JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 77, NO. 5, 2021

EXPERT CONSENSUS DECISION PATHWAY

2020 ACC Expert Consensus Decision Pathway for Anticoagulant and Antiplatelet Therapy in Patients With Atrial Fibrillation or Venous Thromboembolism Undergoing Percutaneous Coronary Intervention or With Atherosclerotic Cardiovascular Disease

A Report of the American College of Cardiology Solution Set Oversight Committee

Writing Committee

Dharam J. Kumbhani, MD, SM, FACC, *Chair*
Christopher P. Cannon, MD, FACC, *Vice-Chair*
Craig J. Beavers, PharmD, FACC
Deepak L. Bhatt, MD, MPH, FACC
Adam Cuker, MD, MS
Ty J. Gluckman, MD, FACC
Joseph E. Marine, MD, FACC
Roxana Mehran, MD, FACC
Steven R. Messe, MD
Nimesh S. Patel, MD
Benjamin E. Peterson, MD, MPH
Kenneth Rosenfield, MD, FACC
Sarah A. Spinler, PharmD, AACC
Vinod H. Thourani, MD, FACC

Solution Set Oversight Committee

Ty J. Gluckman, MD, FACC, *Chair*
Niti R. Aggarwal, MD, FACC
Nicole M. Bhave, MD, FACC
Gregory J. Dehmer, MD, MACC
Olivia N. Gilbert, MD, MSc, FACC
Chayakrit Krittanawong, MD
Dharam J. Kumbhani, MD, SM, FACC
Andrea L. Price, CPHQ, RCIS, AACC
Javier A. Sala-Mercado, MD, PhD
David E. Winchester, MD, MS, FACC
Martha Gulati, MD, MS, FACC—Ex Officio

This document was approved by the American College of Cardiology Clinical Policy Approval Committee in September 2020.

The American College of Cardiology requests that this document be cited as follows: Kumbhani DJ, Cannon CP, Beavers CJ, Bhatt DL, Cuker A, Gluckman TJ, Marine JE, Mehran R, Messe SR, Patel N, Peterson BE, Rosenfield K, Spinler SA, Thourani VH. 2020 ACC expert consensus decision pathway for anticoagulant and antiplatelet therapy in patients with atrial fibrillation or venous thromboembolism undergoing percutaneous coronary intervention or with atherosclerotic cardiovascular disease: a report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol 2021;77:629-58.

Copies: This document is available on the website of the American College of Cardiology (www.acc.org). For copies of this document, please contact Elsevier Inc. Reprint Department via fax (212) 633-3820 or e-mail (reprints@elsevier.com).

ISSN 0735-1097/$36.00 https://doi.org/10.1016/j.jacc.2020.09.011

TABLE OF CONTENTS

PREFACE

The American College of Cardiology (ACC) has a long history of developing documents (e.g., decision pathways, health policy statements, appropriate use criteria) to provide members with guidance on both clinical and nonclinical topics relevant to cardiovascular care. In most circumstances, these documents have been created to complement clinical practice guidelines and to inform clinicians about areas where evidence may be new and evolving or where sufficient data may be more limited. Despite this, numerous care gaps continue to exist, highlighting the need for more streamlined and efficient processes to implement best practices in service to improved patient care.

Central to the ACC's strategic plan is the generation of "actionable knowledge"—a concept that places emphasis on making clinical information easier to consume, share, integrate, and update. To this end, the ACC has evolved from developing isolated documents to the development of integrated "solution sets." Solution sets are groups of closely related activities, policy, mobile applications, decision support, and other tools necessary to transform care and/or improve heart health. Solution sets address

key questions facing care teams and attempt to provide practical guidance to be applied at the point of care. They use both established and emerging methods to disseminate information for cardiovascular conditions and their related management. The success of the solution sets rests firmly on their ability to have a measurable impact on the delivery of care. Because solution sets reflect current evidence and ongoing gaps in care, the associated content will be refined over time to best match changing evidence and member needs.

Expert consensus decision pathways (ECDPs) represent a key component of solution sets. The methodology for ECDPs is grounded in assembling a group of clinical experts to develop content that addresses key questions facing our members across a range of high-value clinical topics (1). This content is used to inform the development of various tools that accelerate real-time use of clinical policy at the point of care. They are not intended to provide a single correct answer; rather, they encourage clinicians to ask questions and consider important factors as they define treatment plans for their patients. Whenever appropriate, ECDPs seek to provide unified articulation of clinical practice guidelines, appropriate use criteria, and other related ACC clinical policy. In some cases, covered topics will be addressed in subsequent clinical practice guidelines as the evidence base evolves. In other cases, these will serve as stand-alone policy.

Ty J. Gluckman, MD, FACC
Chair, ACC Solution Set Oversight Committee

1. INTRODUCTION

Current estimates suggest that approximately one in four individuals will develop atrial fibrillation (AF) during their lifetime (2,3). AF increases the risk of stroke 4- to 5-fold and accounts for 15% to 20% of ischemic strokes (4–6). In addition, strokes associated with AF tend to be more severe, with higher rates of death and severe disability (6,7). For the vast majority of patients with AF, treatment with oral anticoagulant (OAC) therapy is associated with significantly lower stroke rates compared with aspirin or placebo (8–10). Accordingly, current AF guidelines provide strong support for use of OACs, particularly in those at higher stroke risk, such as those individuals with a high CHA_2DS_2-VASc score, presence of certain valvular lesions (e.g., mitral stenosis), or other predisposing factors (11).

Coronary artery disease (CAD) is a common comorbidity in patients with AF, occurring in roughly 25% to 35% of this population (12–15). This percentage is due, in large part, to the multiple shared risk factors of both conditions (e.g., obesity, hypertension, diabetes mellitus). It is estimated that patients on a chronic OAC with CAD are 7 times more likely to have a separate indication for concomitant antiplatelet therapy (APT) than those without CAD (16). In addition, approximately 10% of patients with recent percutaneous coronary intervention (PCI) have concomitant AF (17,18).

Similar to AF, venous thromboembolism (VTE), including deep venous thrombosis and pulmonary embolism, is quite common, with an overall incidence estimated to be 1 to 2 per 1,000 person-years (19). VTE is usually treated with anticoagulant (AC) therapy as well. The drug used and length of treatment depend on the presence or absence of a provoking factor and whether or not the provoking factor is transient (e.g., surgery, pregnancy) or if a chronic condition is present (e.g., cancer, thrombophilia, chronic immobility, or obesity) (20–22). There may similarly be a pathophysiological link between VTE and CAD, and a concomitant indication for APT may exist in both patient populations (23–25).

Choosing the optimal antithrombotic regimen for patients needing an AC and APT can be a challenge for practicing clinicians. Patients with either AF or VTE undergoing PCI have historically been treated with an AC and dual antiplatelet therapy (DAPT) (aspirin and a $P2Y_{12}$ inhibitor [$P2Y_{12}$i])—so called “triple therapy.” Support for this practice came from older trials that suggested that an OAC alone was not an optimal treatment for those undergoing PCI and, similarly, that DAPT was not an optimal treatment for AF or VTE (10,17,26).

Triple antithrombotic therapy, however, significantly increases the risk of bleeding. In fact, it is estimated that the addition of single APT to an OAC increases the risk of bleeding ≥20% to 60% and the addition of DAPT to an OAC further increases the risk 2- to 3-fold (27–33). In absolute numbers, the risk of major bleeding with triple antithrombotic therapy can be as high as 2.2% at 1 month and 4% to 12% at 1 year (34–36). Because major bleeding is associated with an up to 5-fold increased risk of death following an acute coronary syndrome (ACS) (37,38), it is important to identify the optimal antithrombotic therapy for patients with atherosclerotic cardiovascular disease (ASCVD) (39) and concomitant AF or VTE requiring an AC (ASCVD is defined as stroke, transient ischemic attack [TIA], documented CAD with stable angina, ACS, coronary or other arterial revascularization, peripheral vascular disease with or without claudication, and aortic aneurysm) (39). Regardless of the underlying indication for antithrombotic therapy, the ultimate goal is the same—preserving antithrombotic efficacy while mitigating bleeding. Accordingly, the intent of this ECDP is to provide guidance and recommendations regarding the optimal antithrombotic therapy regimen in this patient population.

2. METHODS

The clinical scenarios in this document assume that a given patient has a pre-existing condition dictating the need for AC therapy (AF, VTE) and subsequently develops another condition requiring additional antithrombotic therapy (e.g., CAD with the need for PCI) or, conversely, that the patient is on APT for ASCVD, and subsequently develops AF or VTE, requiring the addition of an AC. Accordingly, the document is divided into 4 sections:

1. A patient with AF receiving an OAC who now needs PCI and APT
2. A patient on APT for ASCVD with new-onset AF requiring an OAC
3. A patient with prior VTE receiving an AC who now needs PCI and APT
4. A patient on APT for ASCVD with a new VTE requiring an AC

Two Heart House Roundtables, which involved multiple stakeholders and focused on this topic, were held in Washington, DC, in 2016 and 2017 and informed many of the discussion points in this document. Additional evidence from pivotal clinical trials and meta-analyses assessing the optimal type and duration of antithrombotic therapy was collated and, where necessary, supplemented by "best practice" recommendations (29,40,41). Because trial data available for patients with VTE are more limited, it is acknowledged that many of the recommendations in this population are extrapolated from trials in patients with AF.

The work of the Writing Committee was supported exclusively by the ACC without commercial support. Writing Committee members volunteered their time to this effort. Conference calls with the Writing Committee were confidential and attended only by committee members and ACC staff. A formal peer review process was completed, consistent with ACC policy, and included expert reviewers nominated by the ACC. A public comment period was also held to obtain further feedback. Following reconciliation of all comments, this document was approved for publication by the Clinical Policy Approval Committee.

The ACC and the Solution Set Oversight Committee (SSOC) recognize the importance of avoiding real or perceived RWI or other entities that may affect clinical policy. The ACC maintains a database that tracks all relevant relationships for ACC members and persons who participate in ACC activities, including those involved in the development of ECDPs. ECDPs follow ACC RWI Policy in determining what constitutes a relevant relationship, with additional vetting by the SSOC.

ECDP writing groups must be chaired or co-chaired by an individual with no relevant RWI. Although vice chairs and writing group members may have relevant RWI, this must constitute less than 50% of the writing group. Relevant disclosures for the writing group and external reviewers can be found in Appendixes 1 and 2. To ensure complete transparency, a full list of disclosure information, including relationships not pertinent to this document, is available in Supplemental Appendix 1. Participants are discouraged from acquiring relevant RWI throughout the writing process.

3. ASSUMPTIONS AND DEFINITIONS

To limit inconsistencies in interpretation, specific assumptions and definitions were considered by the Writing Committee in the development of this document.

3.1. General Clinical Assumptions and Considerations

1. For the purpose of this document, the underlying assumption is that the patient has an indication for both an AC and APT and is deemed to be suitable for the use of both types of antithrombotic therapy together.
2. Patients with VTE have been under-represented in clinical trials comparing outcomes with an AC and APT. Given that the vast majority of the existing literature is on patients with AF undergoing PCI, we have used these results to extrapolate to the VTE population, with inclusion of VTE-specific recommendations related to dosage.
3. Recommendations for patients with AF relate specifically to those with nonvalvular AF and should not be extrapolated to those with valvular AF (a controversial term in itself but most commonly defined as AF associated with moderate to severe mitral stenosis, most frequently rheumatic, or with mechanical heart valves) (42).
4. Certain recommendations may not be applicable in all patients with VTE, such as patients with triple-positive antiphospholipid syndrome, because at least 1 of the direct oral anticoagulants (DOACs) was noted to be inferior to vitamin K antagonists (VKAs) for this indication (43,44).
5. Recommendations for other patient subsets, particularly those excluded from the trials, may not be applicable. This includes patients with prosthetic heart valves (both mechanical and bioprosthetic), recent or ongoing bleeding, known bleeding diatheses, or severe renal insufficiency (estimated creatinine clearance $<$30 ml/min; specific for DOACs, not VKAs).
6. This pathway does not include recommendations utilizing low-dose (referred to as "vascular-dose")

DOACs for secondary cardiovascular prevention, as were studied in the ATLAS-ACS TIMI 51 trial (Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects With Acute Coronary Syndromes–Thrombolysis In Myocardial Infarction 51) and COMPASS trial (Cardiovascular Outcomes for People Using Anticoagulation Strategies); in those trials, there was no other indication for the use of an OAC (25,45).

7. Although this pathway does consider other manifestations of clinical ASCVD beyond PCI for which APT may be recommended, APT can usually be discontinued when AC therapy is initiated.
8. For patients with CAD undergoing PCI, this pathway is disproportionately focused on APT following implantation of a drug-eluting stent (DES). Bare metal stents are no longer the preferred choice, even in high bleeding-risk patients (35,46,47). The choice of DES should take into account the available data regarding individual stent performance with shorter duration of DAPT (48,49).
9. For patients who do receive either a bare metal stent or balloon angioplasty alone, shorter durations of DAPT (≤1 month) are feasible in the setting of stable ischemic heart disease (SIHD); for those receiving PCI in the setting of ACS, the duration of DAPT is the same, irrespective of the type of stent used (according to the 2016 ACC/American Heart Association [AHA] Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease) (50).
10. Although risk scores may be helpful in stratifying patients according to thromboembolic and bleeding risk, these risks frequently overlap and vary over time. These issues highlight the limitations of a generalized approach to treatment (51,52).

3.2. AC and APT Definitions

- AC refers to any anticoagulant in oral or parenteral form.
- APT refers to antiplatelet therapy.
- DAPT refers to dual antiplatelet therapy, most commonly in the form of aspirin and a $P2Y_{12}$i, such as clopidogrel, prasugrel, or ticagrelor.
- DOAC refers to any direct oral anticoagulant. For the sake of this document, the DOACs for consideration are apixaban, dabigatran, edoxaban, or rivaroxaban. Other related terms (although not used in this pathway) include novel oral anticoagulant (NOAC), non-VKA OAC, or target-specific OAC.
- OAC refers to oral anticoagulant therapy, most commonly in the form of a DOAC or VKA.
- SAPT refers to single antiplatelet therapy, most commonly in the form of aspirin or a $P2Y_{12}$i.
- Triple therapy refers to the simultaneous use of aspirin, a $P2Y_{12}$i, and an AC.
- Antithrombotic refers to use of APT and/or AC therapy.

4. PATHWAY SUMMARY GRAPHIC

Figure 1 Provides an overview of what is covered in the ECDP. See each section for more detailed considerations and guidance.

5. DESCRIPTION, RATIONALE, AND IMPLICATION OF PATHWAY

For patients with long-term indications for both an AC and APT, there exists an important need to reduce ischemic/thrombotic events without incurring increased bleeding risk. One approach has been to use triple antithrombotic therapy but with a significantly shorter $P2Y_{12}$i duration. In the ISAR-TRIPLE trial (Triple Therapy in Patients on Oral Anticoagulation After Drug Eluting Stent Implantation), 614 patients on OAC therapy undergoing PCI with a DES were randomized to 6 weeks versus 6 months of clopidogrel on a background of continued treatment with aspirin and OAC therapy (53). Although patients treated with a shortened duration of clopidogrel experienced no significant difference in the rate of ischemic events (hazard ratio: 0.93; 95% CI: 0.43 to 2.05), there was no reduction in the rate of Thrombolysis In Myocardial Infarction major bleeding (hazard ratio: 1.35; 95% CI: 0.64 to 2.84). An alternative approach for patients with indications for both AC therapy and APT has been continued use of an AC and $P2Y_{12}$i (dual antithrombotic therapy), with discontinuation of aspirin at discharge or soon after. This approach has been evaluated in multiple randomized trials that have demonstrated either no significant difference or noninferiority for ischemic endpoints but superior safety compared with triple antithrombotic therapy (**Table 1**) (none of the trials were individually powered for efficacy/thrombotic events).

The decision pathway algorithms created by the Writing Committee are outlined in the following text and reflect the 4 clinical scenarios discussed earlier. The following general principles apply to all sections from here on within this ECDP:

1. Overall, we recommend *against* the routine use of triple antithrombotic therapy for most patients. Accordingly, for patients requiring both an AC and APT, we strongly recommend that the default strategy after recent PCI be dual antithrombotic therapy consisting of an AC and a $P2Y_{12}$i.
2. When triple antithrombotic therapy is to be utilized, we recommend that it be done for a limited duration (shortest period possible) in patients at high thrombotic risk. For instance, if the patient is perceived to

FIGURE 1 Summary Graphic

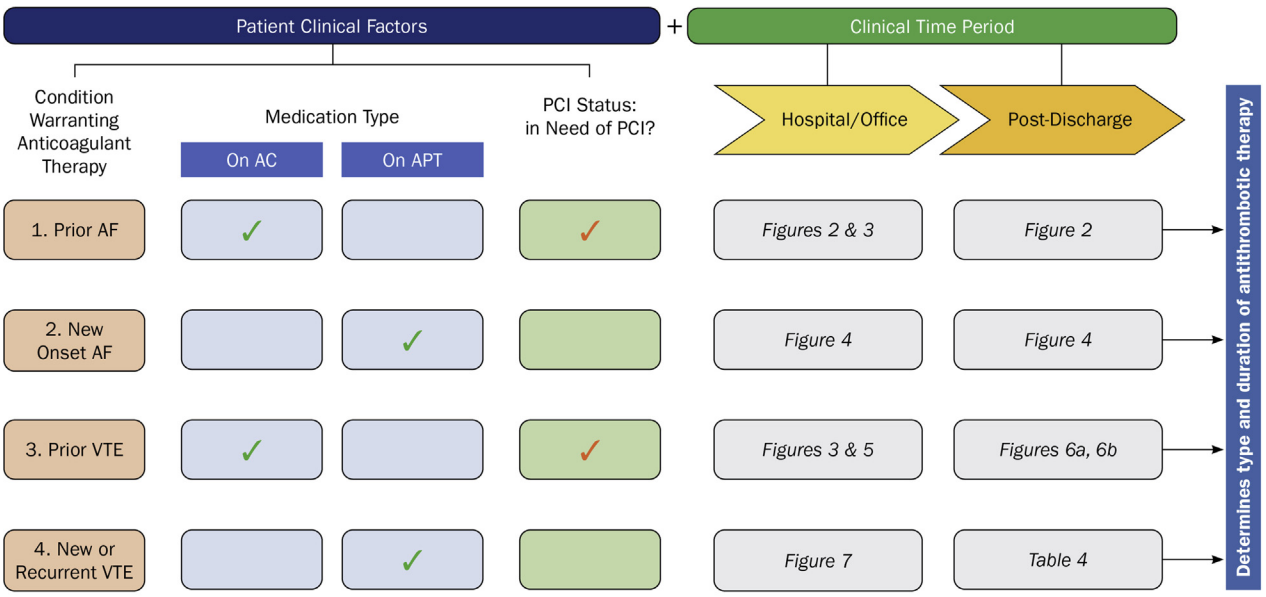


Illustration showing the four scenarios depicted in the pathway and how previous AC therapy and APT, PCI status, and clinical time period determine the type and duration of antithrombotic therapy. The illustration also shows the figures that correspond to each treatment pathway.

AC = anticoagulant; AF = atrial fibrillation; APT = antiplatelet therapy; OAC = oral anticoagulant; PCI = percutaneous coronary intervention; VTE = venous thromboembolism.

be at particularly high risk for coronary thrombosis and bleeding risk is judged to be low, aspirin may be added to a $P2Y_{12}$i and an AC for up to 30 days following PCI (54).

3. In the setting of recent PCI (≤6 months for SIHD, ≤12 months for ACS), the preferred APT is a $P2Y_{12}$i.
4. Consistent with other documents on this topic (55,56), we recommend clopidogrel over other, more potent $P2Y_{12}$is and DOACs over VKAs when combination antithrombotic therapy is needed. Although platelet function and genotype testing for clopidogrel-treated patients has been explored, no clear thrombotic benefit has been identified for routine use and it will not be discussed further in this document (57-60).
5. When aspirin is used in combination with an AC, the daily dose should not exceed 100 mg.
6. If indefinite AC therapy is not indicated, the duration of APT should follow the most recent 2016 ACC/AHA DAPT guidelines once combination antithrombotic therapy is no longer needed (50,61).
7. For patients requiring indefinite AC therapy, we recommend that APT be continued for 1 year post-PCI, as the safety and efficacy of an AC alone after a short duration of APT has not been tested. As an example, if a patient requiring indefinite AC therapy undergoes PCI for SIHD, clopidogrel would be used for 6 months post-PCI (consistent with the 2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease) (50). Beyond this period, SAPT with either aspirin or clopidogrel should be continued for an additional 6 months, along with the AC. Thereafter, AC therapy alone could be used long-term. Recent data from the AFIRE (Atrial Fibrillation and Ischemic events with Rivaroxaban in Patients With Stable Coronary Artery Disease Study) and OAC-ALONE trials (Optimizing Antithrombotic Care in Patients With AtriaL fibrillatiON and Coronary stEnt) provide support for use of an OAC alone among patients with stable CAD who need long-term anticoagulation (62,63). At the same time, if perceived thrombotic risk is high (e.g., prior myocardial infarction, complex lesions, presence of select traditional cardiovascular risk factors, or extensive ASCVD), and the patient is at low bleeding risk, it is reasonable to continue SAPT beyond 12 months (in line with prior ACC/AHA recommendations) (64).

TABLE 1 Randomized Trials of Dual Versus Triple Therapy for AF and PCI (29–33)

Trial Name	WOEST	PIONEER AF-PCI	RE-DUAL PCI	AUGUSTUS	ENTRUST-AF PCI
Patients enrolled	n = 573	n = 2,124	n = 2,725	n = 4,614	n = 1,506
Trial design	Open-label, Randomized	Open-label, Randomized	Open-label, Randomized	2 × 2 factorial randomized*	Open-label, Randomized
Treatment arms	Group 1: VKA (INR per indication) + $P2Y_{12}$i vs. Group 2: VKA (INR 2.0) + aspirin + $P2Y_{12}$i	Group 1: Rivaroxaban (15 mg daily) + $P2Y_{12}$i vs. Group 2: Rivaroxaban (2.5 mg twice daily) + aspirin + $P2Y_{12}$i vs. Group 3: VKA (INR 2–3) + aspirin + $P2Y_{12}$i†	Group 1: Dabigatran (110 mg twice daily) + $P2Y_{12}$i vs. Group 2: Dabigatran (150 mg twice daily) + $P2Y_{12}$i vs. Group 3: VKA (INR 2–3) + aspirin (1–3 months) + $P2Y_{12}$i	Group 1: Apixaban (5 mg twice daily) + $P2Y_{12}$i vs. Group 2: Apixaban (5 mg twice daily) + aspirin + $P2Y_{12}$i vs. Group 3: VKA (INR 2–3) + $P2Y_{12}$i vs. Group 4: VKA (INR 2–3) + aspirin + $P2Y_{12}$i‡	Group 1: Edoxaban (60 mg daily) + $P2Y_{12}$i vs. Group 2: VKA (INR 2–3) + aspirin (1–12 months) + $P2Y_{12}$i§
Predominant $P2Y_{12}$i	Clopidogrel	Clopidogrel	Clopidogrel	Clopidogrel	Clopidogrel
Duration of ASA use in dual therapy arm	4 hours	72 hours	1.6 days	7 days	5 days
Follow-up	12 months	12 months	14 months	6 months	12 months
Indication for OAC therapy	AF (69%) Mechanical valve (10%)	AF (100%)	AF (100%)	AF (100%)	AF (100%)
Indication for APT	PCI for ACS (≈28%) PCI for SIHD (≈72%)	PCI for ACS (≈50%) PCI for SIHD (≈49%)	PCI for ACS (≈50%) PCI for SIHD (≈50%)	PCI for ACS (≈37%) PCI for SIHD (≈39%) Medical treatment for ACS (≈24%)	PCI for ACS (≈52%) PCI for SIHD (≈48%)
Primary outcome	Any bleeding	Clinically significant bleeding	Major bleeding or clinically relevant nonmajor bleeding	Major bleeding or clinically relevant nonmajor bleeding	Major bleeding or clinically relevant nonmajor bleeding
Primary outcome event rate(s), (HR; 95% CI)	19.4% vs. 44.4%; (0.36; 0.26–0.50)	Group 1 vs. 3 16.8% vs. 26.7%; (0.59; 0.47–0.76) Group 2 vs. 3 18.0% vs. 26.7%; (0.63; 0.50–0.80)	Dabigatran 110 mg twice daily vs. WTT 15.4% vs. 26.9%; (0.52; 0.42–0.63) Dabigatran 150 mg twice daily vs. WTT 20.2% vs. 25.7%; (0.72; 0.58–0.88)	Apixaban vs. VKA 10.5% vs. 14.7%; (0.69; 0.58–0.81) Aspirin vs. placebo 16.1% vs. 9.0%; (1.89; 1.59–2.24)	17.0% vs. 20%; (0.83; 0.65–1.05)
Primary ischemic/ thrombotic endpoint	Death, MI, stroke, target vessel revascularization, and stent thrombosis	Death from cardiovascular causes, MI, or stroke	Death, Thromboembolic events (MI, stroke, or systemic embolism), or unplanned revascularization	Death or ischemic event (stroke, MI, stent thrombosis, or urgent revascularization)	Cardiovascular death, stroke, systemic embolic event, MI, or definite stent thrombosis
Event rate for primary ischemic/ thrombotic endpoint (HR; 95% CI)	11.1% vs. 17.6%; (0.60; 0.38–0.94)	Group 1 vs. 3 6.5% vs. 6.0%; (1.08; 0.69–1.68) Group 2 vs. 3 5.6% vs. 6.0%; (0.93; 0.59–1.48)	Dabigatran 110 mg twice daily vs. WTT 15.2% vs. 13.4%; (1.13; 0.90–1.43) Dabigatran 150 mg twice daily vs. WTT 11.8% vs. 12.8%; (0.89; 0.67–1.19)	Apixaban vs. VKA 6.7% vs. 7.1%; (0.93; 0.75–1.16) Aspirin vs. placebo 6.5% vs. 7.3%; (0.89; 0.71–1.11)	7% vs. 6%; (1.06; 0.71–1.69)
TIMI major bleeding (HR; 95% CI)	3.2% vs. 5.6%; (0.56; 0.25–1.27)	Group 1 vs. 3 2.1% vs. 3.3%; (0.66; 0.33–1.31) Group 2 vs. 3 1.9% vs. 3.3%; (0.57; 0.28–1.16)	Dabigatran 110 mg twice daily vs. WTT 1.4% vs. 3.8%; (0.37; 0.20–0.68) Dabigatran 150 mg twice daily vs. WTT 2.1% vs. 3.9%; (0.51; 0.28–0.93)	Apixaban vs. VKA 1.7% vs. 2.1%; (0.78; 0.51–1.20) Aspirin vs. placebo 2.4% vs. 1.3%; (1.93; 1.23–3.03)	2.0% vs. 3.2%; (0.62; 0.33–1.19)
Stroke (HR; 95% CI)	1.1% vs. 2.8%; (0.37; 0.10–1.40)	Group 1 vs. 3 1.3% vs. 1.2% (1.07; 0.39–2.96) Group 2 vs. 3 1.5% vs. 1.2%; (1.36; 0.52–3.58)	Dabigatran 110 mg twice daily vs. WTT 1.7% vs. 1.3%; (1.30; 0.63–2.67) Dabigatran 150 mg twice daily vs. WTT 1.2% vs. 1.0%; (1.09; 0.42–2.83)	Apixaban vs. VKA 0.6% vs. 1.1%; (0.50; 0.26–0.97) Aspirin vs. placebo 0.9% vs. 0.8%; (1.06; 0.56–1.98)	1.3% vs. 1.6%; (0.84; 0.36–1.95)
Myocardial infarction (HR; 95% CI)	3.2% vs. 4.6%; (0.69; 0.29–1.60)	Group 1 vs. 3 3.0% vs. 3.5%; (0.86; 0.46–1.59) Group 2 vs. 3 2.7% vs. 3.5%; (0.75; 0.40–1.42)	Dabigatran 110 mg twice daily vs. 4.5% vs. 3.0%; (1.51; 0.94–2.41) Dabigatran 150 mg twice daily vs. WTT 3.4% vs. 2.9%; (1.16; 0.66–2.04)	Apixaban vs. VKA 3.1% vs. 3.5%; (0.89; 0.65–1.23) Aspirin vs. placebo 2.9% vs. 3.6%; (0.81; 0.59–1.12)	3.9% vs. 3.0%; (1.26; 0.73–2.17)

Continued on the next page

TABLE 1 Continued

Trial Name	WOEST	PIONEER AF-PCI	RE-DUAL PCI	AUGUSTUS	ENTRUST-AF PCI
Stent thrombosis (HR; 95% CI)	1.4% vs. 3.2%; (0.44; 0.14–1.44)	Group 1 vs. 3 0.8% vs. 0.7%; (1.20; 0.32–4.45) Group 2 vs. 3 0.9% vs. 0.7%; (1.44; 0.40–5.09)	Dabigatran 110 mg twice daily vs. WTT 1.5% vs. 0.8%; (1.86; 0.79–4.40) Dabigatran 150 mg twice daily vs. WTT 0.9% vs. 0.9%; (0.99; 0.35–2.81)	Apixaban vs. VKA 0.6% vs. 0.8%; (0.77; 0.38–1.56) Aspirin vs. placebo 0.5% vs. 0.9%; (0.52; 0.25–1.08)	1.1% vs. 0.8%; (1.32; 0.46–3.79)
Cardiovascular death (HR 95% CI)	1.1% vs. 2.5%; (0.43; 0.11–1.66)	Group 1 vs. 3 2.4% vs. 1.9%; (1.29; 0.59–2.80) Group 2 vs. 3 2.2% vs. 1.9%; (1.19; 0.54–2.62)	Dabigatran 110 mg twice daily vs. WTT 3.8% vs. 3.2% (1.17; 0.72–1.89) Dabigatran 150 mg twice daily vs. WTT 2.8% vs. 3.1% (0.84; 0.47–1.51)	Apixaban vs. VKA 2.5% vs. 2.3%; (1.05; 0.0.72–1.52) Aspirin vs. placebo 2.3% vs. 2.5%; (0.92; 0.63–1.33f)	2.3% vs. 2.1%; (1.06; 0.54–2.10)

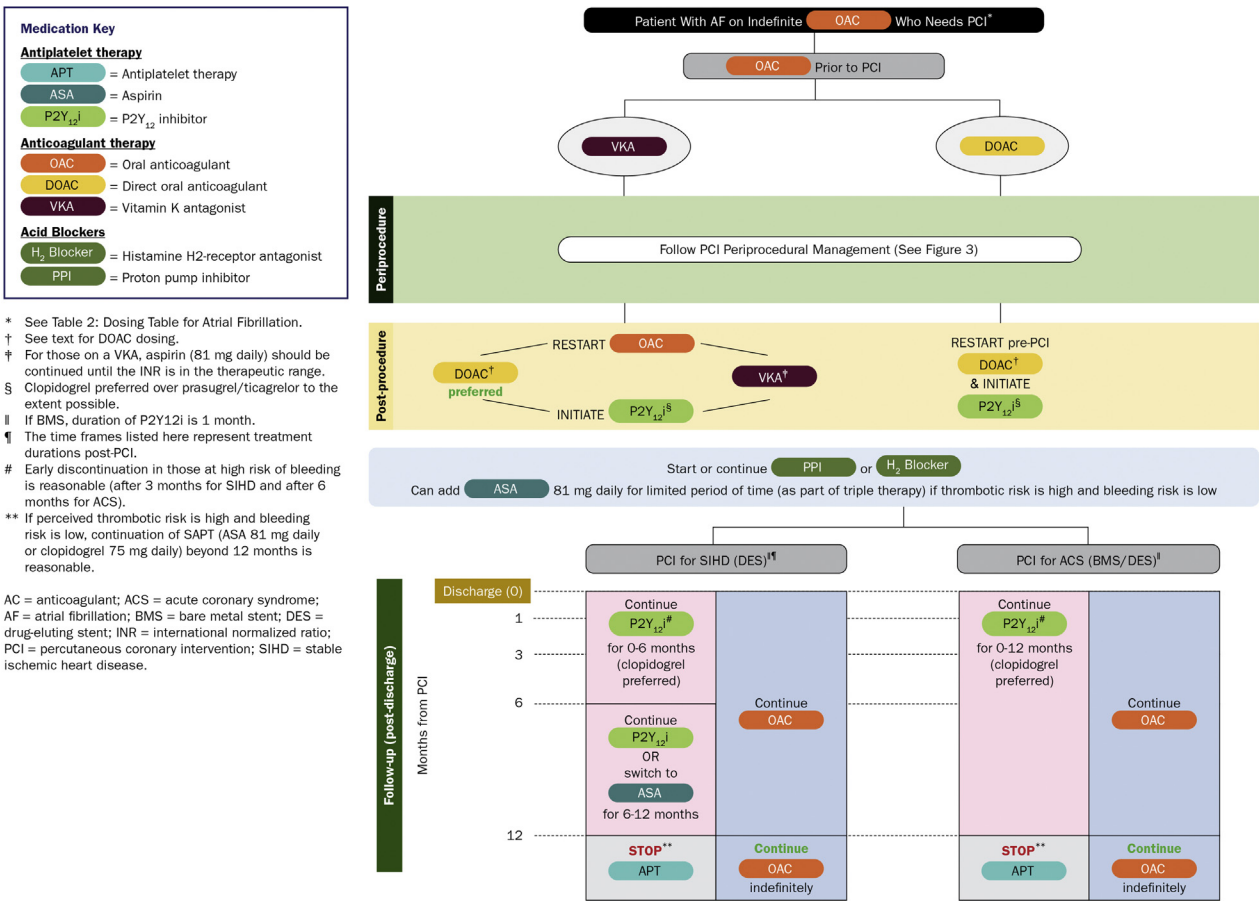
*AUGUSTUS was half double-blind (aspirin) and half open-label. The treatment regimen comparing apixaban with a VKA was open-label; however, the regimen comparing aspirin with matching placebo was double-blind.
† Group 1: Rivaroxaban 15 mg once daily with food (or 10 mg once daily with or without food for CrCl 30 to <50 mL/min) plus P2Y12i for 12 months. Group 2: Rivaroxaban 2.5 mg twice daily with or without food plus DAPT for 1, 6, or 12 months followed by rivaroxaban 15 mg once daily with food (or 10 mg once daily with or without food for CrCl 30 to <50 mL/min) plus low-dose aspirin to 12 months. Group 3: VKA + DAPT for 1, 6, or 12 months followed by VKA + low-dose aspirin to 12 months.
‡ Apixaban 5 mg twice daily reduced to 2.5 mg twice daily for patients with ≥2 of the following: serum creatinine ≥1.5 mg/dL, age ≥80 years, body weight ≤60 kg.
§ Edoxaban 60 mg once daily or 30 mg once daily if CrCl 15-50 mL/min, body weight ≤60 kg, or use of certain P-glycoprotein inhibitors (cyclosporine, dronedarone, erythromycin, ketoconazole, verapamil or amiodarone).
ACS = acute coronary syndrome; AF = atrial fibrillation; ASA = aspirin; AUGUSTUS = Open-Label, 2×2 Factorial, Randomized, Controlled Clinical Trial to Evaluate the Safety of Apixaban vs Vitamin K Antagonist and Aspirin vs Aspirin Placebo in Patients With Atrial Fibrillation and Acute Coronary Syndrome and/or Percutaneous Coronary Intervention; CI = confidence interval; CrCl = creatinine clearance; ENTRUST-AF PCI = Edoxaban-Based Versus Vitamin K Antagonist-Based Antithrombotic Regimen After Successful Coronary Stenting in Patients With Atrial Fibrillation trial; HR = hazard ratio; INR = international normalized ratio; MI = myocardial infarction; $P2Y_{12i}$ = $P2Y_{12}$ inhibitor; P-glycoprotein = permeability glycoprotein; PCI = percutaneous coronary intervention; PIONEER AF-PCI = An Open-Label, Randomized, Controlled, Multicenter Study Exploring Two Treatment Strategies of Rivaroxaban and a Dose-Adjusted Oral Vitamin K Antagonist Treatment Strategy in Subjects With Atrial Fibrillation Who Undergo Percutaneous Coronary Intervention; RE-DUAL PCI = Triple Therapy With Warfarin in Patients With AF That Undergo a PCI With Stenting trial; SIHD = stable ischemic heart disease; TIMI = Thrombolysis In Myocardial Infarction; VKA = vitamin K antagonist; WOEST = What is the Optimal antiplatElet and anticoagulant therapy in patients with oral anticoagulation and coronary StenTing trial; WTT = warfarin triple therapy.

8. For patients deemed to be at high risk of bleeding, discontinuation of SAPT before the recommended duration can be considered (after 3 months for those presenting with SIHD and after 6 months for those presenting with ACS), but the relative risks of stent thrombosis versus bleeding need to be considered.
9. For patients who are not candidates for a DOAC and require treatment with a VKA, it is reasonable to aim for the lower end of the target international normalized ratio (INR) range (i.e., 2.0 to 2.5), with more frequent INR monitoring to reduce bleeding risk (65). Careful attention to time spent in the therapeutic range for patients on a VKA is important.
10. For patients on ≥2 antithrombotic agents, we recommend starting or continuing a proton pump inhibitor (or histamine H_2-receptor antagonist in selected cases) along with avoidance of concomitant nonsteroidal anti-inflammatory drugs to reduce the risk of gastrointestinal (GI) bleeding. Clinicians should be vigilant about discontinuing the proton pump inhibitor (or histamine H_2-receptor antagonist) when the regimen returns to OAC therapy alone, unless there are other indications for continued use. There have been concerns regarding reduced efficacy of clopidogrel with concomitant proton pump inhibitor use, particularly omeprazole (66,67). However, in the only randomized controlled trial on this topic, omeprazole was protective for GI bleeding without an increase in ischemic events (68).
11. For patients undergoing PCI, the characteristics and morphology of the vessel, lesion, and stent location may influence decisions regarding DAPT duration and the safety of shortening it, irrespective of the type of stent used. Higher risk lesion characteristics include bifurcation lesions, thrombus-containing lesions, long lesions, among others, but if there is uncertainty, it should be discussed with an interventional cardiologists on a case-by-case basis.
12. Cost and patient preference may be taken into consideration when making decisions regarding choice of therapy.

5.1. Clinical Scenario 1: Patient With AF on AC Therapy Who Now Needs PCI

For patients with AF who are appropriate candidates for an OAC (refer to the 2019 ACC/AHA/Heart Rhythm Society Guidelines on AF for eligibility), the duration of treatment should be lifelong, unless contraindications are present/develop or alternative therapy such as a left atrial appendage occlusion device is used (11,69,70).

FIGURE 2 Patient With AF on OAC Who Now Needs PCI: Post-Procedure and Long-Term Management of Antithrombotic Therapy



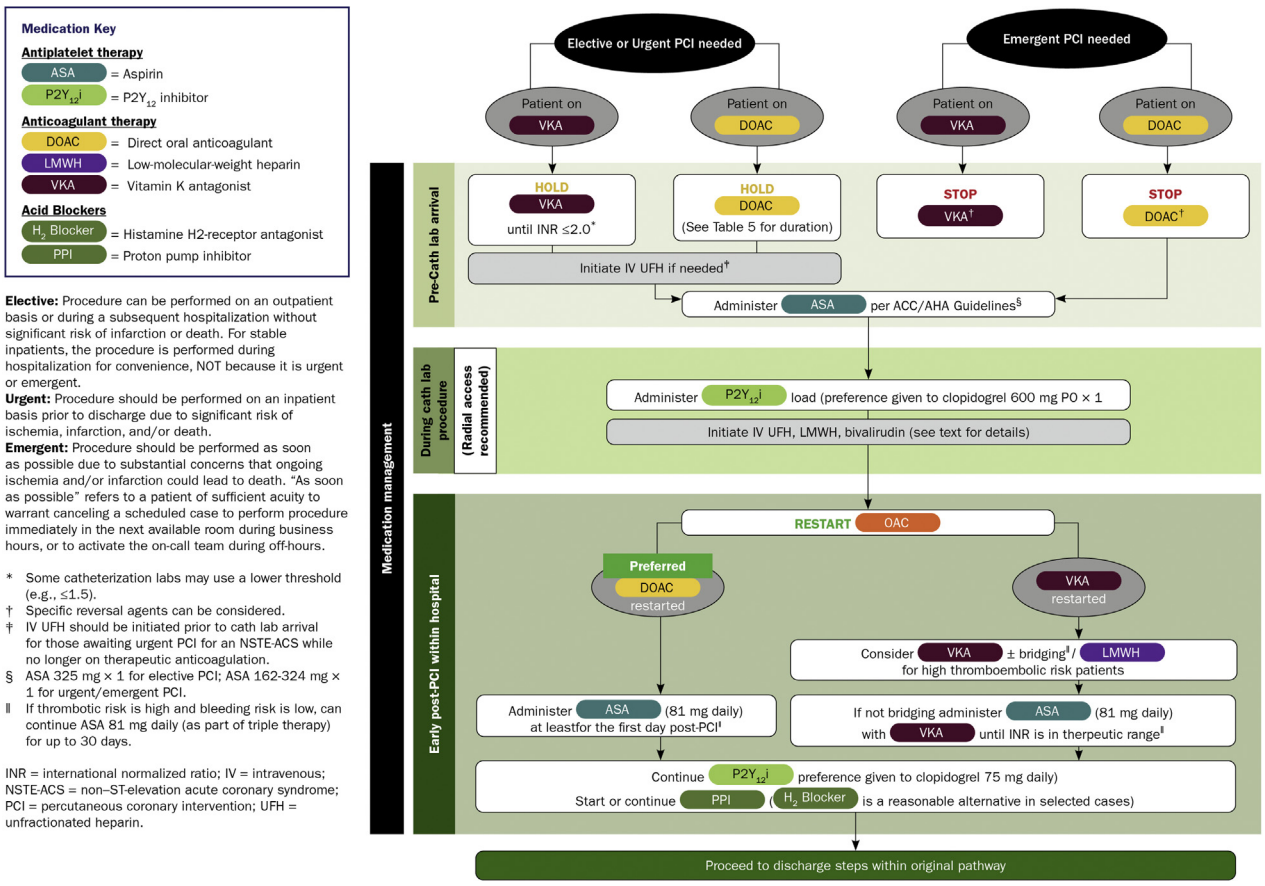
Figures 2 and 3 provide an overview of the patient with pre-existing AF receiving an OAC who presents for PCI. In general, if the patient was on a DOAC before PCI, the same DOAC would be continued afterwards, with the addition of a $P2Y_{12}i$ (clopidogrel is generally preferred). If the patient was on a VKA previously, the VKA could be reinitiated post-PCI, although the preferred option in eligible patients would be to substitute a DOAC instead. Assessment of the type and dose of DOAC can be based on the clinical trial results. An unusual scenario would be a patient who was on a DOAC for AF prior to PCI who then develops a specific allergy or significant renal dysfunction that precludes further use of a DOAC and instead warrants the transition to a VKA, or switching to another DOAC.

Low-dose aspirin is recommended for the duration of the hospitalization, and in general, we recommend discontinuing it prior to/upon discharge in most patients (71). Although the default approach is DAPT, because the risk of stent-related thrombotic complications is greatest in the first month post-PCI, one may consider continuing aspirin (81 mg/day) for 30 days (at which point the patient should switch to an OAC and $P2Y_{12}i$) in those with high thrombotic risk and low bleeding risk. Alternatively, in patients at particularly high stent thrombosis risk (e.g., patients with ACS), ticagrelor may be used in lieu of clopidogrel as the $P2Y_{12}i$ agent of choice, although data on ticagrelor are limited. At this time, we do not recommend prasugrel as a component of a triple-therapy regimen. In 1 small study, triple therapy using a VKA, aspirin, and prasugrel was associated with a 4-fold higher rate of bleeding (72). As discussed in the previous text, the duration of $P2Y_{12}i$ monotherapy should be, in general, 6 months for SIHD and 12 months for ACS.

5.1.1. General Principles

1. The proposed antithrombotic regimen should always account for the patient's ischemic and bleeding risk as well as presentation (SIHD vs. ACS). An individualized approach is important.
2. For OAC therapy post-PCI in patients with AF, a DOAC is preferred, owing to its: a) lower risk of major, fatal, and intracranial bleeding compared with a VKA; b)

FIGURE 3 Patient on AC Who Now Needs PCI: Periprocedural Management of Antithrombotic Therapy



simplicity; c) rapid onset of action; and d) lack of need for bridging anticoagulation (54). **Table 2** shows the dosing recommendations for DOACs in AF.

3. For patients on a VKA for AF with a history of good INR control prior to PCI, continuation of the VKA may be considered post-PCI. For these patients, however:
   a. One can consider continuing aspirin (81 mg/day) post-PCI until the INR is in the therapeutic range (ideally, 2.0 to 2.5, as described in the previous text).
   b. Patients at high risk of stroke (e.g., left atrial or left atrial appendage thrombus, complete INR reversal or parenteral vitamin K administration prior to PCI, very high risk of thromboembolism) may be considered for bridging with parenteral anticoagulation until the INR is in the therapeutic range.
4. Given that the intensity and duration of the $P2Y_{12}$i plays a key role in bleeding complications after PCI, the chosen agent must be evaluated carefully. Because both prasugrel and ticagrelor have been associated with a higher risk of bleeding compared with clopidogrel, we believe preference should be given to clopidogrel after PCI in patients requiring a long-term OAC , although some support for ticagrelor in this setting exists as well (50,65,70,73). Data on the combination of prasugrel with a DOAC are also very scarce. Accordingly, the use of prasugrel should be avoided in patients treated concomitantly with an OAC (72).
5. Although the default approach is for dual antithrombotic therapy, because the risk of stent-related thrombotic complications is greatest in the first month post-PCI, one may consider additional use of aspirin (81 mg/day) for up to 30 days in those with high thrombotic risk and low bleeding risk (50,54,74–76).
6. For patients presenting with an ACS and requiring an OAC for AF, SAPT with a $P2Y_{12}$i should be continued for 12 months (50).
7. For patients presenting with SIHD and requiring an OAC for AF, SAPT with clopidogrel should be continued for 6 months. An additional 6 months of

TABLE 2 Dosing Table for AF (11,78-82)

Agent	Stroke Prevention Atrial Fibrillation	Dosing Adjustments*
Apixaban	5 mg orally twice daily	Dose reduction to 2.5 mg orally twice daily if the patient meets at least 2 of the following 3 characteristics: ■ Age ≥80 years ■ Actual body weight ≤60 kg and/or ■ Serum creatinine ≥1.5 mg/dL Patients with ESKD receiving hemodialysis were not enrolled in clinical trials. However, the prescribing information suggests no dosing adjustment for patients with ESKD, unless they have additional dose reduction characteristics.
Dabigatran	150 mg orally twice daily	Dose reduction to 75 mg orally twice daily if the CrCl (estimated using actual body weight) is 15–30 mL/min. Dose reduction is not recommended for patients with ESKD in the 2019 ACC/AHA/HRS AF guideline focused update.†
	110 mg orally twice daily	The FDA has not approved this dose for use in AF in the United States. In the European label, a twice-daily dose of 110 mg is recommended for patients age ≥80 years and "for consideration" for those age 75-80 years.
Edoxaban	60 mg orally once daily	The 60-mg once-daily dose is for patients with a CrCl (estimated using actual body weight) of 51–95 mL/min (not recommended for patients with a CrCl >95 ml/min). Dose reduction to 30 mg orally once daily if the CrCl is 15–50 mL/min. Patients with ESKD were not enrolled in clinical trials, and the prescribing information provides no dosing recommendations for patients with ESKD.
Rivaroxaban	20 mg orally once daily	Dose reduction to 15 mg orally once daily with the evening meal for patients with CrCl (estimated using actual body weight) ≤50 mL/min. Patients with ESKD were not enrolled in clinical trials. Dose reduction not recommended for patients with ESKD in the 2019 ACC/AHA/HRS AF guideline focused update.†
	15 mg orally once daily	This is the dose that was studied in PIONEER AF-PCI, with adjunctive use of a $P2Y_{12}$i. This dose has not been approved for stroke prevention in AF for those with a CrCl >50 ml/min without concomitant $P2Y_{12}$i use. When this lower, off-label dosing strategy is used in those with CrCl <50, the dose should be adjusted to 10 mg.
VKA	When used with APT INR 2.0–3.0‡	NA

*Dosing information in this table does not take drug-drug interactions into consideration. The reader is encouraged to review the specific drug prescribing information.
†Although the prescribing information provides dosing recommendations for patients with ESKD, the 2019 ACC/AHA/HRS AF guideline focused update recommends apixaban or warfarin for patients with ESKD. Dabigatran, rivaroxaban, and edoxaban are considered Class III (no benefit) in this population.
‡Reasonable to aim for the lower end of the target INR range (i.e., 2.0–2.5). Monitor INR more frequently.

ACC = American College of Cardiology; AF = atrial fibrillation; AHA = American Heart Association; APT = antiplatelet therapy; CrCl = creatinine clearance; ESKD = end-stage kidney disease; FDA = U.S. Food and Drug Administration; HRS = Heart Rhythm Society; INR = international normalized ratio; NA = not applicable; $P2Y_{12}$i = $P2Y_{12}$ inhibitor; PIONEER AF-PCI = An Open-Label, Randomized, Controlled, Multicenter Study Exploring Two Treatment Strategies of Rivaroxaban and a Dose-Adjusted Oral Vitamin K Antagonist Treatment Strategy in Subjects With Atrial Fibrillation Who Undergo Percutaneous Coronary Intervention; VKA = vitamin K antagonist.

SAPT (with either aspirin or clopidogrel) is recommended thereafter for a total of 12 months of SAPT.

8. For patients deemed to be at high risk of bleeding, discontinuation of SAPT before the recommended duration can be considered (after 3 months for those presenting with SIHD and after 6 months for those presenting with ACS), but the relative risks of stent thrombosis versus bleeding need to be considered.
9. If perceived thrombotic risk is high (e.g., prior myocardial infarction, complex lesions, presence of select traditional cardiovascular risk factors, or extensive ASCVD) and the patient is at low bleeding risk, it is reasonable to continue SAPT beyond 12 months (in line with prior ACC/AHA recommendations) (74,77).
10. Although a DES is the preferred stent type for those requiring OAC therapy after PCI, patients with SIHD treated with a bare metal stent should receive at least 1 month of SAPT with a $P2Y_{12}$i.

5.2. Clinical Scenario 2: Patient on APT With a New Diagnosis of AF

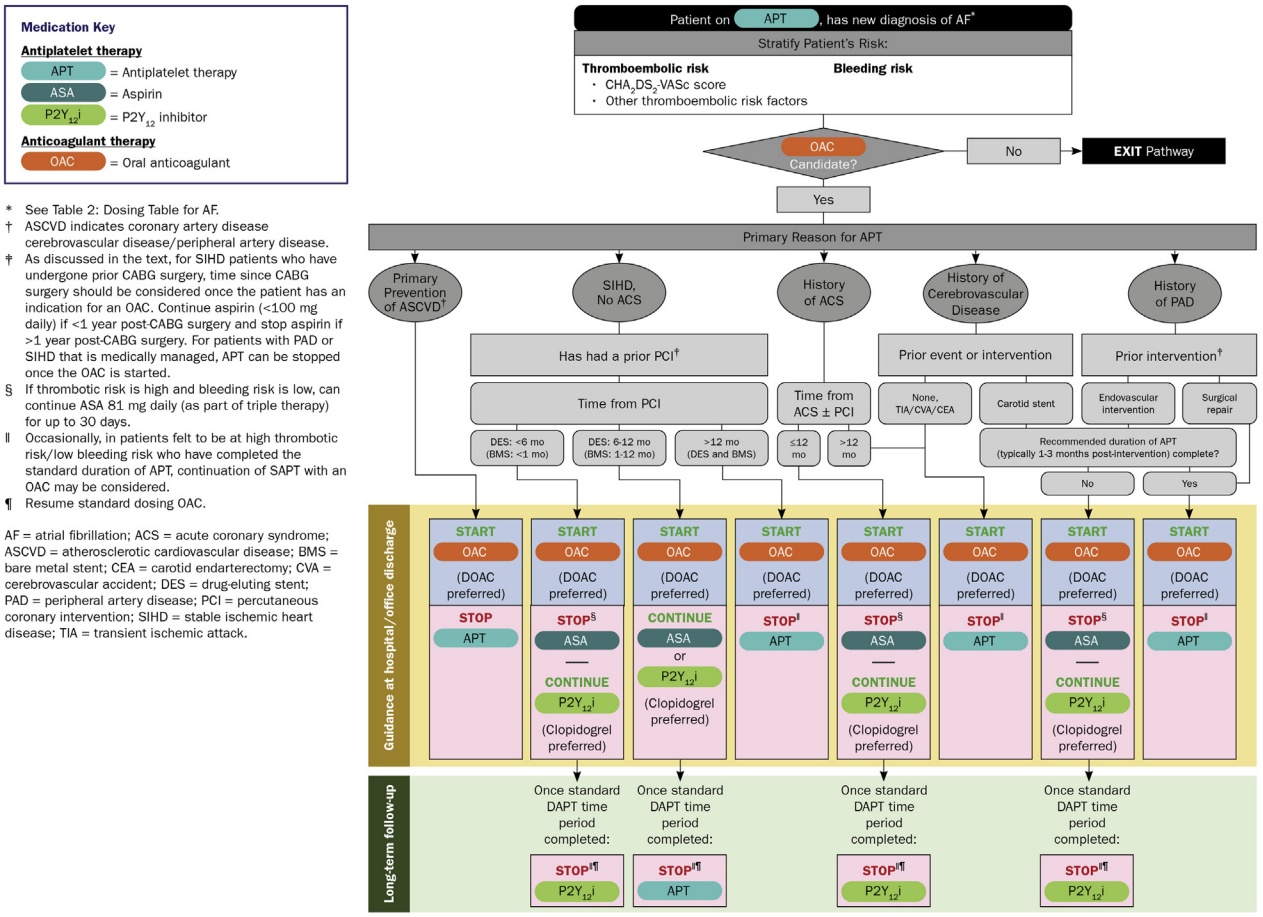
5.2.1. Assessment of Thromboembolic and Bleeding Risk

Figure 4 addresses the antithrombotic management of a patient who is taking APT for cardiovascular, peripheral vascular, or cerebrovascular disease who subsequently develops AF requiring an OAC. In such patients, it is important to first assess their thromboembolic and bleeding risks.

The CHA_2DS_2-VASc score is arguably the most extensively validated and widely used tool to assess the patient's risk of stroke or systemic embolism (Supplemental Table 1). Current ACC/AHA/Heart Rhythm Society guidelines recommend that men with a CHA_2DS_2-VASc score ≥2 and women with a score ≥3 take an OAC (11,82). Patients with lower scores may be considered for OAC therapy based on additional clinical factors (left atrial enlargement, left ventricular hypertrophy, and so on), and patient preference. Patients with AF and certain conditions, such as hypertrophic cardiomyopathy and rheumatic mitral stenosis, are advised to take an OAC regardless of the CHA_2DS_2-VASc score; similar guidance exists for patients undergoing electrical cardioversion or AF ablation (11). The type of AF (paroxysmal vs. persistent), the presence or absence of AF symptoms, and the AF burden do not usually affect OAC decision-making, although the role of OAC therapy in patients with brief, asymptomatic, device-detected AF is uncertain (83).

Whereas several bleeding risk scores (e.g., HAS-BLED, $HEMORR_2HAGES$, and ATRIA) (Supplemental Table 2) and definitions (e.g., ARC-HBR) exist, none are perfectly discriminant (84-88). Some bleeding conditions, such as recent spontaneous intracranial hemorrhage, represent

FIGURE 4 Patient on APT With a New Diagnosis of AF: Discharge and Long-Term Management of Antithrombotic Therapy



* See Table 2: Dosing Table for AF.
† ASCVD indicates coronary artery disease cerebrovascular disease/peripheral artery disease.
‡ As discussed in the text, for SIHD patients who have undergone prior CABG surgery, time since CABG surgery should be considered once the patient has an indication for an OAC. Continue aspirin (<100 mg daily) if <1 year post-CABG surgery and stop aspirin if >1 year post-CABG surgery. For patients with PAD or SIHD that is medically managed, APT can be stopped once the OAC is started.
§ If thrombotic risk is high and bleeding risk is low, can continue ASA 81 mg daily (as part of triple therapy) for up to 30 days.
‖ Occasionally, in patients felt to be at high thrombotic risk/low bleeding risk who have completed the standard duration of APT, continuation of SAPT with an OAC may be considered.
¶ Resume standard dosing OAC.

AF = atrial fibrillation; ACS = acute coronary syndrome; ASCVD = atherosclerotic cardiovascular disease; BMS = bare metal stent; CEA = carotid endarterectomy; CVA = cerebrovascular accident; DES = drug-eluting stent; PAD = peripheral artery disease; PCI = percutaneous coronary intervention; SIHD = stable ischemic heart disease; TIA = transient ischemic attack.

strong contraindications to OAC therapy, whereas others, such as easy bruising, epistaxis, or hemorrhoids, make decision-making regarding OAC management more difficult. It is important to note that OAC therapy has historically been underutilized due to increased concerns about bleeding complications and underestimation of thromboembolic risk (89). After a review of relevant data, the benefits and risks of OAC therapy should be discussed with the patient using shared decision-making, while factoring in the patient's goals and preferences. Some patients at very low risk (i.e., CHA_2DS_2-VASc score of 0 without relevant comorbidities) will: 1) not require an OAC; 2) remain on prescribed APT; and 3) exit the pathway. Patients with a higher thromboembolic risk who also have very high bleeding risk or other appropriate reasons to seek an alternative to OAC therapy may be considered for left atrial appendage occlusion and would also exit the pathway (90,91). **Table 2** shows the dosing for DOACs in AF.

5.2.2. Determining Indication for APT

For patients with AF who have an indication for OAC therapy and an acceptable bleeding risk, the next step involves reassessing the original and current indication(s) for APT. This assessment should include a history and physical examination, looking particularly for symptoms and signs of cardiovascular disease (e.g., angina, recent neurological symptoms, bruits, and so on). It is also very important to ascertain the timing and details around prior cardiovascular events such as myocardial infarction, peripheral or cerebral embolism, and coronary or other arterial interventional procedures.

5.2.3. Management of Antithrombotic Therapy Based on the Indication for APT

1. Primary prevention of ASCVD

- The 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease noted that low-dose aspirin (75 to 100 mg daily) might be

considered for the primary prevention of ASCVD among select adults 40 to 70 years of age who are at higher ASCVD risk but not at increased bleeding risk (92). If such patients were to develop AF requiring OAC therapy, the appropriate management is nearly always to stop APT and start an OAC (93).

2. SIHD

- For patients on SAPT for SIHD, with no history of an ACS and no prior revascularization who develop AF requiring OAC therapy, the appropriate management is nearly always to stop APT and start an OAC.
- For patients on APT for SIHD, with no history of an ACS but who have had a prior PCI, the time since PCI should be assessed.
  - If it has been ≤6 months since PCI, our recommendation for most patients would be to stop aspirin, continue clopidogrel, and start an OAC (with preference given to a DOAC for the reasons given in the previous text [see section 5.1.1]).
  - If it has been 6 to 12 months since PCI, we recommend continuing SAPT with either aspirin or clopidogrel until 1 year post-PCI, along with an OAC.
  - For >12 months post-PCI, OAC alone can be used long-term.
- For patients on APT for SIHD with no history of an ACS but prior coronary artery bypass graft (CABG) surgery, the time since CABG surgery should be assessed. We recommend continuing aspirin (<100 mg/day) if <1 year post-CABG surgery and stopping aspirin >1 year post-CABG surgery (62).

3. History of ACS

- Patients with ACS (unstable angina, non-ST-elevation myocardial infarction, and ST-elevation myocardial infarction) are usually treated with DAPT for 12 months (50,94).
  - If it has been ≤12 months since the ACS, our recommendation for most patients would be to stop aspirin, continue the $P2Y_{12}$i (with preference given to clopidogrel), and start an OAC (with preference given to a DOAC for the reasons given in the previous text (see section 5.1.1).
  - If it has been >12 months since the ACS, APT may be stopped and most patients can be treated with an OAC alone.
  - For patients at high bleeding risk and low ischemic risk, shorter durations of APT can be considered.
  - At the clinician's discretion, selected patients felt to be at higher thrombotic risk due to: a) the nature of the coronary lesion; b) the type, location, number, or length of coronary stents; or c) other clinical factors, and low bleeding risk may continue SAPT (aspirin 81 mg daily or clopidogrel 75 mg daily) beyond 12 months while on an OAC.

4. History of Cerebrovascular Disease

- Cerebrovascular disease is notable for being a heterogeneous condition, encompassing a broad range of clinical syndromes and pathophysiological states, including intracranial small-vessel disease; large-vessel disease involving the extracranial or intracranial vessels; cardioembolism related to AF, an anterior wall motion abnormality, severely reduced left ventricular systolic function, or a patent foramen ovale; illicit drug use; arterial dissection; or less common mechanisms such as hypercoagulability, vasculopathy, or genetic diseases. These conditions may be asymptomatic (detected only on imaging studies) or symptomatic, manifesting as a TIA or stroke/cerebrovascular accident. The antithrombotic therapy used will depend upon the type of cerebrovascular disease, prior symptomatic events, prior interventions, and perceived bleeding risk. For example, in patients with a concomitant diagnosis of cerebral amyloid angiopathy, the risk of recurrent intracranial hemorrhage is very high and generally precludes use of anticoagulation (95). For patients presenting with AF appropriate for an OAC who have a prior history of cerebrovascular disease and are currently receiving APT, the pathway separates patients into 3 broad categories:
  1. For patients on APT for prior TIA or cerebrovascular accident who develop AF requiring OAC therapy, the pathway recommends stopping all APT and treating with an OAC alone (DOAC preferred) when considered safe from the perspective of hemorrhagic transformation, typically between 2 and 14 days following an acute event (74–76). Given that TIA is often the diagnosis when no infarct or hemorrhage is noted on imaging, an OAC can typically be initiated immediately.
  2. For patients who have undergone recent carotid endarterectomy, the pathway recommends stopping all APT and treating with an OAC alone (DOAC preferred) when considered safe from risk of post-operative bleeding, typically 3 to 14 days after surgery.
  3. For patients with carotid stenting within the previous 1 to 3 months, our recommendation for most patients would be to stop aspirin, continue the $P2Y_{12}$i (clopidogrel preferred), and start an OAC (DOAC preferred). If the standard duration of DAPT after carotid stenting has ended (usually 1 to 3 months), all APT may be stopped, and most

TABLE 3 Management Summary for Acute VTE Based on CHEST and International Practice Guidelines (21,102)

Clinical Scenario	Length of Therapy	Anticoagulant Choice
DVT/PE provoked by surgery	3 months	DOAC preferred over VKA
DVT/PE provoked by nonsurgical transient risk factor	3 months	DOAC preferred over VKA
Unprovoked DVT/PE	■ Indefinite therapy if low/moderate bleeding risk ■ 3 months if high bleeding risk	DOAC preferred over VKA
Recurrent unprovoked DVT/PE	■ Indefinite therapy if low/moderate bleeding risk ■ 3 months if high bleeding risk	DOAC preferred over VKA
DVT/PE in setting of active cancer	Indefinite therapy	DOAC preferred over LMWH/VKA*; LMWH preferred over VKA

*The HOKUSAI VTE-Cancer, SELECT-D, ADAM VTE, and Caravaggio trials compared edoxaban, rivaroxaban, and apixaban, respectively, to dalteparin (103-106). VTE recurrence appeared to be lower with a DOAC, but bleeding tended to be similar to slightly higher with similar mortality rates (90). Patients with GI and GU malignancies may have a higher risk of GI or GU bleeding, respectively, with DOACs compared with LMWH. Moreover, DOAC use may pose challenges for oral administration and drug-drug interactions; these recommendations would need to be tailored based on the clinical scenario (99,102).

ADAM-VTE = Apixaban and Dalteparin in Active Malignancy-Associated Venous Thromboembolism trial; Caravaggio = Apixaban for the Treatment of Venous Thromboembolism in Patients With Cancer trial; DOAC = direct oral anticoagulant; DVT = deep vein thrombosis; GI = gastrointestinal; HOKUSAI-VTE Cancer = Edoxaban for the Treatment of Cancer-Associated Venous Thromboembolism; GU = genitourinary; LMWH = low-molecular-weight heparin; PE = pulmonary embolism; SELECT-D = Comparison of an Oral Factor Xa Inhibitor With Low Molecular Weight Heparin in Patients With Cancer With Venous Thromboembolism: Results of a Randomized Trial; VKA = Vitamin K antagonist; VTE = venous thromboembolism.

patients can be treated with an OAC alone (96-97).

5. History of Peripheral Artery Disease

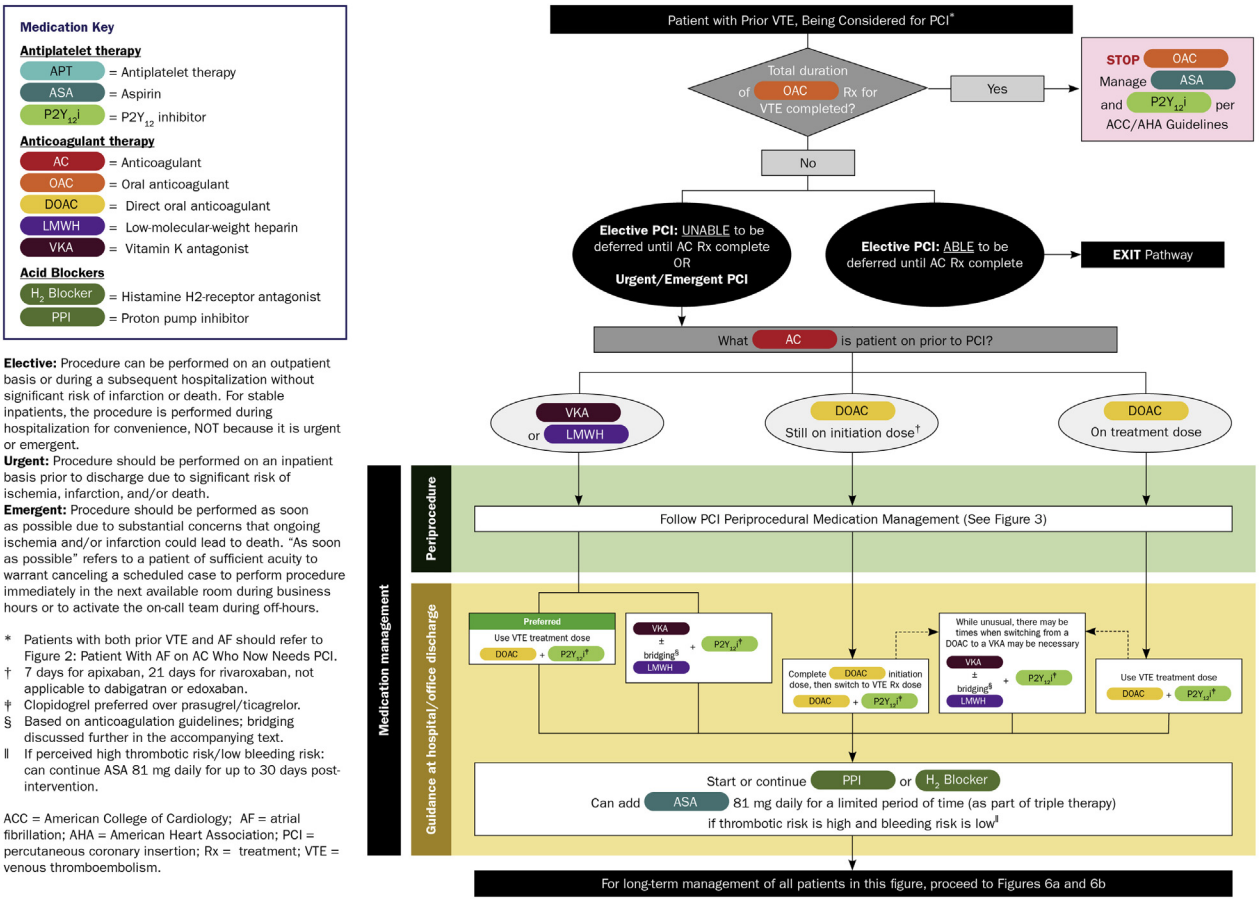
- Similar to cerebrovascular disease, peripheral artery disease (PAD) can encompass a broad range of clinical syndromes and disease states, ranging from aortic disease to peripheral limb ischemia. Use of APT is less well-defined than for CAD, and APT regimens after peripheral interventions can vary.
- Patients with PAD without prior intervention or with prior surgical repair are usually treated with SAPT (usually aspirin or clopidogrel) for primary or secondary prevention of ischemic events (myocardial infarction, stroke). For such patients presenting with AF appropriate for an OAC, the pathway recommends stopping all APT and treating with an OAC alone (DOAC preferred).
- Patients with PAD who have been treated with endovascular intervention/stenting are usually treated with APT for 1 to 3 months. The type and duration of APT is less well-defined and standardized than for coronary interventions. For patients presenting with AF appropriate for an OAC, the pathway recommends continuing or switching to SAPT (either clopidogrel or aspirin, clopidogrel preferred) and treating with an OAC (DOAC preferred). If the standard duration of DAPT after endovascular intervention/stenting has ended (usually 1 to 3 months), all APT may be stopped and most patients can be treated with an OAC alone.

5.3. Clinical Scenario 3: Patient With Prior VTE Being Considered for PCI

VTE refers to proximal lower extremity deep venous thrombosis and/or pulmonary embolism, although thrombosis can affect other venous beds including the deep veins of the upper extremities, splanchnic veins, portal vein, and cerebral sinuses. The standard therapy for acute VTE is anticoagulation (21). The length of treatment depends on the presence or absence of a provoking factor and whether the provoking factor is transient (e.g., surgery, pregnancy) or if a chronic condition (e.g., cancer, chronic immobility) is present (**Table 3**). Additional factors include bleeding risk and patient preference. Current guidelines give preference to a DOAC over a VKA for non-cancer-associated VTE; in contrast, low-molecular-weight heparin (LMWH) or a DOAC (rather than a VKA) are recommended for cancer-associated VTE (**Table 3**) (21). Venous thromboembolism provoked by a transient risk factor can generally be treated for 3 months, whereas unprovoked VTE may be treated indefinitely (21). Two DOACs, apixaban and rivaroxaban, offer the added advantage of reduced-intensity dosing in patients on indefinite anticoagulation whose VTE was ≥6 months ago (rivaroxaban 10 mg daily in EINSTEIN-CHOICE [Reduced-dosed Rivaroxaban in the Long-term Prevention of Recurrent Symptomatic VTE] and apixaban 2.5 mg twice daily in AMPLIFY-EXTEND [Efficacy and Safety Study of Apixaban for Extended Treatment of Deep Vein Thrombosis or Pulmonary Embolism]) (98). In patients with unprovoked VTE who stop anticoagulation after a minimum of 3 months, rather than continuing anticoagulation indefinitely, aspirin is an option for secondary prevention, although it is not as effective as anticoagulation (78).

In patients receiving PCI while on an AC for VTE, triple therapy is associated with an increased risk of major bleeding (99,100). However, there are important limitations in applying the AF recommendations related to OAC therapy and APT to those with VTE. Studies evaluating the use of OAC therapy (either DOACs or VKAs) in patients with VTE have demonstrated lower rates of major bleeding compared with that observed in AF. This suggests that the

FIGURE 5 Patient With Prior VTE Being Considered for PCI: Peri-PCI and Hospital Discharge Management of Antithrombotic Therapy



combined use of an AC and APT may also have a lower risk for major bleeding in those with VTE, but this has not been shown in large randomized trials (101).

For patients with prior VTE needing PCI, the key factors to consider in developing a treatment plan are the desired duration of AC therapy, the urgency of PCI, and, when appropriate, how best to combine AC therapy and APT in a fashion that minimizes bleeding risk (**Figure 5**).

5.3.1. Duration of AC Therapy for VTE

In patients with VTE who require PCI, it is critical to reassess the recommended duration of AC therapy (**Table 3**). Recommendations regarding the duration of AC therapy are adapted from the American College of Chest Physicians Clinical Practice Guidelines and are intended to provide guidance to clinicians and patients but do not substitute for clinical judgment and individualized decision-making (21).

1. We recommend a time-limited course of OAC therapy (**Figures 6A and 6B**) after VTE provoked by surgery or a transient nonsurgical risk factor (e.g., acute medical illness, cast immobilization, exogenous estrogen therapy, pregnancy, or the postpartum state).
2. Based on the considerable risk of recurrent VTE after an unprovoked event or an event provoked by active cancer, we recommend indefinite AC therapy in most such patients if they are at average bleeding risk, and we recommend time-limited AC therapy if they are at increased bleeding risk. Women and patients with normal D-dimer levels have a lower risk of recurrent VTE after a first unprovoked event. Validated clinical decision tools may be helpful to identify those with the highest risk of recurrence who may need extended anticoagulation or those at the lowest risk where anticoagulation may be discontinued (107-109). HERDOO2 is a validated scoring system for identifying female patients at the lowest risk of recurrence (107).
3. In all patients on indefinite therapy, the risks and benefits of continuing AC therapy should be reassessed at least annually.

FIGURES 6A AND 6B Patient With VTE on AC Who Has Undergone PCI (6A: Time-Limited AC; 6B: Indefinite AC): Long-Term Post-Discharge Management of Antithrombotic Therapy

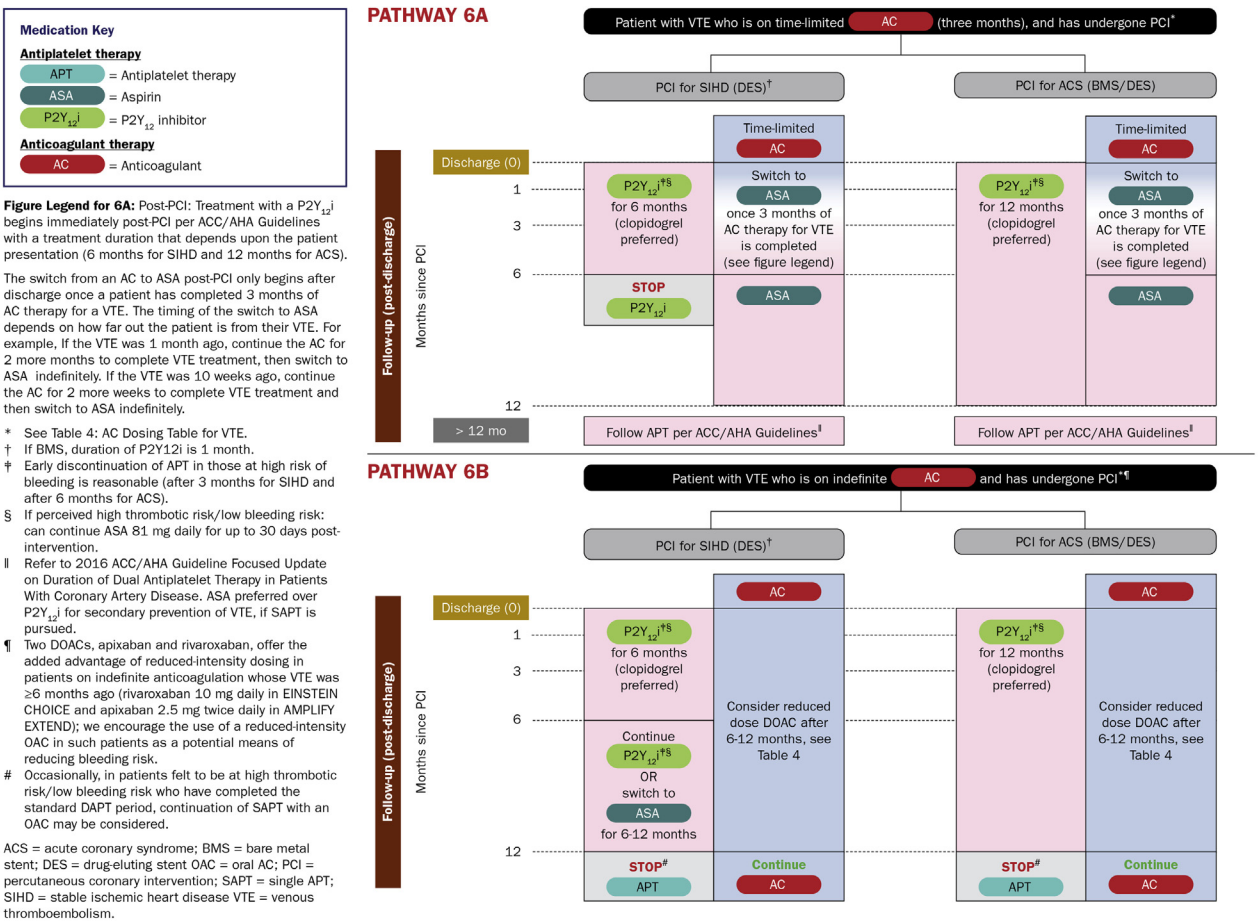


Figure Legend for 6A: Post-PCI: Treatment with a $P2Y_{12}i$ begins immediately post-PCI per ACC/AHA Guidelines with a treatment duration that depends upon the patient presentation (6 months for SIHD and 12 months for ACS).

The switch from an AC to ASA post-PCI only begins after discharge once a patient has completed 3 months of AC therapy for a VTE. The timing of the switch to ASA depends on how far out the patient is from their VTE. For example, If the VTE was 1 month ago, continue the AC for 2 more months to complete VTE treatment, then switch to ASA indefinitely. If the VTE was 10 weeks ago, continue the AC for 2 more weeks to complete VTE treatment and then switch to ASA indefinitely.

* See Table 4: AC Dosing Table for VTE.
† If BMS, duration of P2Y12i is 1 month.
‡ Early discontinuation of APT in those at high risk of bleeding is reasonable (after 3 months for SIHD and after 6 months for ACS).
§ If perceived high thrombotic risk/low bleeding risk: can continue ASA 81 mg daily for up to 30 days post-intervention.
‖ Refer to 2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease. ASA preferred over $P2Y_{12}i$ for secondary prevention of VTE, if SAPT is pursued.
¶ Two DOACs, apixaban and rivaroxaban, offer the added advantage of reduced-intensity dosing in patients on indefinite anticoagulation whose VTE was ≥6 months ago (rivaroxaban 10 mg daily in EINSTEIN CHOICE and apixaban 2.5 mg twice daily in AMPLIFY EXTEND); we encourage the use of a reduced-intensity OAC in such patients as a potential means of reducing bleeding risk.
# Occasionally, in patients felt to be at high thrombotic risk/low bleeding risk who have completed the standard DAPT period, continuation of SAPT with an OAC may be considered.

ACS = acute coronary syndrome; BMS = bare metal stent; DES = drug-eluting stent OAC = oral AC; PCI = percutaneous coronary intervention; SAPT = single APT; SIHD = stable ischemic heart disease VTE = venous thromboembolism.

4. If a patient has completed ≥3 months of a time-limited course of OAC therapy, the OAC should be stopped prior to PCI. However, if the patient is on indefinite AC therapy or is within the first 3 months of a time-limited course of OAC therapy, it may be necessary to continue the AC after PCI depending on the planned duration of AC therapy and the urgency of the procedure. In patients on indefinite AC therapy, it may be feasible to use reduced-dose apixaban or rivaroxaban after 6 months (**Table 4**) (see section 5.3.3).

5.3.2. Urgency of PCI

We categorize PCI into elective, urgent, and emergent. Elective PCI can be safely postponed for several weeks to months (for instance, for SIHD) without placing the patient at significant cardiovascular risk.

1. If a patient within the first 3 months of a time-limited course of OAC therapy for VTE requires elective PCI, we suggest deferring the PCI until the patient has completed their OAC therapy, at which time the OAC can be discontinued.
2. In patients on indefinite AC therapy and in those within the first 3 months of a time-limited course of OAC therapy who require urgent or emergent PCI, it is not possible to permanently discontinue the AC prior to PCI. In such patients, careful consideration of antithrombotic agents and dosing is necessary to minimize bleeding risk.

5.3.3. Combination AC Therapy and APT

Choice of AC therapy, APT, and the dosing of these medications represent key elements of minimizing bleeding risk in patients who require combination therapy.

1. As previously discussed, preference is given to DOACs over VKAs for most patients because of the lower risk of major, intracranial, and fatal bleeding (115). Even if patients are on a VKA prior to PCI, we prefer switching to a DOAC prior to hospital discharge. The DOAC dosing

TABLE 4 Anticoagulation Dosing Table for VTE (78-81,110-114)

Agent	VTE Initial Treatment	VTE Secondary Prevention after Initial Therapy	Dosing Adjustments*
Apixaban	10 mg orally twice daily for the first 7 days of therapy followed by 5 mg orally twice daily.	After ≥6 months of initial therapy, either 5 mg orally twice daily or 2.5 mg orally twice daily can be considered.†	Patients with ESKD receiving hemodialysis were not enrolled in clinical trials. However, the prescribing information states that no dose adjustment is necessary for patients with renal impairment, including those with ESKD.
Dabigatran	150 mg orally twice daily when preceded by 5–10 days of parenteral AC.‡	150 mg orally twice daily.§	Patients with severe renal impairment (a CrCl of ≤30 mL/min) and with ESKD receiving hemodialysis were not enrolled in clinical trials. The prescribing information makes no recommendations for dosing in this population.
Edoxaban	60 mg orally once daily when preceded by at least 5–10 days of parenteral AC.‡	60 mg orally once daily.	Dose reduction to 30 mg once daily for patients with a CrCl (estimated using actual body weight) of 15–50 mL/min or body weight ≤60 kg.
Rivaroxaban	15 mg orally twice daily with food for the first 21 days followed by 20 mg daily with food.	After ≥6 months of initial therapy, either 20 mg orally daily with food or 10 mg orally daily with or without food can be considered.†	Patients with a CrCl of <30 mL/min were excluded from clinical trials. Avoid use in patients with a CrCl of <15 mL/min.
VKA	When used with APT: INR 2.0–2.5‖; bridging with parenteral heparin initially.	When used with APT: Consider INR 2.0–2.5.‖	NA
Dalteparin	In the setting of cancer: 200 units/kg subcutaneously once daily for 1 month, then 150 IU/kg subcutaneously once daily (months 2–6) for extended treatment.	In the setting of cancer: Not FDA-approved for this indication, but use is consistent with NCCN recommendations.	For patients with a CrCl of <30 mL/min, the prescribing information recommends monitoring anti-Factor Xa levels with a target peak level (4–6 hours post-dose) of 0.5–1.5 IU/mL. Patients with ESKD were excluded from clinical trials.
Enoxaparin	In the setting of cancer: 1 mg/kg twice daily or 1.5 mg/kg once daily, subcutaneously.¶#**	In the setting of cancer: Not FDA-approved for this indication, but use is consistent with NCCN recommendations¶#**	Patients with a CrCl of <30 mL/min were excluded from clinical trials. However, the prescribing information recommends a dose reduction to 1 mg/kg subcutaneously once daily for patients with a CrCl (estimated using actual body weight) of <30 mL/min).

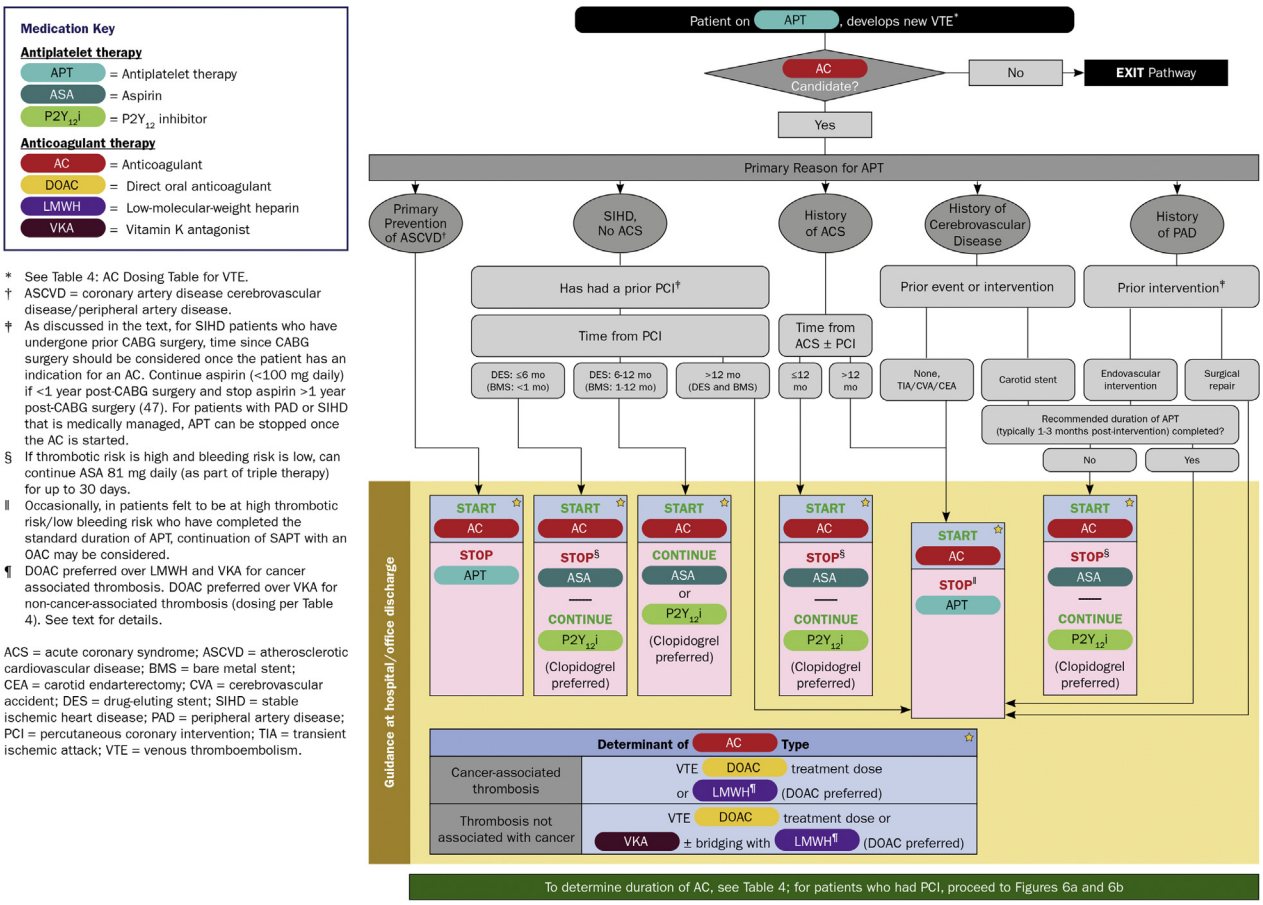
*Dosing information in this table does not take drug-drug interactions into consideration. The reader is encouraged to review the specific drug prescribing information.
†Reduced-dose rivaroxaban (10 mg daily) and apixaban (2.5 mg twice daily) can be considered for secondary prevention of VTE after 6 months of initial treatment.
‡Initial treatment with unfractionated heparin, LMWH, or fondaparinux recommended.
§Dabigatran 110 mg twice daily is approved for use in DVT/PE treatment outside of the United States.
‖Monitor INR more frequently.
¶Long-term treatment with enoxaparin at this dose has not been tested in cancer patients.
#Agent and dosing supported by the NCCN Clinical Practice Guidelines in Oncology for Cancer-Associated Venous Thromboembolic Disease (Version 1.2019).
**Among patients without cancer, enoxaparin is approved for DVT and is also used extensively off-label for treatment of PE

AC = anticoagulation; APT= antiplatelet therapy; CrCl = creatinine clearance; DVT = deep vein thrombosis; ESKD = end-stage kidney disease; FDA = U.S. Food and Drug Administration; INR = international normalized ratio; LMWH = low-molecular-weight heparin; NA = not applicable; NCCN = National Comprehensive Cancer Network; PE = pulmonary embolism; VKA = vitamin K antagonist.

should be VTE-specific, which is typically higher than may be sufficient for stroke prophylaxis in patients with AF. For instance, the VTE maintenance dose of rivaroxaban should be 20 mg daily, not 15 mg daily, as studied in the PIONEER-AF trial (An Open-Label, Randomized, Controlled, Multicenter Study Exploring Two Treatment Strategies of Rivaroxaban and a Dose-Adjusted Oral Vitamin K Antagonist Treatment Strategy in Subjects With Atrial Fibrillation Who Undergo Percutaneous Coronary Intervention) (31). Dosing for the OACs is presented in **Table 4**.

2. An unusual scenario would be a patient who was on a treatment dose of a DOAC for VTE prior to PCI who then develops significant renal dysfunction precluding further use of a DOAC, warranting instead transition to a VKA.
3. In patients requiring a VKA, bridging with LMWH is associated with increased bleeding risk and should therefore be reserved for patients judged to be at very high risk of recurrent VTE (e.g., those within 3 months of a VTE or other thrombophilic states) (116). For all other patients, starting or restarting a VKA after PCI may be undertaken without bridging.
4. Of the 4 DOACs with an approved indication for treatment of VTE, rivaroxaban and apixaban have an initiation dose when used for the management of acute

FIGURE 7 Patient on APT With New VTE: Management of Initial Antithrombotic Therapy at Discharge



VTE (15 mg twice daily for 21 days for rivaroxaban, and 10 mg twice daily for 7 days for apixaban) (**Table 4**). In this scenario, we recommend completing the initiation dose first and then transitioning to the usual treatment dose. Dabigatran and edoxaban require at least 5 days of parenteral lead-in therapy after an acute VTE before they are initiated.

5. For patients with cancer-associated VTE, DOACs are preferred over both LMWH and a VKA as choice of AC therapy, primarily due to better compliance and ease of use; LMWH is preferred over VKA for this indication (**Table 3**) (102–105,117,118). The HOKUSAI VTE-Cancer, SELECT-D, ADAM VTE, and Caravaggio trials compared edoxaban, rivaroxaban, and apixaban to dalteparin, respectively (103–106). VTE recurrence appeared to be lower with a DOAC, but bleeding tended to be similar to slightly higher, with similar mortality rates (90). Patients with GI and genitourinary malignancies may have higher respective risks of GI or genitourinary bleeding with DOACs compared with LMWH (21,102). Moreover, DOAC use may pose challenges for oral administration (for instance, in patients with malabsorption) and drug-drug interactions; these recommendations would need to be tailored based on the clinical scenario (102).

Two DOACs, apixaban and rivaroxaban, offer the added advantage of reduced-intensity dosing in patients on indefinite anticoagulation whose VTE was ≥6 months ago (rivaroxaban 10 mg daily in EINSTEIN-CHOICE and apixaban 2.5 mg twice daily in AMPLIFY-EXTEND) (98,119). We encourage the use of reduced-intensity OAC therapy in such patients as a potential means of reducing bleeding risk.

5.4. Clinical Scenario 4: Patient on APT With New VTE

In the setting of a patient on APT who develops a new or recurrent VTE (**Figure 7**), the selection of AC therapy alone versus a combination of APT and AC therapy and the duration of treatment depends on the indication for APT.

5.4.1. Management of Antithrombotic Therapy Based on the Indication for APT

1. Primary prevention of ASCVD

- The 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease notes that low-dose aspirin (75 to 100 mg daily) might be considered for the primary prevention of ASCVD among select adults 40 to 70 years of age who are at higher ASCVD risk but not at increased bleeding risk (92). If such patients were to develop VTE requiring AC therapy, the appropriate management is nearly always to stop APT and start an AC (75). In the Thrombosis Prevention Trial, low-intensity warfarin alone (INR goal ~1.5 to 1.8) was as effective as aspirin (75 mg daily) at reducing ischemic events but caused more bleeding; the combination of aspirin and warfarin had the highest bleeding risk (120).

2. SIHD

- For patients on SAPT for SIHD, with no history of ACS and no prior revascularization who develop VTE requiring AC therapy, the appropriate management is nearly always to stop APT and start an AC.
- For patients on APT for SIHD, with no history of ACS but prior PCI, the time since PCI should be assessed.
  - If it has been ≤6 months since PCI, our recommendation for most patients would be to stop aspirin, continue clopidogrel, and start an AC (with preference given to a DOAC for reasons given in the previous text [see section 5.1.1]).
  - If it has been 6 to 12 months since PCI, we recommend continuing SAPT with either aspirin or clopidogrel until 1 year post-PCI, along with an OAC.
  - If it has been ≥12 months post-PCI, an OAC alone can be used long-term.
- For patients on APT for SIHD with no history of ACS but who had prior CABG surgery, the time since CABG surgery should be assessed. We recommend continuing aspirin (<100 mg/day) if <1 year post-CABG surgery and stopping aspirin if >1 year post-CABG surgery (62).

3. History of ACS

- Patients with ACS (unstable angina, non-ST-elevation myocardial infarction, and ST-elevation myocardial infarction) are usually treated with DAPT for 12 months after ACS. If these patients were previously on prasugrel or ticagrelor, we recommend switching to clopidogrel (see section 5.1.1. on General Principles).
  - If it has been ≤12 months since the ACS, our recommendation for most patients would be to stop aspirin, continue the $P2Y_{12}$i (with preference given to clopidogrel), and start an AC (with preference given to a DOAC for the reasons given in the previous text [see section 5]).
  - If it has been >12 months since the ACS, APT may be stopped and most patients can be treated with an AC alone.
  - For patients at high bleeding risk and low ischemic risk, shorter durations of APT can be considered.
  - At the clinician's discretion, selected patients felt to be at higher thrombotic risk due to: a) the nature of the coronary lesion; b) the type, location, number, or length of coronary stents; or c) other clinical factors, and low bleeding risk may continue SAPT (aspirin 81 mg daily or clopidogrel 75 mg daily) beyond 12 months while on an AC.

4. History of CVD

See section 5.2.3 for a brief overview of CVD and need for antithrombotic therapy.

- For patients on APT for prior TIA or cerebrovascular accident who develop VTE requiring AC therapy, the pathway recommends stopping all APT and treating with an AC alone (DOAC preferred) when considered safe from the perspective of hemorrhagic transformation, typically between 2 and 14 days following an acute event (93,121,122). Given that TIA is the diagnosis when no infarct or hemorrhage is noted on imaging, an AC can typically be initiated immediately.
- For patients who have undergone recent carotid endarterectomy, the pathway recommends stopping all APT and treating with an AC alone (DOAC preferred) when considered safe from risk of post-operative bleeding, typically 3 to 14 days after surgery.
- For patients with carotid stenting within the previous 1 to 3 months, our recommendation for most patients would be to stop aspirin, continue the $P2Y_{12}$i (clopidogrel preferred), and start an AC (DOAC preferred). If the standard duration of DAPT after carotid stenting has ended (usually 1 to 3 months), all APT may be stopped and most patients can be treated with an AC alone (96,97).

5. History of PAD

- Patients with PAD without prior intervention or with prior surgical repair are usually treated with SAPT (usually aspirin or clopidogrel) for primary or secondary prevention of ischemic events (myocardial infarction, stroke). For such patients presenting with VTE appropriate for an AC, the pathway recommends stopping all APT and treating with an AC alone (DOAC preferred).

- Patients with PAD who have been treated with endovascular intervention/stenting are usually treated with APT for 1 to 3 months. The type and duration of APT is less well-defined and standardized than for coronary interventions. For patients presenting with VTE appropriate for AC therapy, the pathway recommends continuing or switching to SAPT (either clopidogrel or aspirin, clopidogrel preferred) and treating with an AC (DOAC preferred). If the standard duration of DAPT after endovascular intervention/stenting has ended (usually 1 to 3 months), all APT may be stopped and most patients can be treated with an AC alone.

5.5. Periprocedural Management of Patient on AC Therapy Who Now Needs PCI

In general, the periprocedural management of patients on antithrombotic therapy for any invasive procedure is challenging and has been discussed extensively in a prior pathway document, given the complexities involved (123). This current section specifically discusses the periprocedural management of AC therapy and APT around the time of PCI. The main factors to consider include the bleeding risk of the procedure, thrombotic risk, and the overall urgency of the procedure. Reversal agents can be considered depending on the clinical scenario (97,124–127).

5.5.1. Preprocedural Considerations

1. If PCI is elective and can be delayed until treatment with AC therapy is complete (for instance, a low-risk patient with stable angina), then it is preferable to postpone the procedure until then. This situation is most applicable to VTE patients on limited-duration AC therapy because almost all patients with AF will need an OAC indefinitely.
2. In the setting of an emergency (e.g., ST-elevation myocardial infarction or high-risk non-ST-elevation myocardial infarction), AC therapy should be stopped, and PCI should be performed without delay. For patients taking a DOAC, activated clotting time may not be a reliable indicator of anticoagulation (128).
3. For patients awaiting elective or urgent PCI for whom it is safe to defer coronary angiography/PCI for a short time, we recommend the following:
   - For patients on a VKA, defer until the INR is ≤2.0 (some catheterization laboratories may use the lower threshold of ≤1.5). The threshold may also differ based on access choice (for instance, radial vs. femoral) (94,129).
   - For patients on a DOAC, defer based on recommendations in **Table 5.** This table also discusses the role

TABLE 5 Recommendations for Holding a DOAC for Elective PCI*† (102)

a. Apixaban
i. Transradial PCI
≥24 hours if creatinine clearance ≥30 ml/min
≥36 hours if creatinine clearance 15-29 ml/min
Guide duration by agent-specific anti-Xa level or ≥48 hours if creatinine clearance less than 15 ml/min
ii. Transfemoral PCI
≥48 hours if creatinine clearance ≥30 ml/min
Guide duration by agent-specific anti-Xa level or ≥72 hours if creatinine clearance less than 29 ml/min
b. Dabigatran
i. Transradial PCI
≥24 hours if creatinine clearance ≥80 ml/min
≥36 hours if creatinine clearance 50-79 ml/min
≥48 hours if creatinine clearance 30-49 ml/min
≥72 hours if creatinine clearance 15-29 ml/min
Guide duration by dTT or ≥96 hours if creatinine clearance less than 15 ml/min
ii. Transfemoral PCI
≥48 hours if creatinine clearance >80 ml/min
≥72 hours if creatinine clearance 50-79 ml/min
≥96 hours if creatinine clearance 30-49 ml/min
≥120 hours if creatinine clearance 15-29 ml/min
Guide duration by dTT if creatinine clearance less than 15 ml/min
c. Edoxban
i. Transradial PCI
≥24 hours if creatinine clearance ≥30 ml/min
≥36 hours if creatinine clearance 15-29 ml/min
Guide duration by agent-specific anti-Xa level or ≥48 hours if creatinine clearance less than 15 ml/min
ii. Transfemoral PCI
≥48 hours if creatinine clearance ≥30 ml/min
Guide duration by agent-specific anti-Xa level or ≥72 hours if creatinine clearance less than 29 ml/min
d. Rivaroxaban
i. Transradial PCI
≥24 hours if creatinine clearance ≥30 ml/min
≥36 hours if creatinine clearance 15-29 ml/min
Guide duration by agent-specific anti-Xa level or ≥48 hours if creatinine clearance less than 15 ml/min
ii. Transfemoral PCI
≥48 hours if creatinine clearance ≥30 ml/min
Guide duration by agent-specific anti-Xa level or ≥72 hours if creatinine clearance less than 29 ml/min

*Also see section 5.5.1., point 3 (130).
†For those on a DOAC, there is likely no value in bridging, particularly with LMWH because it has similar pharmacokinetic properties to DOAC.

DOAC = direct oral anticoagulant; dTT = diluted thrombin time; LMWH = low-molecular-weight heparin; PCI = percutaneous coronary intervention.

of agent-specific Factor Xa or dilute thrombin time levels in guiding preoperative interruption duration. Agent-specific Factor Xa assays may not be widely available. In the PAUSE (Perioperative Anticoagulation Use for Surgery Evaluation) study, among patients receiving apixaban, dabigatran, or rivaroxaban, a simple perioperative management strategy based on DOAC pharmacokinetic properties, procedure-associated bleeding risk, and the patient's creatinine clearance (CrCl) without coagulation function testing was associated with low rates of major bleeding and arterial thromboembolism (130).

- We recognize that these recommendations will differ based on operator and institutional practice, and they should be tailored as such. It is preferable, however, to have a standardized protocol to minimize the risk of errors.

4. For patients on a VKA presenting with ACS without ST-segment elevation who do not need coronary angiography urgently, it may be necessary to bridge with unfractionated heparin or LMWH in the preangiography time period per the 2014 AHA/ACC Guideline for the Management of Patients With Non-ST-Elevation Acute Coronary Syndromes, particularly as the INR tapers off (94). Unfractionated heparin may have a role in reducing recurrent ischemia/myocardial infarction, even among patients on OAC therapy (131–133). For those on a DOAC, there is likely no value in bridging, particularly with LMWH (which has some similar pharmacokinetic properties to DOACs).
5. All patients should receive aspirin 162 to 325 mg as per the 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction, preferably prior to the catheterization procedure (134,135).
6. A loading dose of a $P2Y_{12}$i should be administered in the periprocedural period. Because clopidogrel is the recommended agent in these patients, a 600-mg loading dose would be used (50).

5.5.2. Procedural Considerations

1. We recommend radial access and other feasible bleeding avoidance strategies (for instance, the use of vascular closure devices for femoral access) to minimize the risk of periprocedural and postprocedural bleeding, particularly in emergency situations in which upstream AC discontinuation is not possible (136). Radial access is also recommended when possible in elective PCI, given the lower bleeding risk (137). Crossover to femoral access may be necessary in 5% to 10% of cases (138).
2. For the purpose of the PCI itself, intraprocedural anticoagulation options include unfractionated heparin, LMWH, or bivalirudin. All 3 agents have a Class I recommendation in ACC/AHA guidelines; dosing guidelines should be followed (94,134,135).
3. A glycoprotein IIb/IIIa inhibitor or cangrelor may be considered based on anatomic and procedural characteristics (for instance, presence of fresh thrombus), particularly among patients not receiving pretreatment with a $P2Y_{12}$i. These medications will, however, likely increase bleeding risk (139,140).
4. As discussed in the previous text, even among patients with high bleeding risk, we recommend using the newest-generation DES over bare metal stents for PCI.

5.5.3. Post-Procedural Considerations

AC therapy should be reinitiated post-PCI after careful evaluation of the patient's bleeding risk and post-procedure complications.

1. From a bleeding perspective, particular emphasis should be given to assessing the access site for adequacy of hemostasis.
2. The following should also be factored into the decision-making: history of recent bleeding; body habitus (for example, obese patients who have undergone transfemoral access); qualitative or quantitative platelet abnormalities; and other abnormalities in coagulation studies.
3. Irrespective of the pre-PCI AC, we recommend using a DOAC post-PCI. If DOAC use is not feasible, then a VKA should be resumed/started.
4. In patients treated with a VKA post-PCI, only a small subset (for instance, those with high thromboembolic risk) should be considered for bridging with parenteral anticoagulation until the INR is in the therapeutic range. In those on a VKA not treated with bridging anticoagulation post-PCI, one should consider continuing low-dose aspirin with a $P2Y_{12}$i until the INR is at goal, after which time aspirin can be stopped. As discussed earlier, although the default approach is for dual therapy, because the risk of stent-related thrombotic complications is greatest in the first month post-PCI, one may consider use of aspirin (81 mg/day) for up to 30 days in those with high thrombotic risk and low bleeding risk.
5. Timing of reinitiation of AC therapy:
   - In most patients, AC therapy can be resumed within 24 hours after PCI. In some patients, this could be as early as the evening of the day of the PCI, but timing will depend on operator and institutional preferences. This decision should be made in collaboration with the interventional cardiologist and managing teams.
   - Post-PCI dosing of AC therapy will depend on the agent used. For a VKA, the dose associated with prior therapeutic INR can be resumed. For DOACs and LMWH, the dose may need to be adjusted based on post-PCI renal function. In addition,

specifically for rivaroxaban use in AF (based on the PIONEER-AF PCI trial), the standard dose should be 15 mg daily if the CrCl is >50 mL/min, with a renally adjusted dose of 10 mg daily if the CrCl is 30-50 mL/min (11,31). Once APT is stopped, the dose of rivaroxaban should be readjusted to the U.S. Food and Drug Administration-approved dose (20 mg daily if there is no renal adjustment, 15 mg if renally adjusted). For all other DOACs, the appropriate U.S. Food and Drug Administration-approved doses can be used as part of combination therapy, as outlined in **Tables 2 and 4**.

- For patients unable to tolerate or take oral medications for a prolonged period post-PCI (for instance, intubated patients), the use of a parenteral AC, such as unfractionated heparin or LMWH, can be considered within 24 hours of PCI (for those at low bleeding risk) or within 48 to 72 hours of PCI (for those at high bleeding risk) (118). Alternatively, crushed tablets can be considered (141).

6. For patients who develop major bleeding, appropriate measures should be initiated to control bleeding. In certain situations, it may be necessary to use appropriate reversal agents to control the bleeding and stabilize the patient (124-127,142).

6. DISCUSSION

The primary objective of this document is to provide a framework for decision-making among patients who require concomitant use of an AC and APT. This is a complex topic, and we have attempted to cite the literature to offer direct guidance when possible and to highlight areas in which clinical judgement is needed. We hope this document will aid in the management of this common yet challenging subset of patients.

PRESIDENT AND STAFF

REFERENCES

1. Januzzi JL Jr., Ahmad T, Binder LG, et al. 2019 methodology for creating expert consensus decision pathways: a report of the American College of Cardiology. J Am Coll Cardiol. 2019;74:1138–50.

2. Lloyd-Jones DM, Wang TJ, Leip EP, et al. Lifetime risk for development of atrial fibrillation: the Framingham Heart Study. Circulation. 2004;110:1042–6.

3. Heeringa J, van der Kuip DA, Hofman A, et al. Prevalence, incidence and lifetime risk of atrial fibrillation: the Rotterdam study. Eur Heart J. 2006;27:949–53.

4. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. Stroke. 1991;22:983–8.

5. Centers for Disease Control and Prevention. What is atrial fibrillation? Available at: https://www.cdc.gov/heartdisease/atrial_fibrillation.htm?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fdhdsp%2Fdata_statistics%2Ffact_sheets%2Ffs_atrial_fibrillation.htm. Accessed December 16, 2020.

6. Dulli DA, Stanko H, Levine RL. Atrial fibrillation is associated with severe acute ischemic stroke. Neuroepidemiology. 2003;22:118–23.

7. Kimura K, Minematsu K, Yamaguchi T, et al. Atrial fibrillation as a predictive factor for severe stroke and early death in 15,831 patients with acute ischaemic stroke. J Neurol Neurosurg Psychiatry. 2005;76:679–83.

8. Hart RG, Benavente O, McBride R, et al. Antithrombotic therapy to prevent stroke in patients with atrial fibrillation: a meta-analysis. Ann Intern Med. 1999;131:492–501.

9. van Walraven C, Hart RG, Singer DE, et al. Oral anticoagulants vs aspirin in nonvalvular atrial fibrillation: an individual patient meta-analysis. JAMA. 2002;288:2441–8.

10. Connolly SJ, Eikelboom J, Joyner C, et al. Apixaban in patients with atrial fibrillation. N Engl J Med. 2011;364:806–17.

11. January CT, Wann LS, Calkins H, et al. 2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol. 2019;74:104–32.

12. Nabauer M, Gerth A, Limbourg T, et al. The Registry of the German Competence NETwork on Atrial Fibrillation: patient characteristics and initial management. Europace. 2009;11:423–34.

13. Steinberg BA, Kim S, Piccini JP, et al. Use and associated risks of concomitant aspirin therapy with oral anticoagulation in patients with atrial fibrillation: insights from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF) Registry. Circulation. 2013;128:721–8.

14. Fox KAA, Velentgas P, Camm AJ, et al. Outcomes associated with oral anticoagulants plus antiplatelets in patients with newly diagnosed atrial fibrillation. JAMA Netw Open. 2020;3:e200107.

15. Nieuwlaat R, Capucci A, Camm AJ, et al. Atrial fibrillation management: a prospective survey in ESC member countries: the Euro Heart Survey on Atrial Fibrillation. Eur Heart J. 2005;26:2422–34.

16. Johnson SG, Witt DM, Eddy TR, et al. Warfarin and antiplatelet combination use among commercially insured patients enrolled in an anticoagulation management service. Chest. 2007;131:1500–7.

17. ACTIVE Writing Group of the ACTIVE Investigators, Connolly S, Pogue J, Hart R, et al. Clopidogrel plus aspirin versus oral anticoagulation for atrial fibrillation in the Atrial fibrillation Clopidogrel Trial with Irbesartan for prevention of Vascular Events (ACTIVE W): a randomised controlled trial. Lancet. 2006;367:1903–12.

18. Depta JP, Cannon CP, Fonarow GC, et al. Patient characteristics associated with the choice of triple antithrombotic therapy in acute coronary syndromes. Am J Cardiol. 2009;104:1171–8.

19. Alotaibi GS, Wu C, Senthilselvan A, et al. Secular trends in incidence and mortality of acute venous thromboembolism: the AB-VTE population-based study. Am J Med. 2016;129:879. e19–25.

20. Kearon C, Ageno W, Cannegieter SC, et al. Categorization of patients as having provoked or unprovoked venous thromboembolism: guidance from the SSC of ISTH. J Thromb Haemost. 2016;14:1480–3.

21. Kearon C, Akl EA, Ornelas J, et al. Antithrombotic therapy for VTE disease: CHEST guideline and expert panel report. Chest. 2016;149:315–52.

22. Baglin T, Luddington R, Brown K, et al. Incidence of recurrent venous thromboembolism in relation to clinical and thrombophilic risk factors: prospective cohort study. Lancet. 2003;362:523–6.

23. Pulmonary Embolism Prevention (PEP) trial Collaborative Group. Prevention of pulmonary embolism and deep vein thrombosis with low dose aspirin: Pulmonary Embolism Prevention (PEP) trial. Lancet. 2000;355:1295–302.

24. Kunutsor SK, Seidu S, Khunti K. Statins and primary prevention of venous thromboembolism: a systematic review and meta-analysis. Lancet Haematol. 2017;4:e83–93.

25. Eikelboom JW, Connolly SJ, Bosch J, et al. Rivaroxaban with or without aspirin in stable cardiovascular disease. N Engl J Med. 2017;377:1319–30.

26. Leon MB, Baim DS, Popma JJ, et al., Stent Anticoagulation Restenosis Study Investigators. A clinical trial comparing three antithrombotic-drug regimens after coronary-artery stenting. N Engl J Med. 1998;339:1665–71.

27. Dentali F, Douketis JD, Lim W, et al. Combined aspirin-oral anticoagulant therapy compared with oral anticoagulant therapy alone among patients at risk for cardiovascular disease: a meta-analysis of randomized trials. Arch Intern Med. 2007;167:117–24.

28. Hansen ML, Sorensen R, Clausen MT, et al. Risk of bleeding with single, dual, or triple therapy with warfarin, aspirin, and clopidogrel in patients with atrial fibrillation. Arch Intern Med. 2010;170:1433–41.

29. Lopes RD, Heizer G, Aronson R, et al. Antithrombotic therapy after acute coronary syndrome or PCI in atrial fibrillation. N Engl J Med. 2019;380:1509–24.

30. Dewilde WJ, Oirbans T, Verheugt FW, et al. Use of clopidogrel with or without aspirin in patients taking oral anticoagulant therapy and undergoing percutaneous coronary intervention: an open-label, randomised, controlled trial. Lancet. 2013;381:1107–15.

31. Gibson CM, Mehran R, Bode C, et al. Prevention of bleeding in patients with atrial fibrillation undergoing PCI. N Engl J Med. 2016;375:2423–4.

32. Cannon CP, Bhatt DL, Oldgren J, et al. Dual antithrombotic therapy with dabigatran after PCI in atrial fibrillation. N Engl J Med. 2017;377:1513–24.

33. Vranckx P, Valgimigli M, Eckardt L, et al. Edoxaban-based versus vitamin K antagonist-based antithrombotic regimen after successful coronary stenting in patients with atrial fibrillation (ENTRUST-AF PCI): a randomised, open-label, phase 3b trial. Lancet. 2019;394:1335–43.

34. Dans AL, Connolly SJ, Wallentin L, et al. Concomitant use of antiplatelet therapy with dabigatran or warfarin in the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) trial. Circulation. 2013;127:634–40.

35. Faxon DP, Eikelboom JW, Berger PB, et al. Antithrombotic therapy in patients with atrial fibrillation undergoing coronary stenting: a North American perspective: executive summa-ry. Circ Cardiovasc Interv. 2011;4:522–34.

36. Paikin JS, Wright DS, Crowther MA, et al. Triple antithrombotic therapy in patients with atrial fibrillation and coronary artery stents. Circulation. 2010;121:2067–70.

37. Steg PG, Huber K, Andreotti F, et al. Bleeding in acute coronary syndromes and percutaneous coronary interventions: position paper by the Working Group on Thrombosis of the European Society of Cardiology. Eur Heart J. 2011;32:1854–64.

38. Suh JW, Mehran R, Claessen BE, et al. Impact of in-hospital major bleeding on late clinical outcomes after primary percutaneous coronary intervention in acute myocardial infarction the HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) trial. J Am Coll Cardiol. 2011;58:1750–6.

39. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2019;73:e285–350.

40. Golwala HB, Cannon CP, Steg PG, et al. Safety and efficacy of dual vs. triple antithrombotic therapy in patients with atrial fibrillation following percutaneous coronary intervention: a systematic review and meta-analysis of randomized clinical trials. Eur Heart J. 2018;39:1726–35a.

41. Capodanno D, Huber K, Mehran R, et al. Management of antithrombotic therapy in atrial fibrillation patients undergoing PCI: JACC state-of-the-art review. J Am Coll Cardiol. 2019;74:83–99.

42. Baumgartner H, Falk V, Bax JJ, et al. 2017 ESC/EACTS guidelines for the management of valvular heart disease. Eur Heart J. 2017;38:2739–91.

43. Ordi-Ros J, Saez-Comet L, Perez-Conesa M, et al. Rivaroxaban versus vitamin K antagonist in antiphospholipid syndrome: a randomized noninferiority trial. Ann Intern Med. 2019;171:685–94.

44. Pengo V, Denas G, Zoppellaro G, et al. Rivaroxaban vs warfarin in high-risk patients with antiphospholipid syndrome. Blood. 2018;132:1365–71.

45. Mega JL, Braunwald E, Mohanavelu S, et al. Rivaroxaban versus placebo in patients with acute coronary syndromes (ATLAS ACS-TIMI 46): a randomised, double-blind, phase II trial. Lancet. 2009;374:29–38.

46. Ariotti S, Adamo M, Costa F, et al. Is bare-metal stent implantation still justifiable in high bleeding risk patients undergoing percutaneous coronary intervention?: a pre-specified analysis from the ZEUS trial. J Am Coll Cardiol Intv. 2016;9:426–36.

47. Urban P, Meredith IT, Abizaid A, et al. Polymer-free drug-coated coronary stents in patients at high bleeding risk. N Engl J Med. 2015;373:2038–47.

48. Sabate M, Cequier A, Iniguez A, et al. Everolimus-eluting stent versus bare-metal stent in ST-segment elevation myocardial infarction (EXAMINATION): 1 year results of a randomised controlled trial. Lancet. 2012;380:1482–90.

49. Lip GY, Windecker S, Huber K, et al. Management of antithrombotic therapy in atrial fibrillation patients presenting with acute coronary syndrome and/or undergoing percutaneous coronary or valve interventions: a joint consensus document of the European Society of Cardiology Working Group on Thrombosis, European Heart Rhythm Association (EHRA), European Association of Percutaneous Cardiovascular Interventions (EAPCI) and European Association of Acute Cardiac Care (ACCA) endorsed by the Heart Rhythm Society (HRS) and Asia-Pacific Heart Rhythm Society (APHRS). Eur Heart J. 2014;35:3155–79.

50. Levine GN, Bates ER, Bittl JA, et al. 2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2016;68:1082–115.

51. Baber U, Mehran R, Giustino G, et al. Coronary thrombosis and major bleeding after PCI with drug-eluting stents: risk scores from PARIS. J Am Coll Cardiol. 2016;67:2224–34.

52. Yeh RW, Secemsky EA, Kereiakes DJ, et al. Development and validation of a prediction rule for benefit and harm of dual antiplatelet therapy beyond 1 year after percutaneous coronary intervention. JAMA. 2016;315:1735–49.

53. Fiedler KA, Maeng M, Mehilli J, et al. Duration of triple therapy in patients requiring oral anticoagulation after drug-eluting stent implantation: the ISAR-TRIPLE trial. J Am Coll Cardiol. 2015;65:1619–29.

54. Lopes RD, Leonardi S, Wojdyla DM, et al. Stent thrombosis in patients with atrial fibrillation undergoing coronary stenting in the AUGUSTUS trial. Circulation. 2019;141:781–3.

55. Angiolillo DJ, Goodman SG, Bhatt DL, et al. Antithrombotic therapy in patients with atrial fibrillation treated with oral anticoagulation undergoing percutaneous coronary intervention. Circulation. 2018;138:527–36.

56. Lip GYH, Collet JP, Haude M, et al. 2018 Joint European consensus document on the management of antithrombotic therapy in atrial fibrillation patients presenting with acute coronary syndrome and/or undergoing percutaneous cardiovascular interventions: a joint consensus document of the European Heart Rhythm Association (EHRA), European Society of Cardiology Working Group on Thrombosis, European Association of Percutaneous Cardiovascular Interventions (EAPCI), and European Association of Acute Cardiac Care (ACCA) endorsed by the Heart Rhythm Society (HRS), Asia-Pacific Heart Rhythm Society (APHRS), Latin America Heart Rhythm Society (LAHRS), and Cardiac Arrhythmia Society of Southern Africa (CASSA). Europace. 2019;21:192–3.

57. Collet JP, Cuisset T, Range G, et al. Bedside monitoring to adjust antiplatelet therapy for coronary stenting. N Engl J Med. 2012;367:2100–9.

58. Price MJ, Berger PB, Teirstein PS, et al. Standard- vs high-dose clopidogrel based on platelet function testing after percutaneous coronary intervention: the GRAVITAS randomized trial. JAMA. 2011;305:1097–105.

59. Trenk D, Stone GW, Gawaz M, et al. A randomized trial of prasugrel versus clopidogrel in patients with high platelet reactivity on clopidogrel after elective percutaneous coronary intervention with implantation of drug-eluting stents: results of the TRIGGER-PCI (Testing Platelet Reactivity In Patients Undergoing Elective Stent Placement on Clopidogrel to Guide Alternative Therapy With Prasugrel) study. J Am Coll Cardiol. 2012;59:2159–64.

60. Claassens DMF, Vos GJA, Bergmeijer TO, et al. A genotype-guided strategy for oral P2Y12 inhibitors in primary PCI. N Engl J Med. 2019;381:1621–31.

61. Levine GN, Bates ER, Blankenship JC, et al. 2015 ACC/AHA/SCAI focused update on primary percutaneous coronary intervention for patients with ST-elevation myocardial Infarction: an update of the 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention and the 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. J Am Coll Cardiol. 2016;67:1235–50.

62. Yasuda S, Kaikita K, Akao M, et al. Antithrombotic therapy for atrial fibrillation with stable coronary disease. N Engl J Med. 2019;381:1103–13.

63. Matsumura-Nakano Y, Shizuta S, Komasa A, et al. Open-label randomized trial comparing oral anticoagulation with and without single antiplatelet therapy in patients with atrial fibrillation and stable coronary artery disease beyond 1 year after coronary stent implantation. Circulation. 2019;139:604–16.

64. Berry NC, Mauri L, Steg PG, et al. Effect of lesion complexity and clinical risk factors on the efficacy and safety of dabigatran dual therapy versus warfarin triple therapy in atrial fibrillation after percutaneous coronary intervention: a subgroup analysis from the REDUAL PCI trial. Circ Cardiovasc Interv. 2020;13:e008349.

65. Rossini R, Musumeci G, Lettieri C, et al. Long-term outcomes in patients undergoing coronary stenting on dual oral antiplatelet treatment requiring oral anticoagulant therapy. Am J Cardiol. 2008;102:1618–23.

66. Angiolillo DJ, Gibson CM, Cheng S, et al. Differential effects of omeprazole and pantoprazole on the pharmacodynamics and pharmacokinetics of clopidogrel in healthy subjects: randomized, placebo-controlled, crossover comparison studies. Clin Pharmacol Ther. 2011;89:65–74.

67. Ho PM, Maddox TM, Wang L, et al. Risk of adverse outcomes associated with concomitant use of clopidogrel and proton pump inhibitors following acute coronary syndrome. JAMA. 2009;301:937–44.

68. Bhatt DL, Cryer BL, Contant CF, et al. Clopidogrel with or without omeprazole in coronary artery disease. N Engl J Med. 2010;363:1909–17.

69. Chatterjee S, Sardar P, Biondi-Zoccai G, et al. New oral anticoagulants and the risk of intracranial hemorrhage: traditional and Bayesian meta-analysis and mixed treatment comparison of randomized trials of new oral anticoagulants in atrial fibrillation. JAMA Neurol. 2013;70:1486–90.

70. Capodanno D, Angiolillo DJ. Management of antiplatelet and anticoagulant therapy in patients with atrial fibrillation in the setting of acute coronary syndromes or percutaneous coronary interventions. Circ Cardiovasc Interv. 2014;7:113–24.

71. Lopes RD, Hong H, Harskamp RE, et al. Optimal antithrombotic regimens for patients with atrial fibrillation undergoing percutaneous coronary intervention: an updated network meta-analysis. JAMA Cardiol. 2020;5:1–8.

72. Sarafoff N, Martischnig A, Wealer J, et al. Triple therapy with aspirin, prasugrel, and vitamin K antagonists in patients with drug-eluting stent implantation and an indication for oral anticoagulation. J Am Coll Cardiol. 2013;61:2060–6.

73. Oldgren J, Steg PG, Hohnloser SH, et al. Dabigatran dual therapy with ticagrelor or clopidogrel after percutaneous coronary intervention in atrial fibrillation patients with or without acute coronary syndrome: a subgroup analysis from the RE-DUAL PCI trial. Eur Heart J. 2019;40:1553–62.

74. Genereux P, Rutledge DR, Palmerini T, et al. Stent thrombosis and dual antiplatelet therapy interruption with everolimus-eluting stents: insights from the Xience V Coronary Stent System trials. Circ Cardiovasc Interv. 2015;8:e001362.

75. Silber S, Kirtane AJ, Belardi JA, et al. Lack of association between dual antiplatelet therapy use and stent thrombosis between 1 and 12 months following resolute zotarolimus-eluting stent implantation. Eur Heart J. 2014;35:1949–56.

76. van Werkum JW, Heestermans AA, Zomer AC, et al. Predictors of coronary stent thrombosis: the Dutch Stent Thrombosis Registry. J Am Coll Cardiol. 2009;53:1399–409.

77. Montalescot G, Brieger D, Dalby AJ, et al. Duration of dual antiplatelet therapy after coronary stenting: a review of the evidence. J Am Coll Cardiol. 2015;66:832–47.

78. Boehringer Ingelheim Pharmaceuticals, Inc. Pradaxa (dabigatran etexilate) [package insert]. Revised November 2019. Available at: https://docs.boehringer-ingelheim.com/Prescribing%20Information/PIs/Pradaxa/Pradaxa.pdf. Accessed June 4, 2020.

79. Daiichi Sankyo, Inc. Savaysa (edoxaban) [package insert]. Revised August 2019. Available at: https://dsi.com/prescribing-information-portlet/getPIContent?productName=Savaysa&inline=true. Accessed June 4, 2020.

80. Janssen Pharmaceuticals, Inc. Xarelto (rivaroxaban) [package insert]. Revised November 2019. Available at: http://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/XARELTO-pi.pdf. Accessed June 4, 2020.

81. Bristol-Myers Squibb Company. Coumadin (warfarin sodium) [package insert]. Revised August 2017. Available at: https://packageinserts.bms.com/pi/pi_coumadin.pdf. Accessed June 4, 2020.

82. January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol. 2014;64:e1–76.

83. Mulder BA, Van Gelder IC, Rienstra M. Device-detected atrial fibrillation. Circulation. 2019;139:2513–5.

84. Apostolakis S, Lane DA, Guo Y, et al. Performance of the HEMORR(2)HAGES, ATRIA, and HAS-BLED bleeding risk-prediction scores in patients with atrial fibrillation undergoing anticoagulation: the AMADEUS (evaluating the use of SR34006 compared to warfarin or acenocoumarol in patients with atrial fibrillation) study. J Am Coll Cardiol. 2012;60:861–7.

85. Pisters R, Lane DA, Nieuwlaat R, et al. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro Heart Survey. Chest. 2010;138:1093–100.

86. Gage BF, Yan Y, Milligan PE, et al. Clinical classification schemes for predicting hemorrhage: results from the National Registry of Atrial Fibrillation (NRAF). Am Heart J. 2006;151:713–9.

87. Fang MC, Go AS, Chang Y, et al. A new risk scheme to predict warfarin-associated hemorrhage: the ATRIA (Anticoagulation and Risk Factors in Atrial Fibrillation) Study. J Am Coll Cardiol. 2011;58:395–401.

88. Urban P, Mehran R, Colleran R, et al. Defining high bleeding risk in patients undergoing percutaneous coronary intervention. Circulation. 2019;140:240–61.

89. Ogilvie IM, Newton N, Welner SA, et al. Underuse of oral anticoagulants in atrial fibrillation: a systematic review. Am J Med. 2010;123:638–45.e4.

90. Holmes DR Jr., Kar S, Price MJ, et al. Prospective randomized evaluation of the Watchman Left Atrial Appendage Closure device in patients with atrial fibrillation versus long-term warfarin therapy: the PREVAIL trial. J Am Coll Cardiol. 2014;64:1–12.

91. Holmes DR, Reddy VY, Turi ZG, et al. Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomised non-inferiority trial. Lancet. 2009;374:534–42.

92. Arnett DK, Blumenthal RS, Albert MA, et al. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2019;74:e177–232.

93. Hindricks G, Potpara TS, Dagres N, et al. 2020 ESC guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS): The Task Force for the Diagnosis and Management of Atrial Fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. Eur Heart J. 2020. https://doi.org/10.1093/eurheartj/ehaa612.

94. Amsterdam EA, Wenger NK, Brindis RG, et al. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014;64:e139–228.

95. DeSimone CV, Graff-Radford J, El-Harasis MA, et al. Cerebral amyloid angiopathy: diagnosis, clinical implications, and management strategies in atrial fibrillation. J Am Coll Cardiol. 2017;70:1173–82.

96. Liapis CD, Bell PR, Mikhailidis D, et al. ESVS guidelines. Invasive treatment for carotid stenosis: indications, techniques. Eur J Vasc Endovasc Surg. 2009;37:1–19.

97. Ricotta JJ, Aburahma A, Ascher E, et al. Updated Society for Vascular Surgery guidelines for management of extracranial carotid disease. J Vasc Surg. 2011;54:e1–31.

98. Weitz JI, Lensing AWA, Prins MH, et al. Rivaroxaban or aspirin for extended treatment of venous thromboembolism. N Engl J Med. 2017;376:1211–22.

99. Andrade JG, Deyell MW, Khoo C, et al. Risk of bleeding on triple antithrombotic therapy after percutaneous coronary intervention/stenting: a systematic review and meta-analysis. Can J Cardiol. 2013;29:204–12.

100. Lamberts M, Olesen JB, Ruwald MH, et al. Bleeding after initiation of multiple antithrombotic drugs, including triple therapy, in atrial fibrillation patients following myocardial infarction and coronary intervention: a nationwide cohort study. Circulation. 2012;126:1185–93.

101. Riva L, Ageno W, Di Pasquale G, et al. Antithrombotic therapy for patients with an indication for oral anticoagulation undergoing percutaneous coronary intervention with stent: the case of venous thromboembolism. Int J Cardiol. 2018;269:75–9.

102. Farge D, Frere C, Connors JM, et al. 2019 international clinical practice guidelines for the treatment and prophylaxis of venous thromboembolism in patients with cancer. Lancet Oncol. 2019;20:e566–81.

103. Raskob GE, van Es N, Verhamme P, et al. Edoxaban for the treatment of cancer-associated venous thromboembolism. N Engl J Med. 2018;378:615–24.

104. Young AM, Marshall A, Thirlwall J, et al. Comparison of an oral factor Xa inhibitor with low molecular weight heparin in patients with cancer with venous thromboembolism: results of a randomized trial (SELECT-D). J Clin Oncol. 2018;36:2017–23.

105. McBane RD 2nd, Wysokinski WE, Le-Rademacher JG, et al. Apixaban and dalteparin in active malignancy-associated venous thromboembolism: The ADAM VTE trial. J Thromb Haemost. 2020;18:411–21.

106. Agnelli G, Becattini C, Meyer G, et al. Apixaban for the treatment of venous thromboembolism associated with cancer. N Engl J Med. 2020;382:1599–607.

107. Rodger MA, Le Gal G, Anderson DR, et al. Validating the HERDOO2 rule to guide treatment duration for women with unprovoked venous thrombosis: multinational prospective cohort management study. BMJ. 2017;356:j1065.

108. Raj L, Presles E, Le Mao R, et al., PADIS-PE Investigators. Evaluation of venous thromboembolism recurrence scores in an unprovoked pulmonary embolism population: a post-hoc analysis of the PADIS-PE trial. Am J Med. 2020;133:e406–21.

109. Tosetto A, Testa S, Martinelli I, et al. External validation of the DASH prediction rule: a retrospective cohort study. J Thromb Haemost. 2017;15:1963–70.

110. Boehringer Ingelheim Limited. Pradaxa (dabigatran) [Summary of product characteristics]. Revised December 2019. Available at: https://www.medicines.org.uk/emc/product/4703/smpc#companyDetails. Accessed February 25, 2020.

111. Pfizer Labs. Fragmin (dalteparin sodium) [package insert]. Revised May 2019. Available at: http://labeling.pfizer.com/ShowLabeling.aspx?id=2293. Accessed June 4, 2019.

112. Sanofi. Lovenox (enoxaparin sodium) [package insert]. December 2018. Available at: http://products.sanofi.us/Lovenox/Lovenox.pdf/. Accessed June 4, 2019.

113. National Comprehensive Cancer Network Guidelines Version 1.2019. Cancer-associated venous thromboembolic disease. Available from: https://www.nccn.org/professionals/physician_gls/pdf/vte.pdf. Accessed June 4, 2019.

114. Bristol-Myers Squibb Company. Eliquis (apixaban) [package insert]. Revised November 2019. Available at: https://packageinserts.bms.com/pi/pi_eliquis.pdf. Accessed January 22, 2019.

115. Chai-Adisaksopha C, Crowther M, Isayama T, et al. The impact of bleeding complications in patients receiving target-specific oral anticoagulants: a systematic review and meta-analysis. Blood. 2014;124:2450–8.

116. Witt DM, Nieuwlaat R, Clark NP, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: optimal management of anticoagulation therapy. Blood Adv. 2018;2:3257–91.

117. Lee AY, Levine MN, Baker RI, et al. Low-molecular-weight heparin versus a coumarin for the prevention of recurrent venous thromboembolism in patients with cancer. N Engl J Med. 2003;349:146–53.

118. Lee AYY, Kamphuisen PW, Meyer G, et al. Tinzaparin vs Warfarin for treatment of acute venous thromboembolism in patients with active cancer: a randomized clinical trial. JAMA. 2015;314:677–86.

119. Agnelli G, Buller HR, Cohen A, et al. Apixaban for extended treatment of venous thromboembolism. N Engl J Med. 2013;368:699–708.

120. The Medical Research Council's General Practice Research Framework. Thrombosis prevention trial: randomised trial of low-intensity oral anticoagulation with warfarin and low-dose aspirin in the primary prevention of ischaemic heart disease in men at increased risk. Lancet. 1998;351:233–41.

121. Lip GYH, Banerjee A, Boriani G, et al. Antithrombotic therapy for atrial fibrillation: CHEST Guideline and Expert Panel Report. Chest. 2018;154:1121–201.

122. Kernan WN, Ovbiagele B, Black HR, et al. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2014;45:2160–236.

123. Doherty JU, Gluckman TJ, Hucker WJ, et al. 2017 ACC expert consensus decision pathway for periprocedural management of anticoagulation in patients with nonvalvular atrial fibrillation: a report of the American College of Cardiology Clinical Expert Consensus Document Task Force. J Am Coll Cardiol. 2017;69:871–98.

124. Cuker A, Burnett A, Triller D, et al. Reversal of direct oral anticoagulants: guidance from the Anticoagulation Forum. Am J Hematol. 2019;94:697–709.

125. Raval AN, Cigarroa JE, Chung MK, et al. Management of patients on non-vitamin K antagonist oral anticoagulants in the acute care and periprocedural setting: a scientific statement from the American Heart Association. Circulation. 2017;135:e604–33.

126. Godier A, Martin AC. Specific antidotes for direct oral anticoagulant reversal: case closed or cold case? Circulation. 2019;140:1445–7.

127. Tomaselli GF, Mahaffey KW, Cuker A, et al. 2020 ACC expert consensus decision pathway on management of bleeding in patients on oral anticoagulants: a report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol. 2020;76:594–622.

128. Heidbuchel H, Verhamme P, Alings M, et al. Updated European Heart Rhythm Association practical guide on the use of non-vitamin K antagonist anticoagulants in patients with non-valvular atrial fibrillation. Europace. 2015;17:1467–507.

129. Bashore TM, Balter S, Barac A, et al. 2012 American College of Cardiology Foundation/Society for Cardiovascular Angiography and Interventions expert consensus document on cardiac catheterization laboratory standards update: a report of the American College of Cardiology Foundation Task Force on Expert Consensus documents developed in collaboration with the Society of Thoracic Surgeons and Society for Vascular Medicine. J Am Coll Cardiol. 2012;59:2221–305.

130. Douketis JD, Spyropoulos AC, Duncan J, et al. Perioperative management of patients with atrial fibrillation receiving a direct oral anticoagulant. JAMA Intern Med. 2019;179:1469–7.

131. Brener SJ, Moliterno DJ, Lincoff AM, et al. Relationship between activated clotting time and ischemic or hemorrhagic complications: analysis of 4 recent randomized clinical trials of percutaneous coronary intervention. Circulation. 2004;110:994–8.

132. Montalescot G, Cohen M, Salette G, et al. Impact of anticoagulation levels on outcomes in patients undergoing elective percutaneous coronary intervention: insights from the STEEPLE trial. Eur Heart J. 2008;29:462–71.

133. Chang RJ, Doherty TM, Goldberg SL. How does warfarin affect the activated coagulation time? Am Heart J. 1998;136:477–9.

134. O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2013;61:e78–140.

135. Levine GN, Bates ER, Blankenship JC, et al. 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. J Am Coll Cardiol. 2011;58:e44–122.

136. Chhatriwalla AK, Amin AP, Kennedy KF, et al. Association between bleeding events and in-hospital mortality after percutaneous coronary intervention. JAMA. 2013;309:1022–9.

137. Roffi M, Patrono C, Collet JP, et al. 2015 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). Eur Heart J. 2016;37:267–315.

138. Pandie S, Mehta SR, Cantor WJ, et al. Radial versus femoral access for coronary angiography/intervention in women with acute coronary syndromes: insights from the RIVAL trial (Radial Vs femorAL access for coronary intervention). J Am Coll Cardiol Cardiovasc Interv. 2015;8:505–12.

139. Vaduganathan M, Harrington RA, Stone GW, et al. Cangrelor with and without glycoprotein IIb/IIIa inhibitors in patients undergoing percutaneous coronary intervention. J Am Coll Cardiol. 2017;69:176–85.

140. Abtan J, Steg PG, Stone GW, et al. Efficacy and safety of cangrelor in preventing periprocedural complications in patients with stable angina and acute coronary syndromes undergoing percutaneous coronary intervention: the CHAMPION PHOENIX trial. J Am Coll Cardiol Cardiovasc Interv. 2016;9:1905–13.

141. Song Y, Chang M, Suzuki A, et al. Evaluation of crushed tablet for oral administration and the effect of food on apixaban pharmacokinetics in healthy adults. Clin Ther. 2016;38:1674–16785.e1.

142. Tomaselli GF, Mahaffey KW, Cuker A, et al. ACC expert consensus decision pathway on management of bleeding in patients on oral anticoagulants: a report of the American College of Cardiology Solution Set Oversight Committee. Am Coll Cardio. 2020;76:594–622.

KEY WORDS ACC Expert Consensus Decision Pathway, anticoagulant therapy, antiplatelet therapy, atherosclerotic cardiovascular disease, atrial fibrillation, DOAC, percutaneous coronary intervention, venous thromboembolism

APPENDIX 1. AUTHOR RELATIONSHIPS WITH INDUSTRY AND OTHER ENTITIES (RELEVANT) — 2020 EXPERT CONSENSUS DECISION PATHWAY FOR ANTICOAGULANT AND ANTIPLATELET THERAPY IN PATIENTS WITH ATRIAL FIBRILLATION OR VENOUS THROMBOEMBOLISM UNDERGOING PERCUTANEOUS CORONARY INTERVENTION OR WITH ATHEROSCLEROTIC CARDIOVASCULAR DISEASE RELATIONSHIPS WITH INDUSTRY AND OTHER ENTITIES

To avoid actual, potential, or perceived conflicts of interest that may arise as a result of industry relationships or personal interests among the writing committee, all members of the writing committee, as well as peer reviewers of the document, are asked to disclose all current healthcare-related relationships, including those existing 12 months before initiation of the writing effort. The ACC Task Force on Expert Consensus Decision Pathways reviews these disclosures to determine what companies make products (on market or in development) that pertain to the document under development. Based on this information, a writing committee is formed to include a majority of members with no *relevant* relationships with industry (RWI), led by a chair with no *relevant* RWI. RWI is reviewed on all conference calls and updated as changes occur. Author RWI pertinent to this document is disclosed in the table below and peer reviewer RWI is disclosed in Appendix 2. Additionally, to ensure complete transparency, authors' *comprehensive disclosure information*—including RWI not pertinent to this document—is available in Supplemental Appendix 1. Disclosure information for the ACC Task Force on Expert Consensus Decision Pathways is also available online at, as well as the ACC disclosure policy for document development.

Committee Member	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Dharam J. Kumbhani *(Chair)*	UT Southwestern Medical Center—Assistant Professor of Medicine	None	None	None	None	None	None
Christopher P. Cannon (*Vice-Chair*)	Brigham and Women's Hospital—Senior Physician; Harvard Medical School—Professor of Medicine	■ Boehringer Ingelheim* ■ Bristol-Myers Squibb ■ Merck* ■ Pfizer ■ Regeneron/ Sanofi*	None	None	■ Boehringer Ingelheim* ■ Bristol-Myers Squibb* ■ Daiichi Sankyo* ■ Janssen Pharmaceuticals* ■ Merck*	None	None
Craig J. Beavers	University of Kentucky College of Pharmacy—Assistant Professor	None	None	None	None	None	None
Deepak L. Bhatt	Brigham and Women's Hospital—Executive Director, Interventional Cardiovascular Programs; Harvard Medical School—Professor of Medicine	None	None	None	■ AstraZeneca* ■ Bristol-Myers Squibb* ■ Chiesi* ■ Eli Lilly and Company* ■ Pfizer* ■ Roche* ■ Sanofi-Aventis*	Merck†	None
Adam Cuker	University of Pennsylvania—Associate Professor of Medicine and Pathology and Laboratory Medicine	None	None	None	■ Bayer ■ Pfizer ■ Sanofi-Aventis	None	None
Ty J. Gluckman	Providence Heart Institute, Providence St. Joseph Health—Medical Director, Center for Cardiovascular Analytics, Research and Data Science (CARDS); Johns Hopkins Hospital—Adjunct Faculty, Ciccarone Center for the Prevention of Heart Disease	■ Boehringer Ingelheim	None	None	None	None	None

Continued on the next page

APPENDIX 1. CONTINUED

Committee Member	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Joseph E. Marine	Johns Hopkins University School of Medicine, Division of Cardiology—Associate Professor of Medicine	None	None	None	None	None	None
Roxana Mehran	Mount Sinai Medical Center—Associate Professor of Nursing; The Icahn School of Medicine—Director of Interventional Cardiovascular Research and Clinical Trials	None	None	None	■ AstraZeneca* ■ Eli Lilly/DSI*	■ Bristol-Myers Squibb ■ Janssen Pharmaceuticals	None
Steven R. Messe	Hospital of the University of Pennsylvania—Associate Professor of Neurology; Hospital of the University of Pennsylvania—Director, Vascular Neurology Fellowship	None	None	None	None	None	None
Nimesh S. Patel	Parkland Health and Hospital System—Fellow in Training, Cardiology	None	None	None	None	None	None
Benjamin E. Peterson	Brigham and Women's Hospital—Clinical Fellow in Interventional Cardiology	None	None	None	None	None	None
Kenneth Rosenfield	Massachusetts General Hospital, Cardiology Division—Section Head, Vascular Medicine and Intervention	None	None	None	None	None	None
Sarah A. Spinler	Binghamton University School of Pharmacy and Pharmaceutical Sciences—Professor and Chair, Department of Pharmacy Practice	■ Portola Pharmaceuticals	■ Bristol-Myers Squibb	None	None	None	None
Vinod H. Thourani	Washington Hospital, Medstar Heart & Vascular Institute—Professor of Surgery; Chair, Department of Cardiac Surgery	None	None	None	None	None	None

This table represents the relationships of committee members with industry and other entities that were determined to be relevant to this document. These relationships were reviewed and updated in conjunction with all meetings and/or conference calls of the writing committee during the document development process. The table does not necessarily reflect relationships with industry at the time of publication. A person is deemed to have a significant interest in a business if the interest represents ownership of ≥5% of the voting stock or share of the business entity or ownership of ≥$5,000 of the fair market value of the business entity, or if funds received by the person from the business entity exceed 5% of the person's gross income for the previous year. Relationships that exist with no financial benefit are also included for the purpose of transparency. Relationships in this table are modest unless otherwise noted. According to the ACC, a person has a *relevant* relationship IF: a) the *relationship or interest* relates to the same or similar subject matter, intellectual property or asset, topic, or issue addressed in the *document;* b) the *company/entity* (with whom the relationship exists) makes a drug, drug class, or device addressed in the *document* or makes a competing drug or device addressed in the *document*; or c) the *person or a member of the person's household* has a reasonable potential for financial, professional or other personal gain or loss as a result of the issues/content addressed in the *document*.

*Significant relationship

†No financial benefit.

UT = University of Texas.

APPENDIX 2. PEER REVIEWER INFORMATION—2020 EXPERT CONSENSUS DECISION PATHWAY FOR ANTICOAGULANT AND ANTIPLATELET THERAPY IN PATIENTS WITH ATRIAL FIBRILLATION OR VENOUS THROMBOEMBOLISM UNDERGOING PERCUTANEOUS CORONARY INTERVENTION OR WITH ATHEROSCLEROTIC CARDIOVASCULAR DISEASE

This table represents the individuals, organizations, and groups that peer reviewed this document. A list of corresponding comprehensive healthcare-related disclosures for each reviewer is available in Supplemental Appendix 2.

Reviewer	Representation	Employment
Dominick J. Angiolillo	Content Reviewer—ACC Expert	University of Florida College of Medicine—Director, Cardiovascular Research
Nicole Martin Bhave	Content Reviewer—Solution Set Oversight Committee	University of Michigan—Assistant Professor of Cardiovascular Medicine
Linda A. Briggs	Content Reviewer—American Association of Nurse Practitioners	George Washington University—Associate Professor
Hugh Calkins	Content Reviewer—ACC Expert	Johns Hopkins Hospital—Professor of Medicine; Director of Electrophysiology
Seemant Chaturvedi	Content Reviewer—American Academy of Neurology	University of Maryland School of Medicine—Stewart J. Greenebaum Endowed Professor of Stroke Neurology
Joaquin E. Cigarroa	Content Reviewer—ACC Expert	Oregon Health & Science University—Professor of Medicine; Chief of Division of Cardiovascular Medicine, School of Medicine
Donald E. Cutlip	Content Reviewer—Roundtable Participant and ACC Expert	Harvard Medical School—Vice Chair, Department of Medicine, Beth Israel Deaconess Medical Center
Gregory J. Dehmer	Content Reviewer—Solution Set Oversight Committee	Virginia Tech Carilion School of Medicine; Carilion Clinic, Cardiology and Carilion Cardiovascular Institute—Medical Director, Quality and Outcomes
Joseph Faiella-Tommasino	Content Reviewer—American Association of Physician Assistants	Touro College—Vice President, PA Program Development and Operations; Chair, Northeast Physician Assistant Programs
John Fanikos	Content Reviewer—American Society of Health-System Pharmacists	Brigham and Women's Hospital—Executive Director of Pharmacy
Olivia N. Gilbert	Content Reviewer—Solution Set Oversight Committee	Wake Forest School of Medicine—Assistant Professor, Advanced Heart Failure and Transplant Cardiology
Bulent Gorenek	Content Reviewer—ACC Electrophysiology Council	Eskisehir Osmangazi University—Professor of Cardiology
Mellanie True Hills	Content Reviewer—StopAfib.org	StopAfib.org—Speaker and CEO; Author, A Woman's Guide to Saving Her Own Life
Richard J. Kovacs	Content Reviewer—ACC Expert	Krannert Institute of Cardiology—Professor of Clinical Medicine
Glenn N. Levine	Content Reviewer—2016 DAPT Chair and 2015 PCI Guideline Focused Update Writing Committee	Baylor College of Medicine—Master Clinician and Professor of Medicine; Director, Cardiac Care Unit, Michael E. DeBakey Medical Center
Andrea L. Price	Official Reviewer— Solution Set Oversight Committee	Indiana University Health—Executive Programs Director; Director, Quality Reporting and Analytics
Yves Rosenberg	Content Reviewer—NHLBI	National Heart, Lung and Blood Institute—Scientific Project Officer
Christian T. Ruff	Content Reviewer—North American Thrombosis Forum and American College of Chest Physicians	Brigham and Women's Hospital—Director of General Cardiology; Investigator, School TIMI Study Group
Andrea M. Russo	Content Reviewer—Heart Rhythm Society	Cooper Medical School of Rowan University—Professor of Medicine; Director, Cardiac Electrophysiology and Arrhythmia Services; Cooper University Hospital—Director, CCEP Fellowship
Matthew William Sherwood	Content Reviewer—ACC Interventional Council	Inova Medical Group—Interventional Cardiology Physician
Deborah Michelle Siegal	Content Reviewer—American Society of Hematologists	McMaster University—Assistant Professor, Department of Medicine, Population Health Research Institute
Toby C. Trujillo	Content Reviewer—ACC Cardiovascular Team Council	University of Colorado Anschutz Medical Campus—Associate Professor, Skaggs School of Pharmacy and Pharmaceutical Sciences; University of Colorado Hospital—Clinical Specialist; Anticoagulation/Cardiology; Co-Chair, Anticoagulation Subcommittee UC Health
Mladen I. Vidovich	Official Reviewer—Board of Governors	University of Illinois—Assistant Professor of Medicine
Marlene S. Williams	Content Reviewer—Association of Black Cardiologists	The Johns Hopkins University—Associate Professor of Medicine; CICU Director, Johns Hopkins Bayview Medical Center, Division of Cardiology

Continued on the next page

APPENDIX 2. CONTINUED

Reviewer	Representation	Employment
David E. Winchester	Content Reviewer—Solution Set Oversight Committee	University of Florida College of Medicine—Associate Professor of Medicine; Malcom Randall VAMC—Staff Cardiologist; Assistant Cardiology Fellowship Program Director, Quality and Research; Co-Director, Advanced Fellowship for Cardiovascular Imaging; Co-Director, University of Florida Health Cardiac Imaging Group
Diane L Wirth	Content Reviewer—Anticoagulation Forum	Grady Healthcare—Interim Executive Director, Cardiovascular Services; Manager Heart Failure Program
Daniel Witt	Content Reviewer—American College of Clinical Pharmacy	College of Pharmacy—Professor and Chair; Assistant Dean of Clinical Affairs, Department of Pharmacotherapy

ACC = American College of Cardiology; CCEP = clinical cardiac electrophysiology; CICU = cardiac intensive care unit; NHLBI = National Heart, Lung, and Blood Institute; PCI = percutaneous coronary intervention.

APPENDIX 3. ABBREVIATIONS

AC = anticoagulant

ACC = American College of Cardiology

ACS = acute coronary syndrome

AHA = American Heart Association

AF = atrial fibrillation

APT = antiplatelet therapy

ASCVD = atherosclerotic cardiovascular disease

CABG = coronary artery bypass graft surgery

CAD = coronary artery disease

DAPT = dual antiplatelet therapy

DES = drug-eluting stent

DOAC = direct oral anticoagulant

ECDP = expert consensus decision pathways

GI = gastrointestinal

INR = international normalized ratio

LMWH = low-molecular-weight heparin

OAC = oral anticoagulant

PAD = peripheral artery disease

$P2Y_{12}i$ = $P2Y_{12}$ inhibitor

PCI = percutaneous coronary intervention

SAPT = single antiplatelet therapy

SIHD = stable ischemic heart disease

TIA = transient ischemic attack

VKA = vitamin K antagonist

VTE = venous thromboembolism