhyankar | Shri BD Mehta Mahavir Heart Institute, Surat, India |
| Dr Sengottuvelu | Apollo Hospitals, Chennai, India |
| Dr Ajit Mullasari | Madras Medical Mission, Chennai, India |
| Dr Halabi Majdi | Ziv Medical Center, Cardiology Department Safed, Israel |
| Prof. Ariel Roguin | Rambam Medical Center, Haifa, Israel |
| Dr Yair Feld | Rambam Medical Center, Haifa, Israel |

| | |
|---|---|
| Prof. Chaim Lotan | Hadassah Ein Karem Medical Center, Jerusalem, Israel |
| Dr Michael Donahue | Policlinico Casilino, Rome, Italy |
| Dr Stefano Garducci | Ospedale di Vimercate Vimercate, Italy |
| Dr Bernhard Reimers | Humanitas Research Hospital, Rozzano, Italy |
| Dr Gennaro Sardella | Policlinico Umberto I, Rome, Italy |
| Dr Alaide Chieffo | San Raffaele Hospital, Milan, Italy |
| Prof. Corrado Tamburino | Ferrarotto Hospital, Catania, Italy |
| Dr Giuseppe Andò | AOU Policlinico Martino, Messina, Italy |
| Dr Luca Testa | Policlinico San Donato, Milan, Italy |
| Dr Maurizio Di Biasi | Sacco Hospital, Milan, Italy |
| Dr Alessandro Sciahbasi | Ospedale Sandro Pertini, Rome, Italy |
| Prof.Dr Paolo Calabro | Azienda Ospedaliera di Caserta Sant Anna e San Sebastiano, Caserta, Italy |
| Dr Gianluigi Minervini | Ospedale Lorenzo Bonomo, Andria, Italy |
| Dr Bruno Loi | Azienda Ospedaliera Brotzu, Cagliari, Italy |
| Dr Franco Fabbiocchi | Centro Cardiologico Monzino IRCCS, Milan, Italy |
| Dr Jacopo Oreglia | ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy |
| Dr Paolo Sganzerla | ASST Bergamo Ovest, Treviglio, Italy |
| Dr Kenji Ando | Fukuoka Kokura Memorial Hospital, Kokura, Japan |
| Dr Yoshiharu Higuchi | Osaka Police Hospital, Osaka, Japan |
| Dr Mamoru Nanasato | Sakakibara Heart Institute, Tokyo, Japan |
| Dr Yuki Ishibashi | St. Marianna University School of Medicine, Kanagawa, Japan |
| Dr Hitoshi Matsuo | Gifu Heart Center, Gifu, Japan |

| | |
|---|---|
| Dr Ruka Yoshida | Japanese Red Cross Nagoya Daini Hospital, Nagoya, Japan |
| Dr Kiyokazu Shimizu | Ichinomiya municipal hospital, Ichinomiya, Japan |
| Dr Haruo Kamiya | Japanese Red Cross Nagoya, Nagoya, Japan |
| Dr Nobuyuki Komiyama | Tokyo, St. Lukes International Hospital, 634 – Japan, Japan |
| Dr Tetsuya Amano | Aichi Medical University Hospital, Nagakuteshi, Japan |
| Dr Toyoaki Murohara | Nagoya University Hospital, Nagoya, Japan |
| Dr Seiji Yamazaki | Sapporo Higashi Tokushukai Hospital, Sapporo, Japan |
| Dr Husam Noor | Bahrain Defence Force Hospital, Riffa, Kingdom of Bahrain |
| Dr Sasko Kedev | University Clinic of Cardiology, Skopje, Macedonia |
| Dr Jakub Podolec | Institute Of Cardiology Jagiellonian University, Krakow, Poland |
| Dr Krzysztof Reczuch | 4 Wojskowy Szpital Kliniczny, Wroclaw, Poland |
| Dr Adian Wlodarczak | Miedziowe Centrum Zdrowia SA, Lubin, Poland |
| Prof. Dariusz Dudek | University Hospital Krakow Poland, Krakow, Poland |
| Dr Pedro Canas da Silva | Hospital de Santa Maria, Lisbon, Portugal |
| Dr Ljupco Mangovski | Institute for Cardiovascular Disease Dedinje, Belgrade, Serbia |
| Dr Dragan Topic | Institute for Cardiovascular Disease Dedinje, Belgrade, Serbia |
| Dr Dragan Debeljacki | Institute of Cardiovascular Diseases, Sremska Kamenica, Serbia |
| Dr Syed Saqib Imran | KhooTeck Puat Hospital, Singapore, Singapore |
| Dr Park Seung-Jung | Asan Medical Center, Seoul, South Korea |
| Dr José Francisco Diaz Fernandez | Juan Ramon Jimenez Hospital, Huelva, Spain |
| Dr Bruno Garcia del Blanco | Hospital Vall Hebron, Barcelona, Spain |
| Dr Vicente Mainar | Hospital General Universitario de Alicante, Alicante, Spain |

| | |
|---|---|
| Dr Ivan Gomez Blazquez | Hospital 12 de Octubre, Madrid, Spain |
| Dr Eduardo Pinar | Universitario Virgen de la Arrixaca, El Palmar, Spain |
| Prof. Javier Escaned Barbosa | Hospital Clinico San Carlos, Madrid, Spain |
| Dr Joan Antoni Gomez | Bellvitge University Hospital, Barcelona, Spain |
| Hospital | |
| Dr Fermin Sainz | Hospital Universitario Valdecilla, Santander, Spain |
| Dr Javier Goicolea | Hospital Universitario Puerta de Hierro, Majadahonda, Spain |
| Dr Ole Fröbert | Orebro University Hospital, Orebro, Sweden |
| Dr Robert Kastberg | Gavle Hospital, Gavle, Sweden |
| Dr Gregor Leibundgut | Kantonsspital Baselland, Liestal, Switzerland |
| Dr Giovanni Pedrazzini | Cardiocentro Ticino, Lugano, Switzerland |
| Dr Ali Garachemani | Lindenhofspital, Bern, Switzerland |
| Dr Patrick Siegrist | University Hospital Zurich, Zurich, Switzerland |
| Prof. Stéphane Cook | HFR Hôpital Cantonal, Fribourg, Switzerland |
| Dr Al Mafragi | Zorgsaam, Terneuzen, Netherlands |
| Dr Jessurun | Treant Zorggroep, Emmen, Netherlands |
| Dr Ruifrok | Treant Zorggroep, Emmen, Netherlands |
| Dr Peter Danse | Rijnstate Ziekenhuis, Arnhem, Netherlands |
| Dr J. Polad | Jeroen Bosch Ziekenhuis, Hertogenbosch, Netherlands |
| Dr Floris Kauer | Albert Schweitzer Ziekenhuis, Dordrecht, Netherlands |
| Dr Clemens von Birgelen | Medisch Spectrum Twente, Enschede, Netherlands |
| Dr Jurrien ten Berg | Antonius Ziekenhuis Nieuwegein, Nieuwegein, Netherlands |
| Dr Sander Ijsselmuiden | Amphia Ziekenhuis, Breda, Netherlands |

| | |
|---|---|
| Dr Samer Somi | Hagahospital, Den Haag, Netherlands |
| Dr Tom Johnson | Bristol Heart Institute, Bristol, United Kingdom |
| Dr Helen Routledge | Worcestershire Royal Hospital, Worcester, United Kingdom |
| Dr Jehangir Din | Royal Bournemouth Hospital, Bournemouth, United Kingdom |
| Dr Shahzad Munir | Heart and Lung Centre – New Cross Hospital, Wolverhampton, United Kingdom |
| Dr John McDonald | Royal Blackburn Hospital, Blackburn, United Kingdom |
| Dr Neville Kukreja | Lee Haynes Research Institute, Lister Hospital, Stevenage, United Kingdom |
| Prof. Mamas Mamas | Royal Stoke University Hospital, Stoke on Trent, United Kingdom |
| Dr Rajiv Das | Freeman Hospital, Newcastle Upon Tyne, United Kingdom |
| Dr Hussain Contractor | Wythenshawe Hospital, Manchester, United Kingdom |
| Dr Aaron Peace | Altnagelvin Hospital, Derry, United Kingdom |
| Dr Rupert Williams | St. George's Hospital, London, United Kingdom |
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**Supplemental Materials**

Data Supplement on MASTER DAPT trial committees and investigators, additional information on the methods, Tables I to IX and Figure I.





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**Table 1.** Baseline Characteristics According to Presence or Absence of Clinical Indication for OAC

| Characteristic | Indication for OAC | | No indication for OAC | |
|---|---|---|---|---|
| | Abbrev DAPT (n=848) | Nonabbrev DAPT (n=818) | Abbrev DAPT (n=1447) | Nonabbrev DAPT (n=1466) |
| Age, years | 73.5 (8.8) | 73.3 (9.5) | 77.7 (8.3) | 77.5 (8.0) |
| Male sex | 636 (75.0%) | 612 (74.8%) | 954 (65.9%) | 969 (66.1%) |
| Body mass index, kg/m² | 28.6 (4.9) | 28.5 (4.8) | 26.5 (4.4) | 26.8 (4.6) |
| Family history of coronary artery disease | 244 (28.8%) | 217 (26.5%) | 312 (21.6%) | 336 (22.9%) |
| Arterial hypertension | 669 (78.9%) | 652 (79.7%) | 1097 (75.8%) | 1135 (77.4%) |
| Uncontrolled hypertension | 50 (5.9%) | 36 (4.4%) | 69 (4.8%) | 81 (5.5%) |
| Diabetes mellitus | 279 (32.9%) | 283 (34.6%) | 475 (32.8%) | 501 (34.2%) |
| Hyperlipidemia | 581 (68.5%) | 559 (68.3%) | 961 (66.4%) | 996 (67.9%) |
| Smoking status | | | | |
| Never | 405 (47.8%) | 395/817 (48.3%) | 781/1442 (54.2%) | 843/1459 (57.8%) |
| Previous | 344 (40.6%) | 348/817 (42.6%) | 530/1442 (36.8%) | 506/1459 (34.7%) |
| Current | 99 (11.7%) | 74/817 (9.1%) | 131/1442 (9.1%) | 110/1459 (7.5%) |
| Left ventricular ejection fraction, % | 51.2 (12.3) (n=805) | 50.2 (12.4) (n=779) | 54.8 (10.7) (n=1364) | 54.6 (11.1) (n=1349) |
| Medical history | | | | |
| Peripheral vascular disease* | 117 (13.8%) | 81 (9.9%) | 126 (8.7%) | 161 (11.0%) |
| Carotid artery disease | 56 (6.6%) | 39 (4.8%) | 64 (4.4%) | 105 (7.2%) |
| Heart failure | 222 (26.2%) | 233 (28.5%) | 207 (14.3%) | 205 (14.0%) |
| Myocardial infarction | 172 (20.3%) | 169 (20.7%) | 262 (18.1%) | 261 (17.8%) |
| PCI | 241 (28.4%) | 197 (24.1%) | 353 (24.4%) | 397 (27.1%) |
| Cerebrovascular event | 124 (14.6%) | 105 (12.8%) | 144 (10.0%) | 197 (13.4%) |
| Stroke | 88 (10.4%) | 76 (9.3%) | 105 (7.3%) | 141 (9.6%) |
| Transient ischemic attack | 42 (5.0%) | 31 (3.8%) | 44 (3.0%) | 53 (3.6%) |
| Undetermined cerebrovascular event | 5 (0.6%) | 5 (0.6%) | 6 (0.4%) | 13 (0.9%) |
| Arterial thromboembolism | 15 (1.8%) | 9 (1.1%) | 16 (1.1%) | 15 (1.0%) |
| Venous thromboembolism | 83 (9.8%) | 83 (10.1%) | 41 (2.8%) | 32 (2.2%) |
| Coronary artery bypass graft surgery | 85 (10.0%) | 74 (9.0%) | 85 (5.9%) | 97 (6.6%) |
| Prosthetic mechanical heart valve | 33 (3.9%) | 47 (5.7%) | 10 (0.7%) | 11 (0.8%) |
| Aortic valve stenosis | 36/763 (4.7%) | 48/735 (6.5%) | 55/1306 (4.2%) | 56/1316 (4.3%) |
| Bleeding before/after qualifying PCI | 76 (9.0%) | 72 (8.8%) | 108 (7.5%) | 103 (7.0%) |
| Chronic pulmonary disease | 101 (11.9%) | 102 (12.5%) | 154 (10.6%) | 181 (12.3%) |
| Chronic kidney disease† | 156 (18.4%) | 156 (19.1%) | 262 (18.1%) | 302 (20.6%) |
| Liver disease | 12 (1.4%) | 14 (1.7%) | 17 (1.2%) | 18 (1.2%) |
| Atrial fibrillation | 726 (85.6%) | 677 (82.8%) | 44 (3.0%) | 43 (2.9%) |
| History of cancer | 96 (11.3%) | 101 (12.3%) | 252 (17.4%) | 250 (17.1%) |
| Active cancer | 24 (2.8%) | 24 (2.9%) | 86 (5.9%) | 102 (7.0%) |
| Hematological or coagulation disorder | 77 (9.1%) | 80 (9.8%) | 213 (14.7%) | 208 (14.2%) |
| Chronic treatment with steroids or NSAIDs | 65 (7.7%) | 76 (9.3%) | 137 (9.5%) | 163 (11.1%) |
| Prior VKA treatment | 317 (37.4%) | 290 (35.5%) | 10 (0.7%) | 9 (0.6%) |
| PRECISE-DAPT score‡ | 24.9 (11.2) | 24.7 (11.3) | 28.0 (10.6) | 27.8 (10.7) |
| Prior bleeding | 61 (7.2%) | 57 (7.0%) | 104 (7.2%) | 98 (6.7%) |

| Characteristic | Indication for OAC | | No indication for OAC | |
|---|---|---|---|---|
| | Abbrev DAPT (n=848) | Nonabbrev DAPT (n=818) | Abbrev DAPT (n=1447) | Nonabbrev DAPT (n=1466) |
| Hemoglobin, g/L | 13.6 (1.8) | 13.6 (1.7) | 13.0 (1.8) | 13.0 (1.8) |
| White blood cell count,‡ $\times 10^9$/L | 8.6 (18.0) | 8.0 (2.7) | 8.1 (4.3) | 8.1 (3.7) (n=1465) |
| Creatinine clearance,§ mL/min/1.73 m² | 71.8 (23.3) | 71.9 (23.1) | 70.1 (24.4) | 70.5 (24.7) |

Data are mean (SD), n (%), or n/n (%) in case of missing data.
Abbrev indicates abbreviated; DAPT=dual antiplatelet therapy; NSAID=nonsteroidal anti-inflammatory drug; OAC=oral anticoagulation medication; PCI=percutaneous coronary intervention; PRECISE-DAPT=predicting bleeding complications in patients undergoing stent implantation and subsequent dual antiplatelet therapy; SD=standard deviation; VKA=vitamin K antagonist.
*Defined as intermittent claudication, peripheral artery bypass for insufficiency, gangrene, acute arterial insufficiency, untreated aneurysm (≥6 cm), ankle brachial index ≤0.90, and aortic plaque.
†Defined as kidney damage (pathologic abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies) or estimated glomerular filtration rate <60 mL/min/1.73 m² for ≥3 months. ‡Calculated at screening visit; n=1 PRECISE Score calculated without risk due to white blood cell. §Modification of Diet in Renal Disease.

**Table 2.** Procedural Characteristics According to Presence or Absence of Clinical Indication for OAC

| Characteristic | Indication for OAC | | No indication for OAC | |
|---|---|---|---|---|
| | Abbreviated DAPT (n=848) | Nonabbreviated DAPT (n=818) | Abbreviated DAPT (n=1447) | Nonabbreviated DAPT (n=1466) |
| Clinical presentation* | | | | |
| Stable angina | 364 (42.9%) | 367 (44.9%) | 558 (38.6%) | 560 (38.2%) |
| Silent ischemia | 101 (11.9%) | 131 (16.0%) | 144 (10.0%) | 143 (9.8%) |
| NSTEMI | 207 (24.4%) | 168 (20.5%) | 388 (26.8%) | 390 (26.6%) |
| STEMI | 67 (7.9%) | 72 (8.8%) | 206 (14.2%) | 193 (13.2%) |
| Unstable angina | 109 (12.9%) | 80 (9.8%) | 151 (10.4%) | 180 (12.3%) |
| Clinical status* | | | | |
| Killip class II, III, or IV | 89 (10.5%) | 90 (11.0%) | 163 (11.3%) | 164 (11.2%) |
| Cardiac arrest | 9 (1.1%) | 12 (1.5%) | 17 (1.2%) | 20 (1.4%) |
| Heart rate, bpm | 76.1 (18.8) | 76.5 (18.2) | 72.0 (14.7) (n=1446) | 72.3 (15.2) (n=1462) |
| SBP, mmHg | 134.7 (24.6) (n=846) | 134.7 (24.4) (n=817) | 139.0 (26.4) (n=1443) | 138.1 (25.5) (n=1461) |
| Procedural characteristics* | | | | |
| Arterial access site | | | | |
| Femoral | 122 (14.4%) | 101 (12.3%) | 238 (16.4%) | 192 (13.1%) |
| Radial | 725 (85.5%) | 715 (87.4%) | 1205 (83.3%) | 1269 (86.6%) |
| Brachial | 1 (0.1%) | 2 (0.2%) | 4 (0.3%) | 5 (0.3%) |
| IABP | 8 (0.9%) | 8 (1.0%) | 16 (1.1%) | 22 (1.5%) |
| LVAD | 1 (0.1%) | 2 (0.2%) | 1 (0.1%) | 4 (0.3%) |
| Total amount of contrast, mL | 168.4 (78.5) (n=841) | 171.0 (81.3) (n=810) | 168.0 (81.5) (n=1434) | 164.5 (78.3) (n=1452) |
| Medications during the procedure* | | | | |
| Unfractionated heparin | 809 (95.4%) | 782 (95.6%) | 1375 (95.0%) | 1390/1465 (94.9%) |
| Bivalirudin | 3 (0.4%) | 1 (0.1%) | 2 (0.1%) | 1/1465 (0.1%) |
| LMWH | 27 (3.2%) | 26 (3.2%) | 36 (2.5%) | 38/1465 (2.6%) |
| Cangrelor | 5 (0.6%) | 2 (0.2%) | 3 (0.2%) | 1/1465 (0.1%) |
| Glycoprotein II/IIIa inhibitor | 28 (3.3%) | 21 (2.6%) | 58 (4.0%) | 55/1465 (3.8%) |
| Total number of PCI† | | | | |
| 1 | 789 (93.0%) | 757 (92.5%) | 1304 (90.1%) | 1309 (89.3%) |
| 2 | 57 (6.7%) | 60 (7.3%) | 134 (9.3%) | 154 (10.5%) |
| 3 | 2 (0.2%) | 1 (0.1%) | 9 (0.6%) | 3 (0.2%) |
| Number of vessels treated per patient* | | | | |
| 1 | 648 (76.4%) | 607 (74.2%) | 1068 (73.8%) | 1042 (71.1%) |
| 2 | 166 (19.6%) | 177 (21.6%) | 317 (21.9%) | 364 (24.8%) |
| 3 | 34 (4.0%) | 34 (4.2%) | 62 (4.3%) | 60 (4.1%) |
| Treated vessel(s) | | | | |
| Left main | 50 (5.9%) | 44 (5.4%) | 76 (5.3%) | 90 (6.1%) |
| LAD artery | 449 (52.9%) | 442 (54.0%) | 791 (54.7%) | 829 (56.5%) |

| Characteristic | Indication for OAC | | No indication for OAC | |
|---|---|---|---|---|
| | Abbreviated DAPT (n=848) | Nonabbreviated DAPT (n=818) | Abbreviated DAPT (n=1447) | Nonabbreviated DAPT (n=1466) |
| Left circumflex artery | 248 (29.2%) | 246 (30.1%) | 404 (27.9%) | 443 (30.2%) |
| Right coronary artery | 301 (35.5%) | 284 (34.7%) | 553 (38.2%) | 522 (35.6%) |
| Bypass graft | 15 (1.8%) | 19 (2.3%) | 23 (1.6%) | 19 (1.3%) |
| Number of treated lesions per patient | | | | |
| 1 | 598 (70.5%) | 561 (68.6%) | 981 (67.8%) | 975 (66.5%) |
| 2 | 182 (21.5%) | 181 (22.1%) | 321 (22.2%) | 341 (23.3%) |
| ≥3 | 68 (8.0%) | 76 (9.3%) | 145 (10.0%) | 150 (10.2%) |
| Number stented lesions per patient | | | | |
| 1 | 612 (72.2%) | 568 (69.4%) | 999 (69.0%) | 997 (68.0%) |
| 2 | 173 (20.4%) | 179 (21.9%) | 313 (21.6%) | 328 (22.4%) |
| ≥3 | 63 (7.4%) | 71 (8.7%) | 135 (9.3%) | 141 (9.6%) |
| At least one complex lesion B2 or C | 543 (64.0%) | 537 (65.6%) | 1019 (70.4%) | 1042 (71.1%) |
| Number of stents per patient | 1.7 (1.1) | 1.7 (1.1) | 1.8 (1.2) | 1.8 (1.1) |
| Total stent length per patient, mm | 37.5 (28.1) | 38.7 (28.1) | 40.3 (29.9) | 40.3 (28.6) |
| Any overlapping stenting | 172 (20.3%) | 149 (18.2%) | 316 (21.8%) | 301 (20.5%) |
| Any bifurcation or trifurcation stenting‡ | 32 (3.8%) | 41 (5.0%) | 51 (3.5%) | 60 (4.1%) |

Data are mean (SD), n (%), or n/n (%) in case of missing data.
bpm indicates beats per minute; DAPT, dual antiplatelet treatment; IABP, intra-aortic balloon pump; LAD, left anterior descending; LMWH, low-molecular-weight heparin; LVAD, left-ventricular assist device; NSTEMI, non-ST-segment elevation myocardial infarction; OAC, oral anticoagulant; PCI, percutaneous coronary intervention; SBP, systolic blood pressure; SD, standard deviation; STEMI, ST-segment elevation myocardial infarction.
*Data from first PCI only.
‡One PCI and up to two staged PCIs. The last PCI was the qualifying PCI 1 month before randomization.
†Left main counted as two vessels.

**Table 3.** Clinical Outcomes at 11 Months Post-Randomization (12-Month Follow-Up) (Intention-To-Treat Population)

| | Clinical indication for OAC | | | | | No clinical indication for OAC | | | | | $P_{interaction}$[‡] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Abbrev DAPT (n=848) | Nonabbrev DAPT (n=818) | HR[*†] (95% CI) | Com-Nougue Difference (95% CI) | Com-Nogue *P* value | Abbrev DAPT (n=1447) | Nonabbrev DAPT (n=1466) | HR[*†] (95% CI) | Com-Nougue Difference (95% CI) | Com-Nogue *P* value | |
| Coprimary composite outcome of all-cause death, myocardial infarction, stroke, bleeding BARC 3 or 5 (NACE) | 68 (8.0) | 78 (9.6) | 0.83 (0.60–1.15) | –1.57 (–4.31 to 1.16) | 0.26 | 104 (7.2) | 104 (7.1) | 1.01 (0.77–1.33) | 0.11 (–1.76 to 1.99) | 0.91 | 0.35 |
| Coprimary composite outcome of all-cause death, myocardial infarction, stroke (MACCE) | 50 (5.9) | 54 (6.7) | 0.88 (0.60–1.30) | –0.74 (–3.09 to 1.60) | 0.53 | 88 (6.1) | 84 (5.7) | 1.06 (0.79–1.44) | 0.37 (–1.35 to 2.09) | 0.67 | 0.45 |
| Coprimary composite outcome of bleeding BARC 2, 3 or 5 | 83 (9.9) | 94 (11.7) | 0.83 (0.62–1.12) | –1.75 (–4.75 to 1.25) | 0.25 | 65 (4.6) | 117 (8.1) | 0.55 (0.41–0.74) | –3.52 (–5.29 to –1.74) | <0.001 | 0.06 |
| Death | 31 (3.7) | 33 (4.1) | 0.90 (0.55–1.47) | –0.40 (–2.26 to 1.46) | 0.67 | 44 (3.1) | 48 (3.3) | 0.93 (0.62–1.40) | –0.23 (–1.50 to 1.05) | 0.73 | 0.93 |
| Cardiovascular death | 16 (1.9) | 21 (2.6) | 0.73 (0.38–1.40) | –0.70 (–2.14 to 0.74) | 0.34 | 21 (1.5) | 23 (1.6) | 0.92 (0.51–1.67) | –0.12 (–1.01 to 0.78) | 0.80 | 0.60 |
| Noncardiovascular death | 11 (1.3) | 7 (0.9) | 1.51 (0.58–3.88) | 0.44 (–0.57 to 1.45) | 0.40 | 18 (1.3) | 21 (1.5) | 0.87 (0.46–1.63) | –0.19 (–1.03 to 0.66) | 0.66 | 0.34 |
| Cerebrovascular accident | 3 (0.4) | 13 (1.6) | 0.22 (0.06–0.77) | –1.26 (–2.23 to –0.30) | 0.01 | 14 (1.0) | 19 (1.3) | 0.75 (0.37–1.49) | –0.33 (–1.12 to 0.45) | 0.40 | 0.10 |
| Stroke[§] | 2 (0.2) | 10 (1.3) | 0.19 (0.04–0.87) | –1.01 (–1.85 to –0.17) | 0.02 | 10 (0.7) | 13 (0.9) | 0.78 (0.34–1.78) | –0.20 (–0.86 to 0.45) | 0.54 | 0.11 |
| Ischemic stroke | 2 (0.2) | 9 (1.1) | 0.21 (0.05–0.99) | –0.89 (–1.69 to –0.09) | 0.03 | 9 (0.6) | 9 (0.6) | 1.01 (0.40–2.55) | 0.00 (–0.58 to 0.58) | 0.99 | 0.09 |
| Hemorrhagic stroke | 0 (0.0) | 2 (0.3) | 0.19 (0.01–3.95) | –0.25 (–0.60 to 0.10) | 0.16 | 1 (0.1) | 3 (0.2) | 0.34 (0.04–3.24) | –0.14 (–0.41 to 0.14) | 0.33 | 1.00 |
| Transient ischemic attack | 1 (0.1) | 3 (0.4) | 0.32 (0.03–3.06) | –0.25 (–0.74 to 0.24) | 0.31 | 4 (0.3) | 6 (0.4) | 0.67 (0.19–2.39) | –0.13 (–0.56 to 0.30) | 0.55 | 0.57 |
| Myocardial infarction | 19 (2.3) | 17 (2.1) | 1.07 (0.56–2.06) | 0.16 (–1.27 to 1.59) | 0.83 | 41 (2.9) | 32 (2.2) | 1.30 (0.82–2.07) | 0.66 (–0.49 to 1.82) | 0.26 | 0.64 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Late definite or probable stent thrombosis | 3 (0.4) | 4 (0.5) | 0.72 (0.16–3.21) | –0.14 (–0.78 to 0.50) | 0.66 | 11 (0.8) | 5 (0.3) | 2.23 (0.78–6.43) | 0.43 (–0.12 to 0.97) | 0.12 | 0.23 |
| Late definite stent thrombosis | 2 (0.2) | 3 (0.4) | 0.64 (0.11–3.82) | –0.14 (–0.68 to 0.41) | 0.62 | 9 (0.6) | 4 (0.3) | 2.28 (0.70–7.41) | 0.36 (–0.14 to 0.85) | 0.16 | 0.24 |
| Late probable stent thrombosis | 1 (0.1) | 1 (0.1) | 0.96 (0.06–15.32) | –0.01 (–0.35 to 0.34) | 0.98 | 2 (0.1) | 1 (0.1) | 2.03 (0.18–22.37) | 0.07 (–0.16 to 0.31) | 0.55 | 0.69 |
| Bleeding BARC classification | | | | | | | | | | | |
| Type 1 | 34 (4.1) | 47 (5.8) | 0.69 (0.44–1.07) | –1.77 (–3.87 to 0.33) | 0.10 | 31 (2.2) | 62 (4.3) | 0.50 (0.33–0.77) | –2.11 (–3.40 to –0.83) | 0.001 | 0.32 |
| Type 2 | 60 (7.2) | 65 (8.1) | 0.88 (0.62–1.24) | –0.91 (–3.48 to 1.66) | 0.49 | 42 (3.0) | 87 (6.0) | 0.48 (0.33–0.69) | –3.07 (–4.59 to –1.56) | <0.001 | 0.02 |
| Type 3 | 26 (3.1) | 33 (4.1) | 0.75 (0.45–1.26) | –0.99 (–2.80 to 0.82) | 0.28 | 27 (1.9) | 26 (1.8) | 1.05 (0.61–1.80) | 0.10 (–0.89 to 1.09) | 0.84 | 0.38 |
| Type 3a | 11 (1.3) | 18 (2.2) | 0.58 (0.28–1.24) | –0.92 (–2.21 to 0.36) | 0.16 | 15 (1.1) | 12 (0.8) | 1.26 (0.59–2.70) | 0.23 (–0.48 to 0.94) | 0.53 | 0.16 |
| Type 3b | 13 (1.6) | 12 (1.5) | 1.04 (0.47–2.27) | 0.07 (–1.12 to 1.26) | 0.91 | 8 (0.6) | 8 (0.6) | 1.01 (0.38–2.70) | 0.01 (–0.54 to 0.56) | 0.98 | 0.97 |
| Type 3c | 3 (0.4) | 3 (0.4) | 0.96 (0.19–4.75) | –0.01 (–0.60 to 0.58) | 0.97 | 4 (0.3) | 6 (0.4) | 0.67 (0.19–2.39) | –0.14 (–0.57 to 0.30) | 0.54 | 0.74 |
| Type 4 | 0 (0.0) | 0 (0.0) | | | – | 0 (0.0) | 0 (0.0) | | | – | |
| Type 5 | 1 (0.1) | 3 (0.4) | 0.32 (0.03–3.07) | –0.26 (–0.75 to 0.23) | 0.30 | 1 (0.1) | 5 (0.4) | 0.20 (0.02–1.73) | –0.27 (–0.61 to 0.06) | 0.11 | 0.77 |
| Type 5a | 0 (0.0) | 1 (0.1) | 0.32 (0.01–7.84) | –0.13 (–0.38 to 0.12) | 0.32 | 0 (0.0) | 1 (0.1) | 0.34 (0.01–8.34) | –0.07 (–0.20 to 0.07) | 0.32 | 1.00 |
| Type 5b | 1 (0.1) | 2 (0.3) | 0.48 (0.04–5.29) | –0.13 (–0.55 to 0.29) | 0.55 | 1 (0.1) | 4 (0.2) | 0.25 (0.03–2.26) | –0.21 (–0.51 to 0.10) | 0.19 | 0.70 |
| Type 3 or 5 | 27 (3.2) | 36 (4.5) | 0.71 (0.43–1.18) | –1.24 (–3.11 to 0.62) | 0.19 | 28 (2.0) | 31 (2.1) | 0.91 (0.55–1.52) | -0.17 (–1.21 to 0.87) | 0.75 | 0.50 |

Data are n (%) unless otherwise specified.
Abbrev indicates abbreviated; BARC, Bleeding Academic Research Consortium; CI, confidence interval; DAPT, dual antiplatelet treatment; HR, hazard ratio; MACCE, major adverse cardiac and cerebral events; NACE, net adverse clinical outcomes; OAC, oral anticoagulant.
*HRs (95% CIs) from Cox's time-to-first event analyses.
†Continuity corrected risk ratios (95% CIs) in case of zero events.
‡Interaction p-value testing for modifying effect of clinical indication 12 months on the HR.
§Includes undetermined strokes.

**Table 4.** Clinical Outcomes Using a Landmark Analysis at 150 Days (6-Month Visit) According to Presence or Absence of Clinical Indication for OAC (Intention-To-Treat)

| | Indication for OAC | | | | | No indication for OAC | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **Abbrev DAPT (n=848)** | **Non-abbrev DAPT (n=818)** | **HR (95% CI)*** | ***P* value** | ***P* interaction †** | **Abbrev DAPT (n=1447)** | **Non-abbrev DAPT (n=1466)** | **HR (95% CI)*** | ***P* value** | ***P* interaction†** |
| Coprimary composite outcome of all-cause death, myocardial infarction, stroke, bleeding BARC 3 or 5 (NACE) | | | | | 0.97 | | | | | 0.59 |
| 0–150 days | 35 (4.1%) | 40 (4.9%) | 0.83 (0.53–1.31) | 0.43 | | 51 (3.5%) | 55 (3.8%) | 0.94 (0.64–1.38) | 0.76 | |
| 151–335 days | 33/811 (4.1%) | 38/771 (4.9%) | 0.82 (0.52–1.31) | 0.41 | | 53/1388 (3.8%) | 49/1409 (3.5%) | 1.09 (0.74–1.61) | 0.65 | |
| Coprimary composite outcome of all-cause death, myocardial infarction, stroke (MACCE) | | | | | 0.58 | | | | | 0.66 |
| 0–150 days | 23 (2.7%) | 22 (2.7%) | 1.00 (0.56–1.80) | 0.99 | | 41 (2.9%) | 42 (2.9%) | 0.99 (0.65–1.53) | 0.98 | |
| 151–335 days | 27/823 (3.3%) | 32/789 (4.1%) | 0.80 (0.48–1.34) | 0.40 | | 47/1398 (3.4%) | 42/1422 (3.0%) | 1.14 (0.75–1.72) | 0.55 | |
| Coprimary composite outcome of bleeding BARC 2, 3, or 5 | | | | | 0.70 | | | | | 0.30 |
| 0–150 days | 56 (6.7%) | 66 (8.1%) | 0.80 (0.56–1.14) | 0.22 | | 30 (2.1%) | 64 (4.4%) | 0.47 (0.30–0.72) | 0.001 | |
| 151–335 days | 27/780 (3.5%) | 28/738 (3.8%) | 0.91 (0.53–1.54) | 0.72 | | 35/1393 (2.5%) | 53/1381 (3.9%) | 0.65 (0.42–0.99) | 0.045 | |
| Bleeding BARC 3 or 5 | | | | | 0.34 | | | | | 0.36 |
| 0–150 days | 14 (1.7%) | 23 (2.8%) | 0.58 (0.30–1.13) | 0.11 | | 12 (0.8%) | 17 (1.2%) | 0.71 (0.34–1.50) | 0.37 | |
| 151–335 days | 13/820 (1.6%) | 13/780 (1.7%) | 0.95 (0.44–2.05) | 0.90 | | 16/1410 (1.1%) | 14/1427 (1.0%) | 1.15 (0.56–2.36) | 0.70 | |
| All-cause death | | | | | 0.33 | | | | | 0.51 |
| 0–150 days | 14 (1.7%) | 11 (1.4%) | 1.22 (0.56–2.69) | 0.62 | | 18 (1.3%) | 23 (1.6%) | 0.79 (0.43–1.47) | 0.46 | |
| 151–335 days | 17/832 (2.0%) | 22/800 (2.8%) | 0.74 (0.39–1.39) | 0.35 | | 26/1421 (1.8%) | 25/1441 (1.7%) | 1.05 (0.61–1.82) | 0.86 | |
| Cerebrovascular accident | | | | | 0.52 | | | | | 0.50 |

| | Indication for OAC | | | | | No indication for OAC | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **Abbrev DAPT (n=848)** | **Non-abbrev DAPT (n=818)** | **HR (95% CI)*** | ***P* value** | ***P* interaction †** | **Abbrev DAPT (n=1447)** | **Non-abbrev DAPT (n=1466)** | **HR (95% CI)*** | ***P* value** | ***P* interaction†** |
| 0–150 days | 2 (0.2%) | 6 (0.7%) | 0.32 (0.07–1.59) | 0.16 | | 6 (0.4%) | 6 (0.4%) | 1.02 (0.33–3.15) | 0.98 | |
| 151–335 days | 1/830 (0.1%) | 7/794 (0.9%) | 0.14 (0.02–1.10) | 0.062 | | 8/1416 (0.6%) | 13/1436 (0.9%) | 0.62 (0.26–1.50) | 0.29 | |
| Myocardial infarction | | | | | 0.79 | | | | | 0.37 |
| 0–150 days | 7 (0.8%) | 7 (0.9%) | 0.96 (0.34–2.74) | 0.94 | | 20 (1.4%) | 19 (1.3%) | 1.07 (0.57–2.01) | 0.83 | |
| 151–335 days | 12/825 (1.5%) | 10/794 (1.3%) | 1.15 (0.50–2.67) | 0.74 | | 21/1402 (1.5%) | 13/1423 (0.9%) | 1.64 (0.82–3.27) | 0.16 | |
| Definite stent thrombosis | | | | – | – | | | | | – |
| 0–150 days | 0 (0.0%) | 1 (0.1%) | | | | 4 (0.3%) | 2 (0.1%) | 2.03 (0.37–11.10) | 0.41 | |
| 151–335 days | 2/832 (0.2%) | 2/799 (0.3%) | 0.96 (0.14–6.79) | 0.96 | | 5/1417 (0.4%) | 2/1439 (0.1%) | 2.53 (0.49–13.05) | 0.27 | |

Abbrev indicates abbreviated; BARC, Bleeding Academic Research Consortium; CI, confidence interval; DAPT, dual antiplatelet treatment; HR, hazard ratio; MACCE, major adverse cardiac and cerebral events; NACE, net adverse clinical outcomes; OAC, oral anticoagulant.

*HRs (95% CIs) from Cox's time-to-first event analyses, using a landmark analysis at 150 days post-randomization.

†Interaction *P* value for randomization (abbreviated vs non-abbreviated DAPT) x period (0 to 150 days vs 150 to 335 days) modifying effect.

## Figure Legends

### Figure 1. Schematic trial design

### Figure 2. Patient Flow

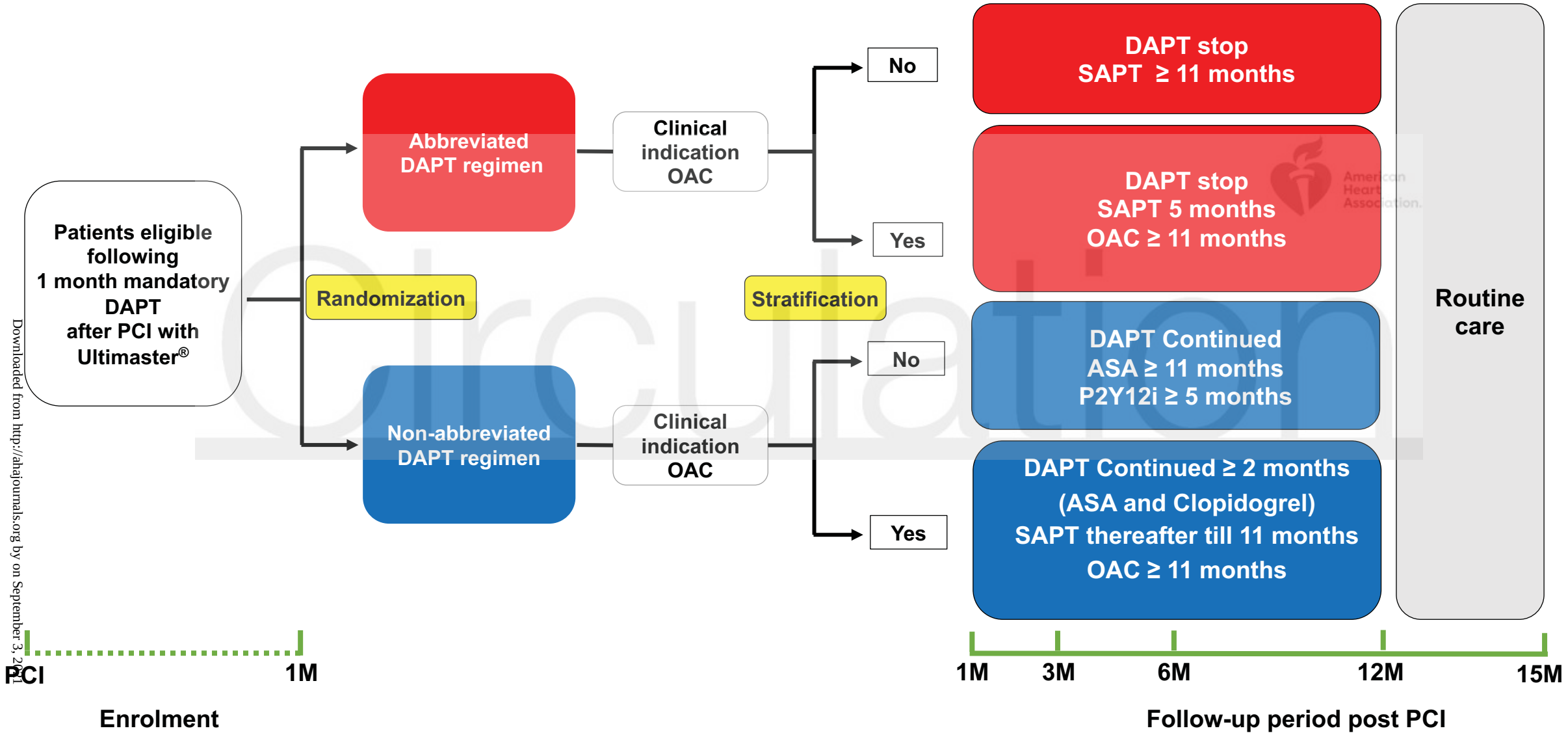
M1=1 month after index coronary stent procedure, meaning the last intended coronary stent implantation. *Did not start within 14 days of randomization, or nonpermitted alternative regimen due to event within 14 days from randomization. †At day 335 or on allowed alternative regimen due to, for example, prior events; if not recorded on exactly day 335, the last information on adherence is used.

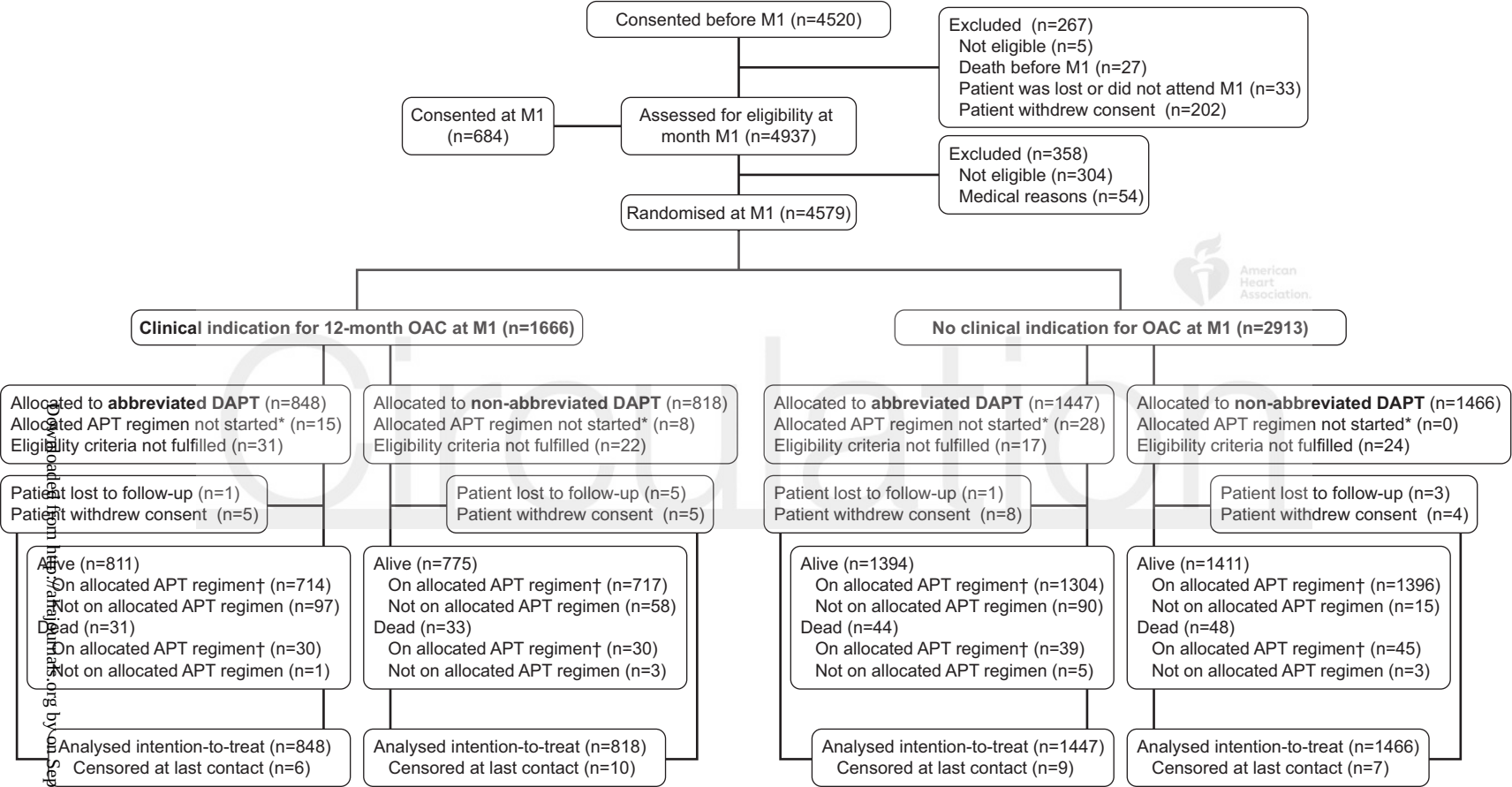


### Figure 3. Antiplatelet Use Per Day Since Randomization for Patients With and Without Oral Anticoagulation Therapy: (A) Patients With an OAC Indication on Abbreviated APT; (B) Patients With an OAC Indication on Nonabbreviated APT; (C) Patients Without an OAC Indication on Abbreviated APT; (D) Patients Without an OAC Indication on Nonabbreviated APT;.

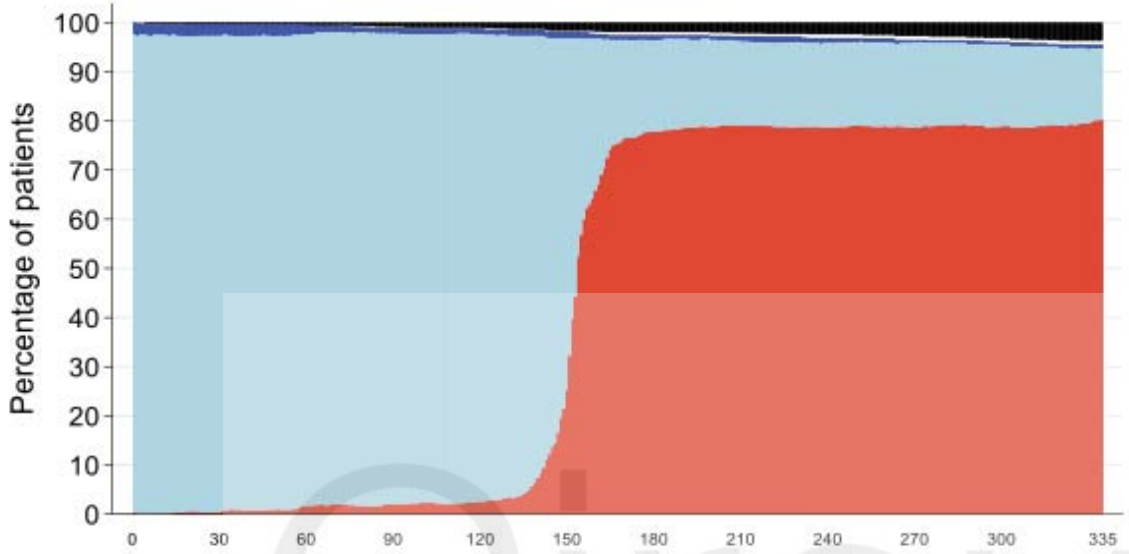
Dark blue = DAPT, light blue = SAPT, red = no APT, black = deceased, white = no information.

### Figure 4. Kaplan-Meier Curves of the three coprimary outcomes at 11 months post-randomization (12-month follow-up): (A) net adverse clinical events; (B) Major Cardiovascular Events; and (C) Major or Clinically Relevant Nonmajor Bleeding

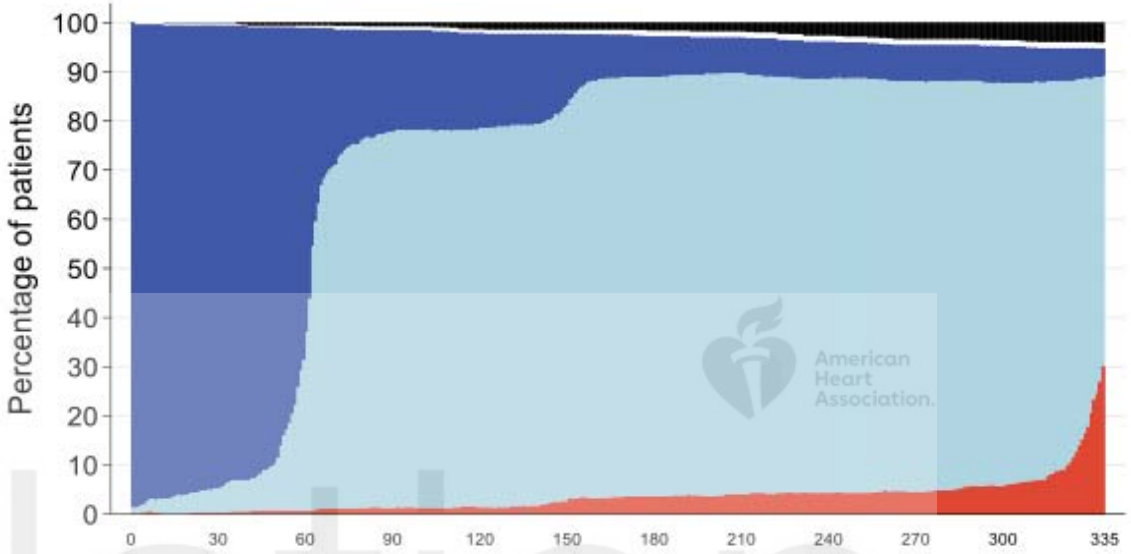




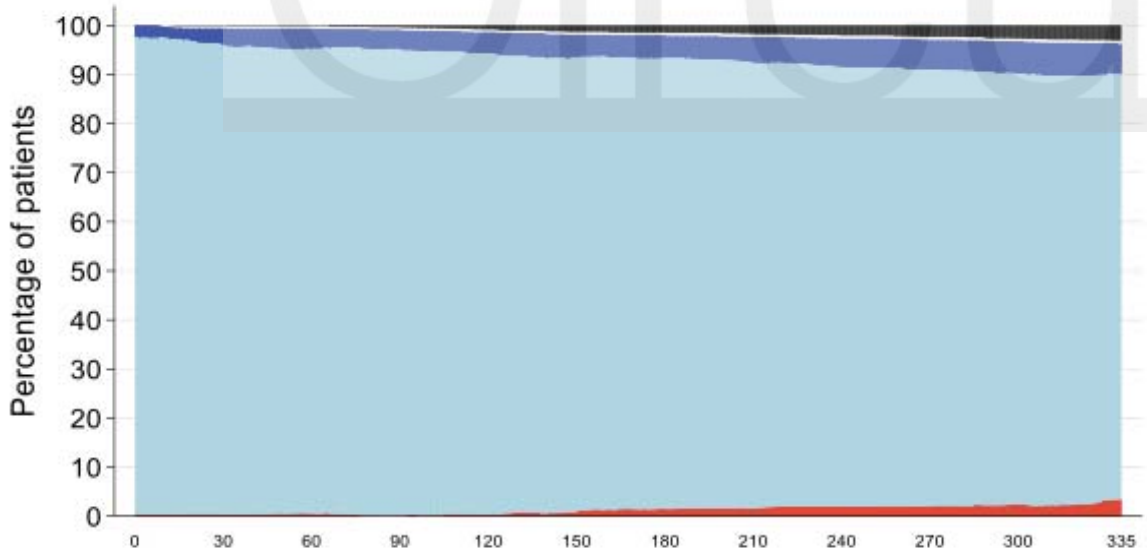
A. Abbreviated OAC subgroup



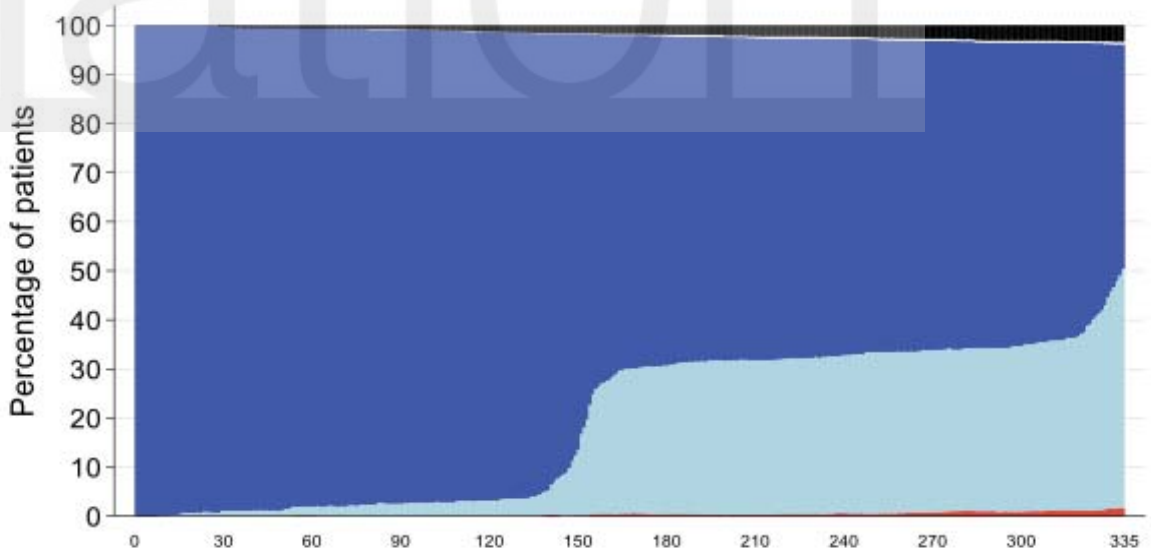

B. Nonabbreviated OAC subgroup

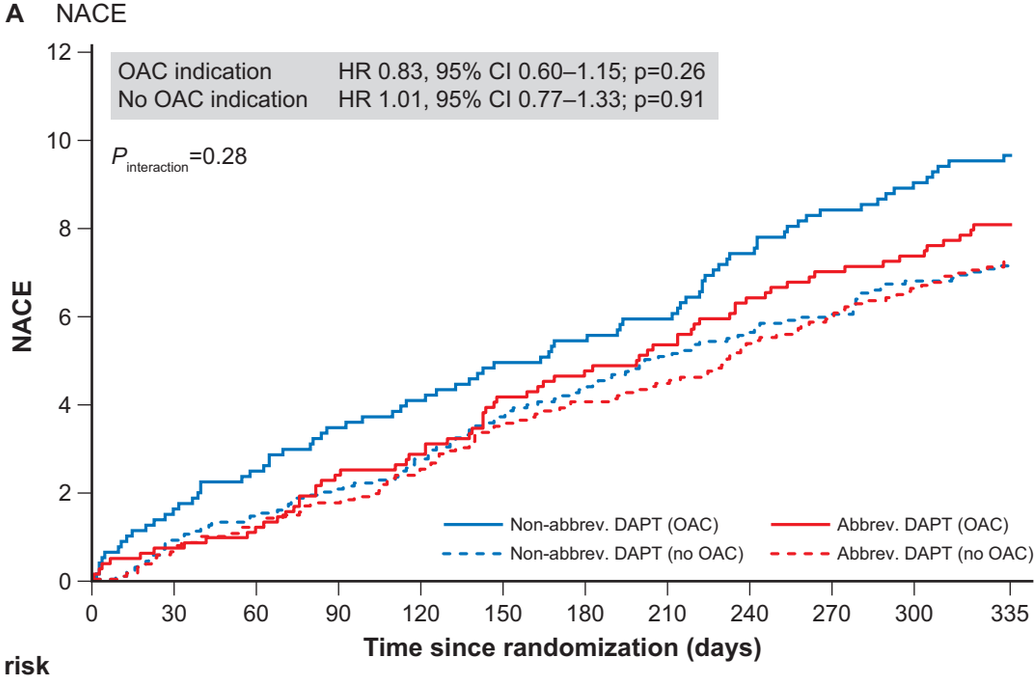



C. Abbreviated non OAC subgroup



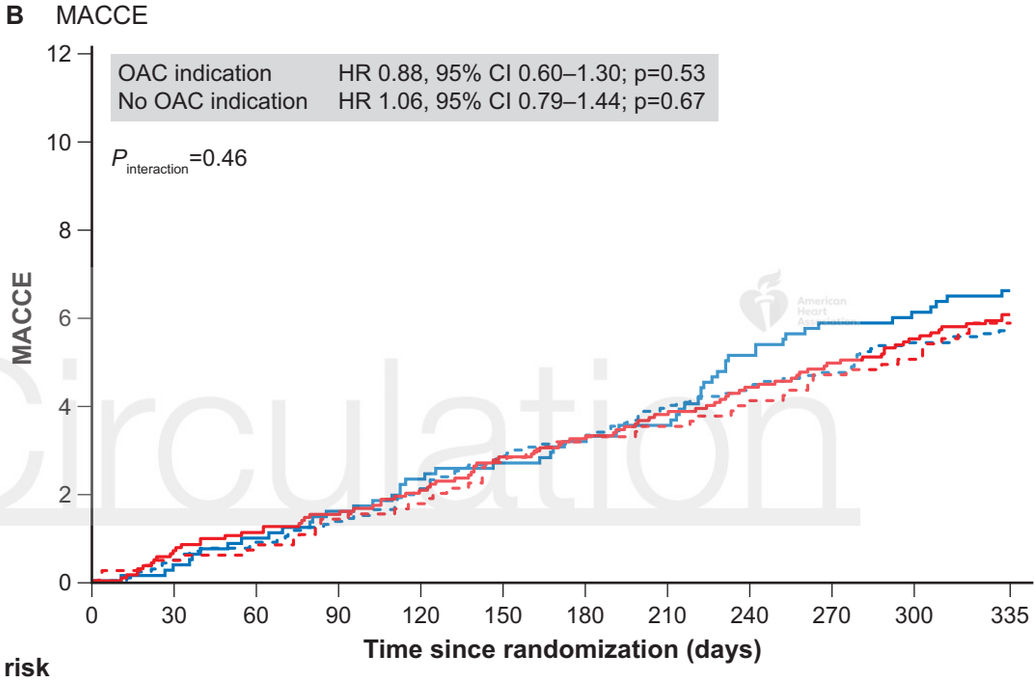

D. Nonabbreviated non OAC subgroup





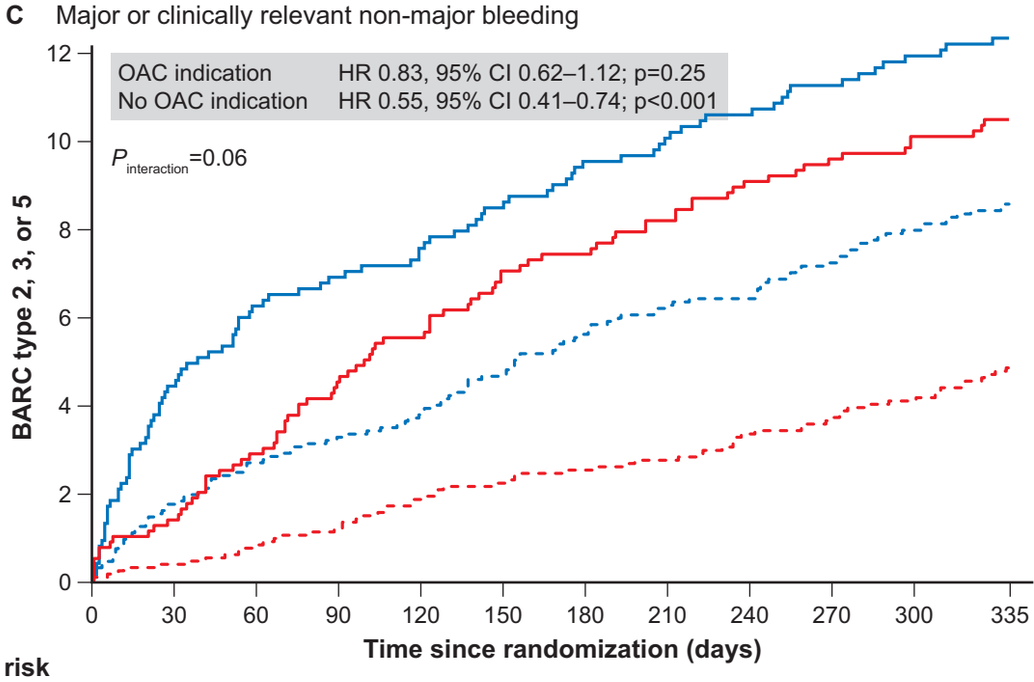

**No. at risk**

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Non-abbrev. DAPT (OAC) | 818 | 802 | 794 | 784 | 779 | 772 | 765 | 761 | 749 | 740 | 735 | 730 |
| Abbrev. DAPT (OAC) | 848 | 841 | 837 | 826 | 822 | 811 | 805 | 800 | 790 | 785 | 782 | 775 |
| Non-abbrev. DAPT (no OAC) | 1466 | 1453 | 1444 | 1435 | 1425 | 1411 | 1399 | 1387 | 1377 | 1371 | 1360 | 1354 |
| Abbrev. DAPT (no OAC) | 1447 | 1432 | 1425 | 1415 | 1404 | 1388 | 1381 | 1375 | 1362 | 1353 | 1344 | 1333 |




**No. at risk**

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Non-abbrev. DAPT (OAC) | 818 | 812 | 806 | 799 | 793 | 790 | 783 | 780 | 767 | 760 | 758 | 754 |
| Abbrev. DAPT (OAC) | 848 | 843 | 840 | 834 | 831 | 823 | 817 | 815 | 809 | 804 | 801 | 792 |
| Non-abbrev. DAPT (no OAC) | 1466 | 1459 | 1453 | 1445 | 1434 | 1424 | 1415 | 1403 | 1394 | 1389 | 1379 | 1374 |
| Abbrev. DAPT (no OAC) | 1447 | 1432 | 1426 | 1418 | 1410 | 1398 | 1392 | 1384 | 1375 | 1367 | 1359 | 1349 |




**No. at risk**

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Non-abbrev. DAPT (OAC) | 818 | 780 | 764 | 755 | 748 | 740 | 729 | 724 | 715 | 704 | 698 | 693 |
| Abbrev. DAPT (OAC) | 848 | 834 | 821 | 804 | 796 | 780 | 774 | 768 | 759 | 754 | 748 | 740 |
| Non-abbrev. DAPT (no OAC) | 1466 | 1440 | 1422 | 1411 | 1399 | 1382 | 1365 | 1353 | 1345 | 1331 | 1317 | 1306 |
| Abbrev. DAPT (no OAC) | 1447 | 1435 | 1428 | 1419 | 1406 | 1393 | 1387 | 1382 | 1371 | 1363 | 1354 | 1338 |