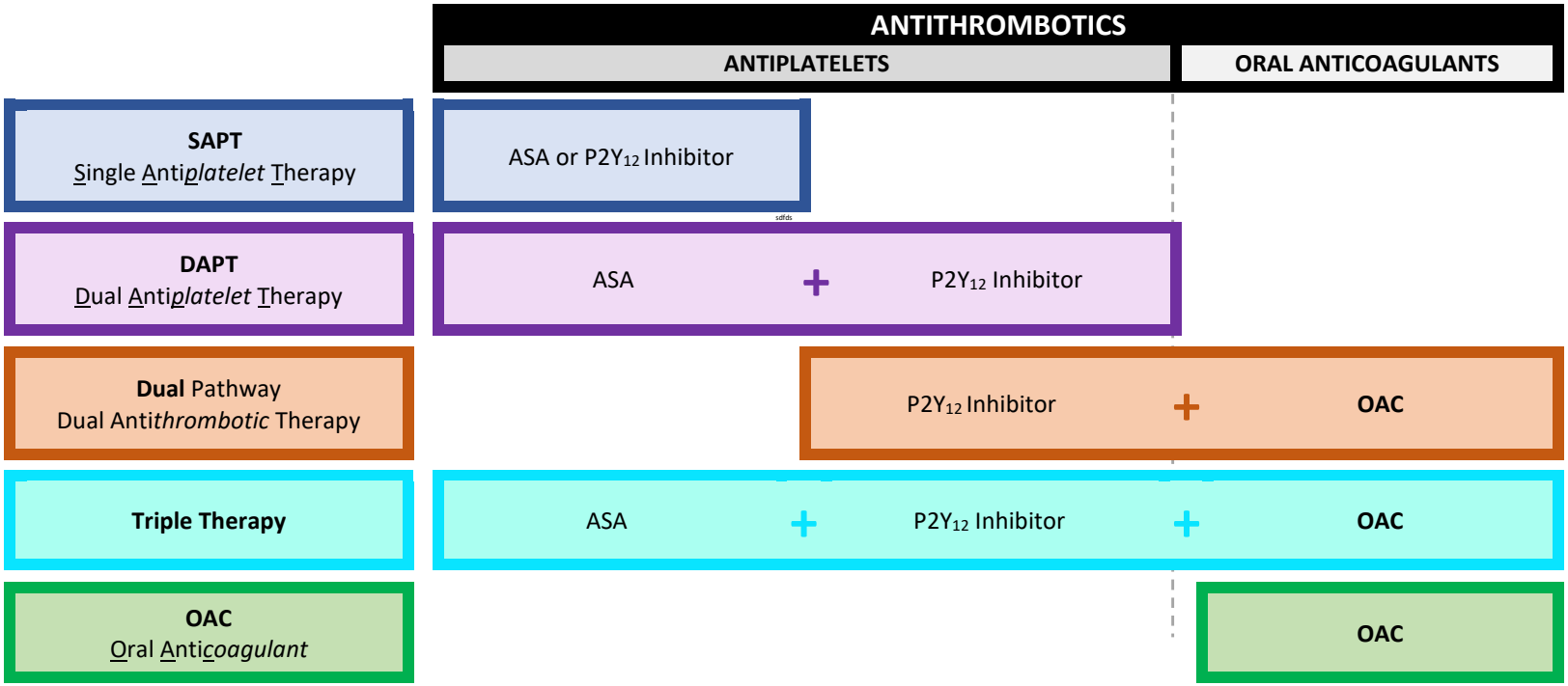
The following tables summarize guideline recommendations for the combination of antithrombotics; however, this is not a comprehensive list. A more conservative approach may be chosen for some older individuals after weighing the benefit versus bleed risk, quality of life, life expectancy and sometimes, palliative considerations. Individuals who are on more than one antithrombotic are at risk of a gastrointestinal bleed and may benefit from gastroprotection with a proton pump inhibitor, once daily, (e.g. pantoprazole PANTOLOC 40mg daily).

## SB ASA IN PRIMARY PREVENTION

3 Major Randomized Controlled Trials (RCTs) from 2018 provided improved clarity on the role of ASA in primary prevention – ARRIVE, ASPREE, ASCEND – Average age 64, 74, and 64 respectively. They suggested little to no benefit in prevention of CV events, with clear increased risk of major bleeding. Risk of bleeding particularly elevated in older age group (ASPREE - ARI 1.03%, NNH 100). The recent CCS AP 2023 meta-analysis found for every 1000 patients using ASA for primary prevention over 5 years, 4 fewer MACE events and 5 more extracranial major bleed events. Routine use of ASA is therefore not recommended in primary prevention. Shared decision making is needed as some individuals with high atherosclerotic risk and low bleeding risk may still opt for use ASA. See Q&A summary for more discussion.

### Figure: Antithrombotic Classification & Terminology




**Antiplatelets:**

SB **ASA** ASPIRIN

**$P2Y_{12}$ inhibitors:**

- S Clopidogrel PLAVIX
- SB Prasugrel EFFIENT
- SB Ticagrelor BRILINTA

In older adults, especially those ≥75 years old, S clopidogrel is typically the preferred $P2Y_{12}$ Inhibitor of choice, given the lower bleed risk compared to SB ticagrelor & SB prasugrel

**Oral Anticoagulants (OAC):**

**Vitamin K Antagonist (VKA)**

- B Warfarin COUMADIN

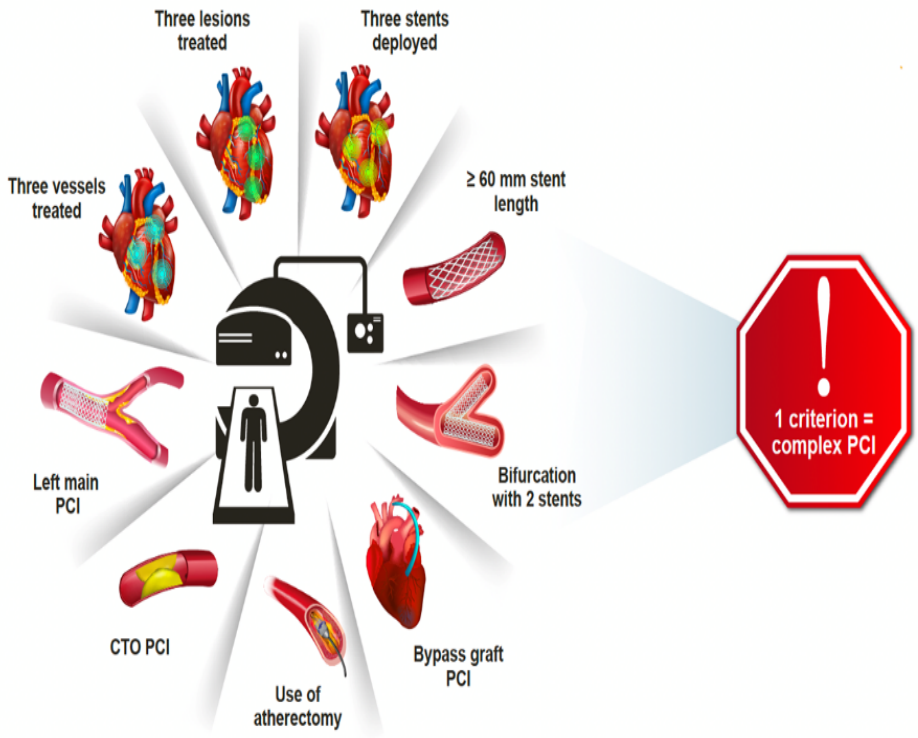
**Direct Oral Anticoagulant (DOAC)**

- S Apixaban ELIQUIS
- SB Dabigatran PRADAXA
- SB Edoxaban LIXIANA
- SB Rivaroxaban XARELTO

**SB – See STOPP&Beers Criteria considerations on page XX**

# Considerations for Thrombotic and Bleeding Risks

## Criterion for Complex Percutaneous Coronary Intervention




The selection of antiplatelet/anticoagulant, their intensity, and duration of use, depends on many factors including, bleed risk, complexity of cardiac intervention (e.g. PCI complexity), patient values and preferences.

Scoring tools, which help consider risk of bleed versus potential benefit of higher potency agents or longer duration of therapy, can be useful in shared decision making discussions. A complex PCI may warrant longer DAPT duration. If 1 major or 2 minor bleeding criterion or met, as laid out by the BARC Academic Research consortium, a patient may be considered high bleed risk (HBR) which may warrant shortened DAPT duration.

Regimens must be tailored to individual patients, and cardiologist guidance is essential.

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| Major Criterion<br>Any 1 major = HBR | OR | Minor Criterion<br>Any 2 minor = HBR |
|---|---|---|
| End-stage chronic kidney disease (CKD) (eGFR ≤30 mL/min/1.73m²) | | Moderate CKD (eGFR 30-59 mL/min/1.73m²) |
| Liver cirrhosis with portal hypertension | | ✖ |
| Active malignancy‡ (excluding non-melanoma skin cancer) within the past 12 months | | ✖ |
| Spontaneous bleeding with hospitalization or transfusion <6 months, or any time if recurrent | | Spontaneous bleeding with hospitalization or transfusion <12 months not meeting major criterion |
| Chronic bleeding diathesis | | ✖ |
| Hemoglobin <110 g/L | | Hemoglobin 110-129 g/L for men and 110-119 g/L for women |
| Moderate or severe baseline thrombocytopenia† (platelet count <100 x $10^9$/L) | | ✖ |
| Prior spontaneous ICH / Prior traumatic ICH <12 months / bAVM / Stroke <6 months | | Any ischemic stroke at any time not meeting the major criterion |
| Anticipated use of long-term anticoagulation* | | ✖ |
| ✖ | | Long-term use of oral NSAIDs or steroids |
| Non-deferrable major surgery on DAPT | | ✖ |
| Recent major surgery or trauma <30 days before PCI | | ✖ |
| ✖ | | Age ≥75 years |

## STOPP & Beers Considerations & Additional Comments*

**ASA:** Beers Major bleed risk markedly increased in older age. Risks generally agreed to outweigh benefits in primary prevention, however, beneficial role of ASA is well established in secondary prevention in the setting of cardiovascular disease. STOPP, not recommended in primary prevention of cardiovascular disease

**Apixaban:** STOPP CrCl <15mL/min, P-glycoprotein (P-gp) efflux inhibitors ↑ bleed risk (amiodarone, azithromycin, carvedilol, cyclosporin, dronedarone, itraconazole, ketoconazole (systemic), macrolides, quinine, ranolazine, tamoxifen, ticagrelor)

**Clopidogrel:** STOPP as long-term secondary stroke prevention with ASA (>4 weeks) in the absence of PCI in last 12 months, or concurrent ACS, or high grade symptomatic carotid arterial stenosis. In combination with anticoagulants (warfarin or DOACs) in chronic A-fib, unless there is concurrent coronary artery stents, or high grade coronary artery stenosis.

**Dabigatran:** Beers Avoid if CrCl < 30mL/min; Increased risk of GI bleeding compared with warfarin (based on head-to-head clinical trials) and of GI bleeding and major bleeding compared with apixaban (based on observational studies and meta-analyses) in older adults when used for long-term treatment of nonvalvular atrial fibrillation (NVAF) or VTE. STOPP CrCl <30mL/min, diltiazem & verapamil ↑ bleed risk, P-gp efflux inhibitors ↑ bleed risk (amiodarone, azithromycin, carvedilol, cyclosporin, dronedarone, itraconazole, ketoconazole (systemic), macrolides, quinine, ranolazine, tamoxifen, ticagrelor)

**Edoxaban:** Beers Avoid if CrCl <15mL/min or > 95 mL/min; STOPP, P-gp efflux inhibitors ↑ bleed risk (amiodarone, azithromycin, carvedilol, cyclosporin, dronedarone, itraconazole, ketoconazole (systemic), macrolides, quinine, ranolazine, tamoxifen, ticagrelor)

**Prasugrel**: Beers use caution in adults ≥75 years old; increased risk of bleeding in older adults compared to clopidogrel; benefits in highest-risk older adults (e.g. those with prior MI or DM) may offset risk when used for its approved indication of ACS to be managed with PCI. QE = moderate, SR = weak. Prasugrel is contraindicated in individuals with a history of stroke or TIA. STOPP, combination with anticoagulants (warfarin or DOACs) in chronic A-fib, unless there is concurrent coronary artery stents, or high grade coronary artery stenosis.

**Ticagrelor**: Beers use caution in adults ≥75 years old; increased risk of bleeding in older adults compared to clopidogrel; cardiovascular benefits may outweigh risk in some older adults. STOPP, combination with anticoagulants (warfarin or DOACs) in chronic A-fib, unless there is concurrent coronary artery stents, or high grade coronary artery stenosis.

**Rivaroxaban:** Beers Avoid if CrCl < 15mL/min; At doses used for long-term treatment of VTE or NVAF, rivaroxaban appears to have a higher risk of major bleeding and GI bleeding in older adults than other DOACs, particularly apixaban. STOPP, P-gp efflux inhibitors ↑ bleed risk (amiodarone, azithromycin, carvedilol, cyclosporin, dronedarone, itraconazole, ketoconazole (systemic), macrolides, quinine, ranolazine, tamoxifen, ticagrelor)

**Warfarin:** Beers Higher risk of major bleeding (especially intracranial) compared to DOACs, with similar or lower effectiveness in treatment of NVAF or VTE; for older adults, it may be reasonable to continue warfarin for those who have been using long-term, with well-controlled INRs (i.e., >70% time in the therapeutic range) and no adverse effects.

**NB – all above agents share the following STOPP:** in the case of concurrent risk of significant major bleeding (uncontrolled severe hypertension, bleeding diathesis, recent-non-trivial spontaneous bleeding) **See full references of 2023 Beers Criteria, and STOPP/START for complete descriptions.*

## Elective Percutaneous Coronary Intervention (PCI) - i.e. not after a heart attack

### ANTITHROMBOTIC REGIMEN / DURATION

**DAPT**
**ASA + $P2Y_{12}$ Inhibitor**

→

**SAPT**
**$P2Y_{12}$ Inhibitor***
OR **ASA**

**DURATION**

| Minimum Duration | Standard Duration | Extended Duration |
|---|---|---|
| DAPT x 1-3 months | DAPT x 6 to 12 months | DAPT up to 3 more yrs (In addition to standard 1 yr) |
| Consider in HBR pts | | |
| CCS AP 2023 WR, MQ | CCS AP 2018 SR, MQ | CCS AP 2018 WR, MQ |

↓

Step-down to SAPT with $P2Y_{12}$ Inhibitor (*clopidogrel preferred in HBR CCS AP 2023) or ASA indefinitely (or until risk > benefit), unless the individual requires an OAC

LQ = Low Quality Evidence; MQ = Moderate Quality Evidence; SR = Strong Recommendation; WR = Weak Recommendation

### THERAPEUTIC OPTIONS

**MINIMUM DURATION CONSIDERATIONS**

- Those with major bleed-post-PCI are at 3-5x increased risk of death. Shortened DAPT (1 to 3 months) may be appropriate in those with **High Bleed Risk (HBR)**. If an individual requires less than the standard duration, reassure him/her that shortened DAPT (< 6 months) had less bleeding, and no difference in MACE, death, or stent thrombosis in patients > 65 years. Meta-Analyses; CCS AP'23

**EXTENDED DURATION CONSIDERATIONS**

- May be considered in individuals at **high risk of thrombotic events & low risk of bleeding**.
- Compared to standard duration DAPT, extended DAPT ↓ the risk of MI and stroke, but ↑ bleeding. Meta-Analyses

See page XXX for thrombotic & bleeding risk factors.

### COMMENTS

- Individuals with a history of previous ACS, multi-vessel disease, & complex PCI should receive at least 12 months (i.e. standard duration). Meta-Analyses
- The **DAPT** study compared 30 to 12 months of DAPT after insertion of a drug-eluting stent. ~57% of patients had a non-ACS indication for their index PCI. Extended DAPT (i.e. 30 months) ↓ the risk of stent thrombosis (NNT=100) and major adverse cardiovascular & cerebrovascular events (NNT=63), but ↑ the risk of moderate-severe bleeding (NNH=112).
- See the notes on the **COMPASS** trial on page XX for another step-down option in individuals with stable CAD.

# PCI after Acute Coronary Syndrome (ACS) - i.e. STEMI, NSTEMI, Unstable Angina (UA)

## ANTITHROMBOTIC REGIMEN / DURATION

**DAPT**
**ASA + $P2Y_{12}$ Inhibitor**
(ticagrelor or prasugrel preferred to clopidogrel)
CCS AP 2023 WR LQ

→ **SAPT**
**$P2Y_{12}$ Inhibitor Or ASA**
CCS AP 2023

Consider if tolerated 1 month potent DAPT without thrombotic event

→ **De-escalated DAPT**
**ASA + clopidogrel**
CCS AP 2023 WR MQ

### DURATION

| Minimum Duration | Standard Duration | Extended Duration |
|---|---|---|
| DAPT x 1-3 months | DAPT x 12 months (CCS AP 2018 SR, MQ) | DAPT up to 3 more yrs (In addition to standard 1 yr) (CCS AP 2018 SR, HR) |
| Consider in patients who are at HBR, without complex PCI. | **De-escalate** If tolerated at least one month potent DAPT without thrombotic event, can consider de-escalation to ASA + clopidogrel (CCS AP 2023 WR, MQ) | If continuing prasugrel or clopidogrel DAPT, use standard dose. |
| See figure above on page XXX (CCS AP 2023 WR, MQ) | | If continuing ticagrelor, dose reduction needed |

↓ ↓ ↓

Step-down to SAPT with $P2Y_{12}$ Inhibitor (*clopidogrel preferred in HBR (CCS AP 2023)) or ASA indefinitely (or until risk > benefit), unless the individual requires an OAC

LQ = Low Quality Evidence; MQ = Moderate Quality Evidence; SR = Strong Recommendation; WR = Weak Recommendation

**SAPT**: Recent meta-analysis[1] comparing ASA vs $P2Y_{12}$ inhibitor monotherapy (62% clopidogrel, 38% ticagrelor) in patients with CAD, over 2 years, suggests reduced risk of CV death, MI, and stroke with $P2Y_{12}$ inhibitor, with similar bleed risk. Until more evidence is available, $P2Y_{12}$ inhibitor is preferred agent to ASA when stepping down to **SAPT**. CCS AP 2023

SB – See STOPP&Beers Criteria considerations on page XX

## THERAPEUTIC OPTIONS

### DAPT THERAPEUTIC OPTIONS

If using clopidogrel or prasugrel, the dosing for DAPT regimen is the same regardless of the duration:

SB **ASA** ASPIRIN 81mg daily +
S **clopidogrel** PLAVIX 75mg daily CURE, PCI-CURE, DAPT

**or**

**ASA** ASPIRIN 81mg daily +
SB **prasugrel** EFFIENT 10mg daily TRITON, DAPT
*Prasugrel generally avoided in those ≥75 years old

**or**

**ASA** ASPIRIN 81mg daily +

**Standard Duration:** SB **ticagrelor** BRILINTA **90mg*** BID (PLATO)

**Extended Duration:** (i.e. after 12 months) **ticagrelor** BRILINTA **60mg*** BID PEGASUS

### COMMENTS

**Minimum Duration of DAPT:**

- Recent RCTs (**MASTER DAPT**) and **Meta-Analyses** CCS AP'23 in those at HBR, have demonstrated that shortened DAPT (1-3 months) reduced major bleeding, without statistically significant difference in MACE, death, or stent thrombosis, compared to standard DAPT (6-12 months).

**De-escalation of DAPT:**
**ticagrelor/ prasugrel → clopidogrel**

- In those tolerating 1 month of potent DAPT, with ASA + ticagrelor or ASA + prasugrel, without recurrent thrombotic event, can consider de-escalation to ASA + clopidrogrel CCS AP'23 WR MQ

- The **TOPIC** study (open-label, single centre, RCT, 646 patients, from France, with ACS & PCI) de-escalated patients from ASA + ticagrelor or ASA + prasugrel to ASA + clopidogrel after 1 month. At 12 months, those switched to clopidogrel had reduced bleeding (BARC ≥2; NNT 9) without increased ischemic events.

## COMMENTS CONTINUED

**De-escalation of DAPT continued:**

- The **TALOS-AMI** study (open-label RCT, 2697 South Korean patients with ACS & PCI, ~12% ≥75yrs old) found de-escalation from ASA + ticagrelor to ASA + clopidogrel led to no difference in composite of CV death, MI, or stroke at the end of 12 months. No difference in stent thrombosis. Bleed events (BARC 2,3, or 5) were significantly reduced with clopidogrel arm (NNT 38)

**Extended Duration:**

- In individuals who tolerate 1 year of DAPT without a major bleed & are not at a high risk of bleeding, DAPT may be extended for up to another 3 years. CCS AP 2018 SR, HQ, DAPT, PEGASUS
- Reassess ischemic & bleeding risk annually.
- The **DAPT** study compared 30 to 12 months of DAPT after insertion of a drug-eluting stent (~65% ASA + clopidogrel, ~35% ASA + prasugrel; 26% had an ACS indication for their index PCI). Extended DAPT (i.e. 30 months) reduced the risk of stent thrombosis (NNT=100) and major adverse cardiovascular & cerebrovascular events (NNT=63), but increased the risk of moderate-severe bleeding (NNH=112).
- The **PEGASUS** study compared ASA + ticagrelor 60mg BID to ASA + placebo x ~3 years, in patients who completed 12 months of DAPT post-MI. Ticagrelor 60mg BID ↓ the risk of CV death, MI & stroke (NNT=79) but ↑ the risk of major bleeding (NNH=81). Although 60mg BID vs 90mg BID doses were not directly compared in the trial, the efficacy between the two doses was similar, but the risk of bleeding was greater with the 90mg BID dose.

Note, for DAPT in medically managed ACS (no PCI), ticagrelor preferred over clopidogrel[CCS AP'23 WR, LQ – Post hoc analysis of PLATO] and clopidogrel preferred over prasugrel, CCS AP'23 SR, MQ but must consider bleed risk factors, particularly in older adults.

# Elective PCI - i.e. not after a heart attack - in individuals WITH Atrial Fibrillation, but, WITHOUT high-risk features (see figure on pageXX)

| ANTITHROMBOTIC REGIMEN / DURATION | THERAPEUTIC OPTIONS | COMMENTS |
|---|---|---|
| **Age <65 years + $CHADS_2$ = 0**<br><br>**i.e OAC NOT INDICATED FOR A-FIB**<br><br>See A-Fib section for more information on the $CHADS_2$ score | **DAPT** ASA + $P2Y_{12}$ Inhibitor → **SAPT** $P2Y_{12}$ Inhibitor Or ASA<br><br>**DURATION**<br>**Minimum Duration** DAPT x 1-3 months Consider in HBR pts CCS AP 2023 WR, MQ<br>**Standard Duration** DAPT x 6 to 12 months CCS AP 2018 SR, MQ<br>**Extended Duration** DAPT up to 3 more yrs (In addition to standard 1 yr) CCS AP 2018 WR, MQ<br><br>↓ ↓ ↓<br>Step-down to SAPT with $P2Y_{12}$ Inhibitor (*clopidogrel preferred in HBR CCS AP 2023) or ASA indefinitely (or until risk > benefit), unless the individual requires an OAC<br><br>LQ = Low Quality Evidence; MQ = Moderate Quality Evidence; SR = Strong Recommendation; WR = Weak Recommendation | • Refer to earlier section – Elective PCI – page XX – as those with $CHADS_2$ = 0 are typically treated the same<br><br>• Approximately 20% of individuals with AF will require a PCI.<br>• DAPT is more effective than warfarin in reducing coronary events after PCI; however, warfarin is more effective than DAPT in reducing the risk of stroke in individuals with AF. As such, antiplatelets are often combined with an anticoagulant after PCI in individuals with AF.<br><br>• For individuals with AF who are less than 65 years old and have a $CHADS_2$ score of 0, the risk of stroke is approximately 0.7% per year. Therefore, DAPT without an OAC is recommended in this population to:<br>1) ↓ the risk of thrombotic events after PCI,<br>2) ↓ the risk of stroke in this lower-risk group, and 3) ↓ the risk of bleeding (compared to combined therapy with an OAC). | • Patients with HBR may be appropriate for shorter duration DAPT, 1-3 months CCS AP 2023 WR, MQ; CCS AF 2020<br><br>• Once DAPT for PCI is complete, if individual remains <65 years of age with $CHADS_2$ score = 0, step down to SAPT with $P2Y_{12}$ Inhibitor or SB ASA<br><br>• See the notes on the **COMPASS** trial on page XX for another step-down option in individuals with stable CAD, who remain $CHADS_2$ score = 0.<br><br>• If after DAPT completion, the individual is **≥65** years of age or has a $CHADS_2$ score of 1 or more, therapy like to switch to OAC alone, CCS AP'18 SR, HQ; ACC-AHA'23 |
| **Age ≥65 years or $CHADS_2$ ≥ 1**<br><br>**i.e. OAC IS INDICATED FOR A-FIB**<br><br>See AF section for more information on the $CHADS_2$ score | **Dual Pathway** OAC + $P2Y_{12}$ Inhibitor (Clopidogrel preferred) CCS AF 2020 SR, HQ CCS AP 2023 WR, MQ<br><br>**DURATION**<br>**BMS:** at least 1 month, up to 12 months<br>**DES:** at least 3 months, up to 12 months CCS AP 2018 WR, MQ; CCS AF 2018 WR, MQ<br><br>**OAC** CCS AP 2018 SR, HQ; ACC-AHA'23<br>**Dual Pathway** CCS AP 2018 WR, LQ<br>**High thrombotic risk & low bleed risk** | **DUAL PATHWAY OPTIONS**<br>**(OAC + $P2Y_{12}$ Inhibitor)**<br><br>S **Apixaban** ELIQUIS 5mg* BID + S **clopidogrel** PLAVIX 75mg daily<br>*2.5mg BID if ≥2: ≥80 years old, <60kg, SCr ≥133umol/L AUGUSTUS<br><br>**or**<br><br>SB **Dabigatran** PRADAXA 110mg* or 150mg BID + **clopidogrel** PLAVIX 75mg daily RE-DUAL PCI<br>*consider in those ≥80 years old or at high risk of bleeding<br><br>**or**<br><br>SB **Edoxaban** LIXIANA **30mg* or 60mg** daily + clopidogrel 75mg daily<br>* consider if CrCl 15-50mL/min, ≤60kg, potent P-gp inhibitor ENTRUST-AF PCI<br><br>**or**<br><br>SB **Rivaroxaban** XARELTO 15mg* daily + **clopidogrel** PLAVIX 75mg daily<br>*if CrCl 30 to 50mL/min: rivaroxaban 10mg daily<br>(**NOTE:** 10mg is not evidence based for stroke prevention) PIONEER AF-PCI<br><br>**or**<br><br>B **warfarin** COUMADIN + **clopidogrel** PLAVIX 75mg daily WOEST | • Dual pathway had less bleeding than triple therapy in clinical trials, but none of the studies had enough patients enrolled to properly evaluate efficacy (i.e. reduction in thrombotic events). AUGUSTUS, PIONEER AF-PCI, RE-DUAL PCI, WOEST<br><br>• The vast majority of trials assessing dual pathway used clopidogrel as $P2Y_{12}$ inhibitor. As there is limited evidence in combining OAC with SB prasugrel or SB ticagrelor, clopidogrel is the preferred agent. CCS AP 2023<br><br>• Dual pathway in this population, without high-risk features, suggested to continue for at least 1 month, and up to 12 months. CCS AF 2020 WR, LQ |

S B – See STOPP&Beers Criteria considerations on page XX

## ACS - i.e. STEMI, NSTEMI/UA, - & PCI in individuals WITH Atrial Fibrillation or WITH high-risk elective PCI (see pageXX )

**Age < 65 years + $CHADS_2$ = 0**

Refer to ACS + PCI section on page (2 EARLIER) (i.e. an OAC is not required). CCS AF'20 WR, MQ

- The risk of stroke in these individuals is ~ 0.7% per year.
- Therefore, DAPT without an OAC is recommended to 1) ↓ the risk of thrombotic events after PCI, 2) ↓ the risk of bleeding (compared to combined therapy with an OAC).
- If $CHADS_2$=1 and age <65 years old, DAPT regimen may be considered, especially if the individual low end of stroke risk (e.g. isolated hypertension). CCS AF'20

## ACS, i.e. STEMI, NSTEMI/UA, - & PCI in individuals WITH Atrial Fibrillation or WITH high-risk elective PCI (see page XX )

**Age ≥ 65 years or $CHADS_2$ ≥ 1**

**Triple Therapy**
**OAC (DOAC preferred) + $P2Y_{12}$ Inhibitor**
**(clopidogrel preferred CCS AF'20) + ASA**
CCS AP 2023 SR, LQ; CCS AF 2020 SR, LQ

**DURATION**
1 to 30 days CCS AF'20 SR, LQ, ACC-AHA'23

ASA beyond 30 days offers no additional benefit, but does increase bleed risk CCS AP 2023

Average duration of ASA ~ 7 days before stopping CCS AP 2023

**Dual Pathway**
**OAC (DOAC preferred) + $P2Y_{12}$ Inhibitor**
**(clopidrogrel preferred)**
CCS AP 2023 WR, MQ; CCS AF 2020 SR, HQ

**DURATION**
From 1 to 12 months post-cardiac stent insertion
CCS AF 2020 WR, LQ

**OAC**
CCS AP 2023 WR, LQ
(OAC alone preferred pathway for most after 12 months)

**Dual Pathway**
CCS AP 2018 WR, LQ
**High thrombotic risk & low bleed risk**

### TRIPLE THERAPY OPTIONS
(reduced intensity OAC + DAPT)

B **Warfarin** Coumadin (INR 2-2.5) +
SB **ASA** Aspirin 81mg daily + S **clopidogrel** Plavix 75mg daily WOEST

**or**

S**Apixaban** Eliquis 5mg* BID + **ASA** Aspirin 81mg daily + **clopidogrel** Plavix 75mg daily
*2.5mg BID if ≥2: ≥80 years old, <60kg, SCr ≥133umol/L

**or**

SB **Rivaroxaban** Xarelto 2.5mg BID + **ASA** Aspirin 81mg daily + **clopidogrel** Plavix 75mg daily PIONEER AF-PCI
(**NOTE**: 2.5MG bid is not evidence based for stroke prevention)

### DUAL PATHWAY OPTIONS
**(OAC + $P2Y_{12}$ Inhibitor)**

**Apixaban** Eliquis 5mg* BID + **clopidogrel** Plavix 75mg daily
*2.5mg BID if ≥2: ≥80 years old, <60kg, SCr ≥133umol/L
AUGUSTUS

**or**

SB **Dabigatran** Pradaxa 110mg* or 150mg BID + **clopidogrel** Plavix 75mg daily RE-DUAL PCI
*consider in those ≥80 years old or at high risk of bleeding

**or**

SB **Edoxaban** Lixiana **30mg* or 60mg** daily + **clopidogrel** 75mg daily
* Consider if CrCl 15-50mL/min, ≤60kg, potent P-gp inhibitor
ENTRUST-AF PCI

**or**

**Rivaroxaban** Xarelto 15mg* daily + **clopidogrel** Plavix 75mg daily *If CrCl 30 to 50mL/min: rivaroxaban 10mg daily
(**NOTE**: 10mg is not evidence based for stroke prevention) PIONEER AF-PCI

**or**

**Warfarin** Coumadin + **clopidogrel** Plavix 75mg daily WOEST

- Dual pathway had less bleeding than triple therapy in clinical trials, but none of the studies had enough patients enrolled to properly evaluate efficacy (i.e. reduction in thrombotic events). AUGUSTUS, PIONEER AF-PCI, RE-DUAL PCI, WOEST
- Meta-analysis found that for every 1000 pts treated, dual pathway would result in 23 fewer major bleeds, but 4 more thrombosis and 8 MACE events compared to triple therapy. CCS AP 2023
- Of note, 2023 CCS AP guidelines suggest moving directly to dual pathway following PCI, rather than continuing triple therapy post discharge (standard practice includes at least one dose of ASA at the time of PCI, or daily while in hospital until discharge).
- Strategies for reducing the risk of bleeding while on triple therapy:
  - Short duration of ASA (1 to 30 days)
  - Use a proton-pump inhibitor (e.g. pantoprazole 40mg daily).
  - Clopidogrel is the preferred $P2Y_{12}$ inhibitor as it has a lower risk of bleeding compared to ticagrelor & prasugrel, and has the most data when in combination with an OAC.
  - Use walking aids for those with gait or balance disorders.
  - Avoid NSAIDS.
  - Control blood pressure.

S B – See STOPP&Beers Criteria considerations on page XX

## Additional Considerations

- As an alternate step-down option, some with stable CAD could consider the **COMPASS** study approach: **rivaroxaban** 5mg BID vs **rivaroxaban** 2.5mg BID + **ASA** 100mg daily vs **ASA** 100mg daily alone, in patients with stable CAD (i.e. no ACS event in the past 12 months) or PAD (~90% had stable CAD, and ~2/3 had a history of MI). Rivaroxaban + ASA ↓ CV death, MI, & stroke more than ASA alone (NNT=77), but ↑ major bleeding (NNH=84). As such, rivaroxaban 2.5mg BID + ASA may be an alternative to extended DAPT in individuals with stable CAD.

**The Canadian Cardiovascular 2018 Antiplatelet Guidelines recommend:**

- **Standard DAPT Duration (12 months):** ASA + ticagrelor or prasugrel over clopidogrel in ACS patients who receive PCI. CCS AP 2018 SR, HQ Ticagrelor and prasugrel are considered more potent antiplatelets, and therefore reduced the risk of vascular death, myocardial infarction and stroke more than clopidogrel, but also increased the risk of bleeding. PLATO, TRITON
- **Extended DAPT Duration (> 12 months, and up to 3 years):** ASA + ticagrelor or clopidogrel is preferred over prasugrel, based on the number of patients who received extended DAPT with these agents in the landmark trials. CCS 2018 SR, HQ for ticagrelor PLATO & clopidogrel DAPT, CCS 2018 WR, MQ for prasugrel DAPT

**The Canadian Cardiovascular 2023 Antiplatelet Guidelines recommend:**

- **Shortened DAPT** (1-3 months) in patients with HBR undergoing PCI for ACS or elective PCI, with step down to SAPT in those who do not have ischemic or bleeding events in the first month, recalling that patients with complex PCI (see figure on page xxx) may not be suitable candidates for shortened DAPT. CCS AP 2023 WR, MQ

## Non-Cardioembolic Ischemic Stroke or TIA Secondary Prevention (also see Atrial Fibrillation section on page XX for cardioembolic stroke prevention)

**SAPT**

**DURATION:** Long-term, or until risk exceeds benefit

**If acute high-risk TIA, or minor ischemic stroke (without high risk of bleed)**

**DAPT**
**ASA + clopidogrel** → **SAPT**

**DURATION:** DAPT x **21 days** CSBPR'22 SR, HQ, then SAPT indefinitely CSBPR'22 SR, HQ

**OR**

**DAPT**
**ASA + ticagrelor** → **SAPT**

**DURATION:** DAPT x **30 days** CSBPR'22 SR, MQ; THALES, then SAPT indefinitely CSBPR'22 SR, HQ

**SAPT THERAPEUTIC OPTIONS**

SB **ASA** ASPIRIN 81mg daily

**or**

S **clopidogrel** PLAVIX 75mg daily

**or**

AGGRENOX (dipyridamole + ASA) 200mg / 25mg po BID

**DAPT THERAPEUTIC OPTIONS**

**ASA** ASPIRIN 81mg daily +
**clopidogrel** PLAVIX 75mg daily

**or**

**ASA** ASPIRIN 81mg daily +
SB ***ticagrelor** BRILINTA **90mg BID**

*Higher bleed risk with this option, and higher cost

**SAPT after DAPT options:** as above

- If an individual has a stroke while on ASA, it is reasonable to continue
- clopidogrel once DAPT is complete.

- **Monotherapy for most**: initiated as soon as possible after imaging excludes hemorrhage, within 24hrs ideally.
  All are appropriate options; tailor to the individual. CSBPR'20
- **DAPT for some:**
  - Those with **acute high-risk TIA, or minor ischemic stroke** (non-cardioembolic), with low bleed risk, consider **DAPT** x 21 days (clopidogrel) or **DAPT** x 30 days (ticagrelor) then **SAPT**. CSBPR'22 Level A
  - Those with stroke or TIA due to atherosclerotic stenosis of ≥70%, and low bleed risk, **DAPT** x 3 months (ASA + clopidogrel), then **SAPT.** CSBPR'20 Level B, SAMMPRIS
- Duration of **DAPT** should be limited to 21 to 90 days as bleeding risk increases without added benefit beyond this duration.
  - The **POINT** study compared DAPT to ASA for 90 days. DAPT ↓ the risk of ischemic stroke (NNT 67) but ↑major bleeds (NNH 200). Benefit was greatest during the first 7 and 30 days.
  - The **CHANCE** study compared DAPT to ASA for 21 days, followed by clopidogrel vs ASA until Day 90 in Chinese patients. DAPT ↓ the risk of stroke (NNT 29) without ↑ the risk of bleeding.
  - The **MATCH** and **SPS3** studies compared extended DAPT to **SAPT:** **MATCH:** DAPT vs clopidogrel x 18 months; **SPS3:** DAPT vs ASA x 3.4 yrs. No difference in benefit in either study, but DAPT ↑ major bleeding (NNH=50), (NNH=32) in both respectively. Both studies enrolled pts late (26 and 62 days post event respectively). Greatest benefit of DAPT is within first 30 days.

SB **Prasugrel** is contraindicated in patients with a history of stroke or TIA, due to the ↑ risk of harm / no benefit in patients with a history of stroke / TIA. TRITON, CCS AP 2023

S B – See Beers **Criteria considerations on page XX**

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## Search Terms

| | |
|---|---|
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| Antiplatelet | 6 |
| Antithrombotic | 6 |
| ASA | 6 |
| Clopidogrel | 6 |
| DAPT | 6 |
| Primary prevention | 6 |
| SAPT | 6 |
| Anticoagulant | 7 |
| Antiplatelet | 7 |
| Bleed risk | 7 |
| DAPT | 7 |
| Anticoagulant | 8 |
| Antiplatelet | 8 |
| Apixaban | 8 |
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| Clopidogrel | 8 |
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| DAPT | 8 |
| Edoxaban | 8 |
| PCI | 8 |
| Percutaneous coronary intervention | 8 |
| Prasugrel | 8 |
| Rivaroxaban | 8 |
| SAPT | 8 |
| Ticagrelor | 8 |
| Warfarin | 8 |
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| Acute coronary syndrome | 9 |

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| Antiplatelet | 9 |
| ASA | 9 |
| ASPIRIN | 9 |
| BRILINTA | 9 |
| Clopidogrel | 9 |
| DAPT | 9 |
| EFFIENT | 9 |
| NSTEMI | 9 |
| PCI | 9 |
| PEGASUS | 9 |
| Percutaneous coronary intervention | 9 |
| PLAVIX | 9 |
| Prasugrel | 9 |
| SAPT | 9 |
| STEMI | 9 |
| Ticagrelor | 9 |
| Unstable angina | 9 |
| Anticoagulant | 10 |
| Antiplatelet | 10 |
| Apixaban | 10 |
| Atrial fibrillation | 10 |
| Clopidogrel | 10 |
| COMPASS | 10 |
| COUMADIN | 10 |
| Dabigatran | 10 |
| DAPT | 10 |
| Edoxaban | 10 |
| ELIQUIS | 10 |
| LIXIANA | 10 |
| PCI | 10 |
| Percutaneous coronary intervention | 10 |
| PIONEER | 10 |
| PLAVIX | 10 |
| PRADAXA | 10 |
| Rivaroxaban | 10 |
| SAPT | 10 |

| | |
|---|---|
| Warfarin | 10 |
| XARELTO | 10 |
| ACS | 11 |
| Anticoagulant | 11 |
| Antiplatelet | 11 |
| Apixaban | 11 |
| ASA | 11 |
| ASPIRIN | 11 |
| Atrial fibrillation | 11 |
| COUMADIN | 11 |
| Dabigatran | 11 |
| DAPT | 11 |
| Edoxaban | 11 |
| ELIQUIS | 11 |
| LIXIANA | 11 |
| NSTEMI | 11 |
| PLAVIX | 11 |
| PRADAXA | 11 |
| Rivaroxaban | 11 |
| STEMI | 11 |
| Triple therapy | 11 |
| Warfarin | 11 |
| XARELTO | 11 |
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| Anticoagulant | 12 |
| Antiplatelet | 12 |
| ASA | 12 |
| ASPIRIN | 12 |
| BRILINTA | 12 |
| CHANCE | 12 |
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| COMPASS | 12 |
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| Dipyridamole | 12 |
| MATCH | 12 |
| PLAVIX | 12 |
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| | |
|---|---|
| Stroke | 12 |
| TIA | 12 |
| Ticagrelor | 12 |

## GERI-RXFILES ANTIPLATELETS & ANTICOAGULANTS: DUAL & TRIPLE THERAPY REFERENCES

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**Antiplatelets & Anticoagulants: DAPT, Dual & Triple Therapy**

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