# Making Goldilocks Happy

**Not too short, not too long, but JUST RIGHT**

Duration of Dual Antiplatelet Therapy (DAPT) & Triple Therapy for Cardiovascular & Cerebrovascular Indications

March 2016

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1) **ANTITHROMBOTICS are sometimes COMBINED to reduce risk of thrombosis.**
2) Combination antithrombotic use should be for a DEFINITE DURATION.
3) If therapy is TOO SHORT or TOO LONG, there is increased risk of HARM.
4) ALL health care providers have a role in ACHIEVING the duration that’s JUST RIGHT.

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**Phase I: Initial Therapy**

The specialist will select the intended duration of therapy, & will specify if therapy is to be extended.

Initial prescription is usually for:

**Phase II: Step Down**

Once the intended duration is complete, therapy should be stepped down as directed by the specialist.

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**Tipping Point for Benefit vs Harm:**

When DAPT or TRIPLE THERAPY extends beyond the recommended duration, the balance between benefit & harm shifts.

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<table>
<thead>
<tr>
<th>DAPT coronary stent</th>
<th>TRIPLE THERAPY AF + stent*</th>
<th>DAPT cerebrovascular</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clopidogrel + ASA</strong> or Prasugrel + ASA or Ticagrelor + ASA</td>
<td>Warfarin + Clopidogrel + ASA</td>
<td>Clopidogrel + ASA (single antiplatelet therapy also still an option)</td>
</tr>
<tr>
<td><strong>x 12 months</strong></td>
<td><strong>x 1 to 6 months rarely up to 12 months</strong></td>
<td><strong>x 21 days for ischemic stroke</strong> or <strong>x 90 days for intracranial stent</strong></td>
</tr>
<tr>
<td><strong>ASA x life-long</strong> DAPT may be extended up to 30 months see inside</td>
<td><strong>Warfarin + Clopidogrel</strong> (warfarin + ASA or DAPT also an option) up to 12 months post stent then Warfarin x life-long</td>
<td><strong>single antiplatelet x life-long</strong></td>
</tr>
</tbody>
</table>

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8 fewer myocardial infarctions
6 more major bleeds
per 1,000 patients treated/year with potentially 2 more deaths

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**ISCHEMIC STROKE**

21 days of DAPT ↓ risk of stroke in a Chinese population

DAPT >90 days ↑ risk of major bleeds & all-cause mortality

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**SUGGESTED SYSTEM CHANGES TO PROMOTE ADHERENCE & APPROPRIATE DURATION**

- **Specialist:** write the indication, intended duration & directions for step-down therapy on the original prescription & consult note
- **Primary Care Prescriber:** enter the indication, intended duration & step-down therapy into the patient chart paper/electronic medical record
- **Pharmacist:**
  - enter indication, intended duration & step-down therapy into the patient profile
  - add the intended duration to the prescription label
  - may send refill requests to the primary care prescriber if the specialist indicated life-long therapy (rare, see below)

**ENCOURAGE PATIENT ADHERENCE TO THE INTENDED DURATION**

- identify & address reversible causes of non-adherence
- ensure the patient is taking ASA as part of the **DAPT** or **TRIPLE THERAPY** regimen
- use a **proton-pump inhibitor** for patients at high risk of a GI bleed:
  - potential drug interaction between clopidogrel & (es)omeprazole; conflicting evidence
    - all patients while on **TRIPLE THERAPY**
    - those on **DAPT** with a high risk of a GI bleed
    - reassess need for the PPI when therapy is stepped down

**Harms of starting too late / stopping too early for patients who are on DAPT after a coronary stent is inserted:**
- a delay in filling the initial **DAPT** prescription even >1 day after discharge ↑ the risk of mortality & MI NNH=16
- premature discontinuation of **DAPT** ↑ the risk of stent thrombosis, especially within the first 6 months of therapy

**IF YOU IDENTIFY PATIENTS WHO HAVE BEEN ON:**

**CARDIAC:**
- DAPT for >12 months or **TRIPLE THERAPY** > 6 months

**CEREBROVASCULAR:**
- DAPT for >21 days ischemic stroke or >90 days intracranial stent

**Find out:**
- What is the indication?
- How long has the patient been on **DAPT** or **TRIPLE THERAPY**?
- What was the intended duration? Has the specialist extended therapy or indicated it was life-long?
- Has a new event occurred since therapy was started?

Primary care prescribers should consider discontinuing **DAPT** or **TRIPLE THERAPY** if therapy is beyond the intended duration, & the specialist has not extended treatment. Too long may do more harm than good (see front cover).

In select cases, **DAPT** may be prescribed as life-long therapy. For example:
- Atrial fibrillation patients with a CHADS\textsubscript{2} score ≤1 (risk factors change over time), or who are unable to take an oral anticoagulant e.g. warfarin, apixaban, dabigatran, rivaroxaban
- Patients with a history of recurrent cardiovascular or cerebrovascular events
- Patients with peripheral artery disease who are at high vascular risk & low bleed risk (ASA or clopidogrel preferred over DAPT)

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**DURATION of DUAL ANTIPLATELET THERAPY (DAPT) & TRIPLE THERAPY (TT)**

The focus of this chart is the duration of therapy. A specialist will select the intended duration of therapy when initiating treatment. If the duration of therapy is unclear/unknown, the specialist should be consulted. Optimize risk factor management (e.g. weight loss, smoking cessation, healthy eating, exercise, BP/BG/lipid control) to help ↓ risk of subsequent cardiac &/or cerebrovascular events.

### DAPT: CARDIOVASCULAR INDICATIONS

<table>
<thead>
<tr>
<th>INDICATION</th>
<th>THERAPEUTIC OPTIONS &amp; MAINTENANCE DOSES</th>
<th>MINIMUM DURATION need compelling reason</th>
<th>STANDARD DURATION</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary Stent + Stable CAD / Elective PCI</td>
<td>ASA 81mg po daily + Clopidogrel 75mg po daily</td>
<td>BMS: 2-4 weeks DES: 3-6 months</td>
<td>6-12 months, then ASA</td>
<td>Stent thrombosis (ST) can lead to MI &amp;/or death. DAPT ↓ risk of recurrent MI &amp; ST after stent placement. The majority of patients will receive a standard duration of DAPT x 12 months after a coronary stent.</td>
</tr>
<tr>
<td>Coronary Stent + NSTEACS (UA or NSTEMI)</td>
<td>ASA 81mg po daily + Clopidogrel* 75mg po daily</td>
<td>BMS: 1 month DES: 3-6 months</td>
<td>12 months, then ASA</td>
<td>Compared to BMS, DES ↓ the risk of in-stent restenosis &amp; the need for target vessel revascularization procedures.</td>
</tr>
<tr>
<td>Coronary Stent + STEMI</td>
<td>ASA 81mg po daily + Clopidogrel* 75mg po daily or Current-Oasis or ASA 81mg po daily + Prasugrel 10mg po daily or ASA 81mg po daily + Ticagrelor 90mg po BID</td>
<td>12 months, then ASA</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Clopidogrel vs Prasugrel vs Ticagrelor: why might a cardiologist select one over the other for patients with coronary stents?

CCS'12 recommend ticagrelor or prasugrel over clopidogrel, based on:
- **PLATO**: Ticagrelor vs clopidogrel in ACS (≤60% coronary stent) x 12 months  
  - Ticagrelor ↓ risk of vascular death/MI/stroke NNT=53, ↑ risk of bleeding (non-CABG major bleeding NNT=167, & fatal bleeding [non-intracranial NNT=500, intracranial NNT=1112]), ↑ risk of dyspnea NNH=17
- **TRITON**: Prasugrel vs clopidogrel in ACS+PCI (≥95% coronary stent) x 14.5mos  
  - Prasugrel ↓ risk of vascular death/MI/stroke NNT=46, ↑ risk of bleeding (major NNH=167, life-threatening NNH=200 or fatal NNH=334 bleed).
- **Prasugrel**: only indicated in ACS patients who undergo PCI. It is contraindicated in patients with a history of stroke/TIA. For patients <60kg or ≥75 years old, could consider 5mg once daily, CCS'12 however this dose has never been studied & the 10mg tablet is not scored.
- Cost: DAPT x 1 month with clopidogrel $30, prasugrel $104, ticagrelor $113

<table>
<thead>
<tr>
<th>ACS + CABG ± Coronary Stent</th>
<th>ASA 81mg po daily + clopidogrel 75mg po daily or ASA 81mg po daily + ticagrelor 90mg po BID</th>
<th>No stent: 6 - 12 months, then ASA</th>
<th>Stent: 12 months, then ASA</th>
<th>- Ticagrelor preferred over clopidogrel, CCS'12 (15% CABG), based on PLATO (10% underwent CABG).</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACS Medically Managed</td>
<td>If using clopidogrel: NSTEACS: 1 month STEMI: 14 to 30 days</td>
<td>12 months then ASA</td>
<td></td>
<td>- Prasugrel not recommended due to very little evidence.</td>
</tr>
<tr>
<td>(i.e. no PCI or CABG)</td>
<td></td>
<td></td>
<td></td>
<td>- Ticagrelor preferred over clopidogrel, CCS'12 (15% CABG), based on PLATO (~25% were medically managed).</td>
</tr>
<tr>
<td>Peripheral Artery Disease</td>
<td>ASA 81mg po daily + clopidogrel 75mg po daily</td>
<td>Long-term therapy with</td>
<td></td>
<td>- Prasugrel not recommended; TRILOGY failed to show a benefit in this population, vs clopidogrel.</td>
</tr>
<tr>
<td>No stent</td>
<td></td>
<td>single antiplatelet preferred, or DAPT</td>
<td></td>
<td>- Use of fibrinolytics: clopidogrel is recommended.</td>
</tr>
</tbody>
</table>

**BLEEDING RISK**
- Bleeding ↑ risk of morbidity & mortality, from fatal bleeds to nuisance bleeding which can lead to premature discontinuation of DAPT resulting in ↑ risk of harm (e.g. ↑ risk of ST post-coronary stent).
- Unfortunately, there are no validated risk scores for estimating bleeding when DAPT is initiated.
- **DAPT for coronary stents**: the DAPT Score Calculator is a validated tool which compares risk of thrombosis to bleeding, if considering therapy >1 year. The HASBLED & REACH scores may provide perspective on bleeding risk, but limitations exist. See Online Extras.
- ↑ risk of bleeding with prasugrel & ticagrelor (ticagrelor C2 if history of intracranial bleed).

**GASTROPROTECTION** ½ to ¾ of bleeds caused by DAPT are GI bleeds
- Consider a PPI for those on DAPT with a higher than average risk of a GI bleed, ESGE'15 NSTEACS (8)  
  - history of GI ulcer/bleed, or ↓2 of the following risk factors: age ≥65years old, dyspepsia, GERD, H.pylori infection, or chronic NSAID or corticosteroid use, or chronic alcohol use (others: SSRI use, smoking)
- Omeprazole (& esomeprazole) may prevent CYP 2C19 conversion of clopidogrel to its active form. Some evidence suggests this is not clinically significant. Consider pantoprazole, rabeprazole or lanzoprazol. **Reassess need for PPI when DAPT is stopped.**

There may be a small ↑ risk in ischemic events when DAPT d/c; risk of ST ↑ 0.4% to 0.7% & MI ↑ 2% to 3% x months after DAPT stopped. **Unclear if rebound ischemic or unmasking delayed endothelialization.**

Restarting DAPT after initial tx complete: Clopidogrel + ASA: no benefit. Ticagrelor 60mg BID (not available in Canada) vs placebo x3yrs ↓ death/ MI/stroke NNT=77 but ↑ major bleed NNH=64.
**DURATION of DAPT & TT continued**

### COST & FORMULARY STATUS

<table>
<thead>
<tr>
<th>DAPT = P2Y12 Inhibitor + ASA</th>
<th>Formulary coverage is limited to 1 year in SK</th>
<th>$/30days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clopidogrel PLAVIX, g = ▼ 75mg daily + ASA ASPIRIN, g 81mg daily</td>
<td></td>
<td>$30</td>
</tr>
<tr>
<td>Prasugrel EFFIENT 5-10mg daily + ASA ASPIRIN, g 81mg daily</td>
<td></td>
<td>$104</td>
</tr>
<tr>
<td>Ticagrelor BRILINTA ▼ 90mg BID + ASA ASPIRIN, g 81mg daily</td>
<td></td>
<td>$113</td>
</tr>
<tr>
<td>Warfarin + Antiplatelet</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warfarin COUMADIN, g + Clopidogrel PLAVIX, g = ▼ 75mg daily (preferred)</td>
<td></td>
<td>$41</td>
</tr>
<tr>
<td>Warfarin COUMADIN, g + ASA ASPIRIN, g 81mg daily</td>
<td></td>
<td>$19</td>
</tr>
<tr>
<td>Triple Therapy = Warfarin + ASA + Clopidogrel</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warfarin COUMADIN, g + ASA 81mg daily + Clopidogrel PLAVIX, g = ▼ 75mg daily</td>
<td></td>
<td>$45</td>
</tr>
</tbody>
</table>

### SWITCHING BETWEEN CLOPIDOGREL vs TICAGRELOR vs PRASUGREL

- CCS’12 Antithrombotic Guidelines suggest against switching the P2Y12 inhibitor initially selected at discharge unless there is a compelling reason e.g. ST, bleed, CV event. ORNL
- Information on switching is primarily based on pharmacodynamic & registry studies.
- The risk of ST is greatest during the 1st month.
- Most likely reason for switching from: (see Online Extras for a summary of all options)
  - **Clopidogrel → ticagrelor or prasugrel**: clinical failure (e.g. stent thrombosis despite adherence to therapy). A loading dose (LD) would likely be administered, in the hospital.
  - **Ticagrelor → clopidogrel**: dyspnea (rule out HF) or cost concerns. Suggested to give a LD 24hrs after the last ticagrelor dose (pharmacodynamic study showed a residual effect 12hrs after the last dose).
- **Loading Doses for switching**: clopidogrel 300mg x1; ticagrelor 180mg x1; prasugrel 60mg x1

### DAPT: CEREBROVASCULAR INDICATIONS (not comprehensive)

<table>
<thead>
<tr>
<th>Indication</th>
<th>Antithrombotic Options &amp; Maintenance Doses</th>
<th>Duration of DAPT</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiomebolic Stroke in AF OAC preferred over DAPT</td>
<td>ASA 75-325mg po daily + Clopidogrel 75mg po daily</td>
<td>Lifelong</td>
<td>- DAPT may be considered if CHADS2 or CHA2DS2-VASc score &lt;2 or unable to take OAC. See AF chart page 18.</td>
</tr>
<tr>
<td>Intracranial Artery Stenosis (Secondary Prevention)</td>
<td>Note: - Prasugrel CI in patients with a history of stroke/TIA. TRITON</td>
<td>90 days</td>
<td>- Indicated for severe stenosis (70-99%) of a major intracranial artery.</td>
</tr>
<tr>
<td>Non-Cardioembolic Stroke (Secondary Prevention)</td>
<td>T bacon: no benefit</td>
<td>21 days</td>
<td>- SAMMPRIS: DAPT x 90 days ± stent, then ASA 81-325mg daily. DAPT was started within 30 days of stroke/TIA.</td>
</tr>
</tbody>
</table>

### TRIPLE THERAPY (TT = Warfarin + ASA + Clopidogrel) consult with cardiologist

- TT should only be used in consultation with a cardiologist.
- The efficacy & safety data for TT is primarily based on observational studies & a few small open-label RCTs (good evidence lacking).
- Patients who require DAPT (i.e. coronary stent) + an OAC, e.g.:
  - AF with CHADS2 or CHA2DS2-VASc score ≥2. If CHADS2 <2, DAPT may be sufficient for both ST & AF stroke prevention.
  - Non-AF indications: hypercoagulable disorder, LV mural thrombus, mechanical valve prosthesis, VTE [recent or recurrent], & potentially anterior apical akinesis/dyskinesia
- The cardiologist will consider indication for TT, risk of bleed, risk of thrombosis & stent type (if applicable) when determining the duration of therapy. A few examples:
  - AF (CHA2DS2 score ≥2) + coronary stent examples:
    - TT may be as short as 1 month if: HASBLED 2, with a BMS.
    - TT may be 3 to 6 months if: HASBLED ≥2, with a DES.
    - Although rare, TT may be up to 12 months (e.g. very high risk of thrombosis with a low bleed risk).
  - ISAR-TRIPLE: 6 weeks vs 6 months of TT in AF + DES patients; no difference in death/MI/ST/stroke/major bleeding, or major bleeding on its own. ½ stable CAD, majority new-DES.
  - Dual Antiplatelets for TT:
    - ASA 75-100mg/d plus clopidogrel 75mg/day are the preferred antiplatelets, regardless of indication for TT.
    - Prasugrel: avoid due to ↑ risk of bleeding, compared to clopidogrel in DAPT TRITON & TT studies.
    - Ticagrelor: avoid due to ↑ risk of bleeding (more potent agent) PLATO & very limited (n=27) evidence in TT.

### HOW LONG WILL TRIPLE THERAPY BE PRESCRIBED?

- The cardiologist will consider indication for TT, risk of bleed, risk of thrombosis & stent type (if applicable) when determining the duration of therapy. A few examples:
  - AF (CHA2DS2 score ≥2) + coronary stent examples:
    - TT may be as short as 1 month if: HASBLED 2, with a BMS.
    - TT may be 3 to 6 months if: HASBLED ≥2, with a DES.
    - Although rare, TT may be up to 12 months (e.g. very high risk of thrombosis with a low bleed risk).
  - ISAR-TRIPLE: 6 weeks vs 6 months of TT in AF + DES patients; no difference in death/MI/ST/stroke/major bleeding, or major bleeding on its own. ½ stable CAD, majority new-DES.

### WHICH MEDICATIONS SHOULD BE USED IN TRIPLE THERAPY?

- The evidence for TT is primarily with warfarin, ASA + clopidogrel.
- **Oral Anticoagulants (OAC) for TT:**
  - **Warfarin:** the preferred OAC, regardless of indication for TT.
  - **Dabigatran:** if warfarin cannot be used, there is a small amount of evidence for dabigatran 110mg BID in AF patients. **RELY sub-study:** n=812 (4.5%) on DAPT & dabigatran or warfarin at some time during the study; underpowered. Dabigatran has also been evaluated in a TT regimen for ACS secondary prevention; ↑ risk of bleed with no benefit. **REDDEM**
  - **Rivaroxaban:** 2.5mg BID as part of a TT for ACS secondary prevention. ↓ composite of CV death, MI, stroke, NNT=63 but ↑ risk of bleeding. **NNH=83** over 2 years. **ATLAS**, this is not an approved indication & 2.5mg tablet is not available.
  - **Apixaban:** studied as part of TT for ACS secondary prevention. Trial terminated early as ↑ bleed risk with no benefit. **APRAISE 2**

### STEPPING DOWN FROM TRIPLE THERAPY

- Annual rate of major bleeds on TT is 10%. Nose, skin & GI bleeds are most common. 1 in 10 bleeds are fatal (¾ intracranial, ¼ GI).
- After a bleed, antithrombotics should be reassessed / restarted when safe to do so.
- Strategies to ↑ the risk of bleeding with Triple Therapy:
  - Limit TT to recommended definite duration.
  - Correct reversible HASBLED risk factors (e.g. uncontrolled HTN, labile INRs, concomitant NSAID use, & alcohol excess/abuse).
  - Consider target INR of 2-2.5 [unless mechanical valve] & TTR >70%. Monitor INR 2-3 weeks.
  - Use ASA <100mg/day.
  - Use a PPI for gastroprotection (e.g. pantoprazole 40mg po daily).
  - Avoid prasugrel & ticagrelor as ↑ bleed risk vs clopidogrel.
  - Avoid apixaban & rivaroxaban. If dabigatran is used (warfarin preferred), use lowest AF dose (110mg BID).
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COMPLETE LIST OF ABBREVIATIONS

- EDS = edematous in SK
- AB = ankle-brachial index
- ACS = acute coronary syndrome
- AF = atrial fibrillation
- AR = absolute risk increase
- ASA = acetylsalicylic acid
- BMS = bare-metal stent
- BP = blood pressure
- CABG = coronary artery bypass graft
- CAD = coronary artery disease
- CNCS = central nervous system
- CV = cardiovascular
- d/c = discontinue
- DES = drug-eluting stent
- DM = diabetes
- g = generic
- G1DES = 1st generation drug-eluting stent
- GERD = gastroesophageal reflux disease
- GI = gastrointestinal
- HF = heart failure
- houroh = hour
- HTN = hypertension
- INR = international normalization ratio
- LD = loading dose
- LV = left ventricular
- MI = myocardial infarction
- new-DES = newer drug-eluting stent
- mos = months
- NA = not applicable
- NNT = number needed to treat
- NS = non-statistically significant
- NSAID = non-steroidal anti-inflammatory drug
- NSTEACS = non-ST elevated ACS
- OAC = oral anticoagulant
- PAD = peripheral artery disease
- PCI = percutaneous coronary intervention
- PPI = proton-pump inhibitor
- pt = patient
- RCT = randomized controlled trial
- SAPT = single antiplatelet therapy
- SK = Saskatchewan
- SSRI = selective serotonin reuptake inhibitor
- ST = stent thrombosis
- TIA = transient ischemic attack
- TT = triple therapy
- TX = treatment
- VKA = vitamin K antagonist
- VL-ST = very late stent thrombosis
- VTE = venous thromboembolism
- yr = years old
- yo = years old

RXFILES RELATED DOCUMENTS

- DAPT (DAPT 12 vs 30 months) Trial Summary (http://www.rxfiles.ca/rxfiles/uploads/documents/DAPT-Trial-12vs30months.pdf)

RxFiles Duration of DAPT & TT Online Extras: L Kosar MSc, K Koziol BSP, A Martens BSP, D Shmyr BSP © www.RxFiles.ca Apr 2016

DAPT SCORE CALCULATOR (www.daptstudy.org)

- The DAPT Score Calculator is a validated tool to help identify patients who may benefit from extended DAPT (i.e. beyond 1 year after a drug-eluting stent) [not for those with a bare-metal stent].
- The calculator should not be used at the time of coronary stent insertion. Instead, it may be used by a cardiologist after the patient has been on DAPT for 12 months.
- The score is based on the DAPT study – i.e. DAPT x 12 vs 30 months in patients with drug-eluting stent who were compliant & event-free after 12 months of DAPT (i.e. no MI, stent thrombosis, stroke, repeat revascularization, or major bleed).
- Balances risk of thrombosis (i.e. MI or stent thrombosis) vs bleeding.
- Risk of bleeding for the calculator was based solely on age.
- Variables that were risk factors for both thrombosis & bleeding were excluded from the calculator (e.g. HTN, CKD, & PAD).
- The score ranges from -2 to 10:
  - Score <2: bleed NNH=64 > ischemic risk NNT=153, DAPT x 12 months then stop.
  - Score ≥2: ischemic NNT=34 > bleeding risk NNH=272. May consider DAPT >12 months

VARIABLE | POINTS
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**Patient Characteristics**
Age: ≥75 years of age | -2
65-74 years of age | -1
<65 years of age | 0
Diabetes Mellitus | 1
Cigarette smoker within past 2 years | 1
Prior PCI or Prior MI | 1
History of HF or LVEF <30% | 2

**Index Procedure Characteristic**
MI at presentation | 1
Vein graft PCI | 2
Stent diameter <3mm | 1
Paclitaxel stent =1 point | 1

CKD = chronic kidney disease
DAPT = dual antiplatelet therapy
HTN = hypertension
HF = heart failure
LVEF = left ventricular ejection fraction
MI = myocardial infarction
NNH = number needed to harm
NNT = number needed to treat
PAD = peripheral artery disease
PCI = percutaneous coronary intervention
SWITCHING P2Y12 INHIBITORS (Clopidogrel vs Prasugrel vs Ticagrelor)

- The Canadian Cardiovascular Society 2012 Antiplatelet Guidelines suggest against switching the P2Y12 inhibitor initially selected at discharge unless there is a compelling reason e.g. stent thrombosis, bleed, cardiovascular event.

- The following information is based primarily on pharmacodynamics studies & registries. Unfortunately, the timeframe for “acute phase” and “chronic phase” was not defined in the publications. Of note, the risk of stent thrombosis is greatest during the first month.

- Clopidogrel & prasugrel bind to the P2Y12 receptors at the same site where ADP binds – thus blocking ADP. Ticagrelor, on the other hand, binds to the P2Y12 receptor at a different site than ADP & induces a conformational change making the receptor inactive. As such, when switching between clopidogrel & prasugrel, it is a saturable process. Once all of the receptor sites are blocked, any additional drug is eliminated from the systemic circulation.

- Loading Doses for Switching: clopidogrel 300mg x1; ticagrelor 180mg x1; prasugrel 60mg x 1

- Switching from clopidogrel → ticagrelor or prasugrel: (e.g. clinical failure [e.g. stent thrombosis] despite adherence to therapy)
  - Acute Phase: administer loading dose (unless active bleeding) regardless of clopidogrel timing/dose
  - Chronic Phase: omit loading dose, start maintenance dose 24 hours after last clopidogrel dose.
  - In the PLATO trial (ticagrelor vs clopidogrel in ACS), 46% of the patients in the ticagrelor arm received a dose of clopidogrel prior to randomization. The loading dose of ticagrelor (180mg x 1) was administered to all of these patients.
  - In the TRITON-TIMI trial (prasugrel vs clopidogrel in ACS + PCI), all of the patients in the prasugrel arm were “P2Y12 inhibitor naïve”.

- Switching from ticagrelor → clopidogrel or prasugrel: (e.g. dyspnea or cost concerns)
  - Acute Phase: administer loading dose (unless active bleeding) 24 hours after the last dose of ticagrelor.
  - Chronic Phase: omit loading dose, start maintenance dose 24 hours after last prasugrel dose.
  - In the PLATO trial (ticagrelor vs clopidogrel in ACS), 46% of the patients in the ticagrelor arm received a dose of clopidogrel prior to randomization. The loading dose of ticagrelor (180mg x 1) was administered to all of these patients.

- Switching from prasugrel → clopidogrel: (e.g. history of stroke or TIA not known at time of stent insertion or cost concerns)
  - Acute Phase: administer loading dose (unless active bleeding) 24 hours after the last dose of prasugrel.
  - Chronic Phase: omit loading dose, start maintenance dose 24 hours after last prasugrel dose.

P2Y12 inhibitor=clopidogrel, prasugrel or ticagrelor TIA=transient ischemic stroke

STRENGTH OF RECOMMENDATIONS & LEVELS OF EVIDENCE

CARDIOVASCULAR INDICATIONS – DAPT

Stable CAD / Non-ACS / Stable Ischemic Heart Disease / Established CAD & Elective PCI

- Ideally, DAPT with ASA 81mg po daily + clopidogrel 75mg po daily 6 months
  - Minimum Durations:
    - BMS: ↑ risk of bleeding, scheduled for non-cardiac surgery: minimum DAPT x 1 month ACC/AHA'16 (IA), CCS'12 (SR/HQ), ESC/EACTS'14 (IB), ACCF/AHA/SCAI'11 (IB), CHEST'12 (2C)
    - BMS: very high risk of bleeding – minimum DAPT x 2 weeks ACC/AHA'16 (IB), CCS'12 (CR/LQ), ACCF/AHA/SCAI'11 (IB)
    - DES: ↑ risk of bleeding, scheduled for non-cardiac surgery, OAC: minimum 3 ACC/AHA'16 (IB-LD), CCS'12 (CR/LQ) to 6 months ACC/AHA'16 (IB-R), ESC/EACTS'14 (IB, A), CHEST'12 (IA)
  - ASA 81mg po daily indefinitely ESC/EACTS'14 (IA), AHA/ACC'14 (IB), ACCF/AHA/SCAI'11 (IA)

NSTEACS & PCI

- Ideally, DAPT x 12 months ACC/AHA'16 (IB-R), ESC'15 (IA), AHA/ACC'14, CCS'12 (SR/HQ), CHEST'12(IIb)
  - Clopidogrel ESC'15 (IB), AHA/ACC'14 (IB), CCS'12 (SR/HQ), which is preferred for those requiring oral anticoagulation ACC/AHA'16 (RA, B), ACCF/AHA/SCAI'11 (IB), CCS'12 (SR/HQ)
  - Prasugrel preferred over clopidogrel if PCI planned ACC/AHA'16 (IB-RA, A), ESC'15 (IB), AHA/ACC'14 (IB), CCS'12 (SR/HQ).
  - Ticagrelor, which is preferred over clopidogrel in those with moderate-to-high risk of ischemic events ACC/AHA'16 (IB-R), AHA/ACC'14 (IB), CCS'12 (CR/LQ)
    - Longest DAPT >12 months (balance ischemic & bleeding risks) ACC/AHA'16 (IB-R), AHA/ACC'14 (IB), CCS'12 (CR/LQ)
    - Shorter DAPT of 3 to 6 months after DES if high bleeding risk ACC/AHA'16 (IB-R, B), AHA/ACC'14 (IB), CCS'12 (SR/HQ), CHEST'12 (2B)
  - Minimum DAPT: BMS x 1 month, new-generation DES 3 to 6 months ACC'15 (IB)
  - ASA 81mg po daily indefinitely; ensure 81mg po daily if using ticagrelor. If ASA allergy or intolerance, use clopidogrel indefinitely.
STRENGTH OF RECOMMENDATIONS & LEVELS OF EVIDENCE continued

STEMI & PCI

- Ideally, DAPT x 12 months
  - Clopidogrel ESC/EACTS'14 (IB), ACC/AHA'13, CCS'12 (SR/HQ), CHEST'12 (IB)
  - Prasugrel ESC/EACTS'14 (IB), ACC/AHA'13 (IB), CCS'12 (SR/HQ)
  - Ticagrelor ESC/EACTS'14 (IB), ACC/AHA'13 (IB), CCS'12 (SR/HQ)
  Options listed alphabetically:
  - Ideally, DAPT x 12 months ACC/AHA'16 (IB-R), ACC/AHA'16 (IIa, B-R), ACCF/AHA'13 (IB)
  - Clopidogrel ESC/EACTS'14 (IB), ACC/AHA'13 (IB), CCS'12 (SR/HQ)
  - Prasugrel ACC/AHA'16 (IB), ACCF/AHA'13 (IB), CCS'12 (SR/HQ)
  - Ticagrelor ACC/AHA'16 (IB), ACCF/AHA'13 (IB), CCS'12 (SR/HQ)

- Avoid if a history of stroke/TIA, high bleed risk & use 5mg daily if ≥75 years or weigh ≤60kg. ACC/AHA'16 (III, B-R), ACCF/AHA'13 (IIIB)

- If a history of stroke/TIA, ACC/AHA'16 (III, B-R), ACCF/AHA'13 (IIIB)

- Prasugrel is preferred over clopidogrel ESC/EACTS'14 (IB), ACCF/AHA'13 (IB), CCS'12 (SR/HQ) if not a high bleed risk. ACC/AHA'16 (IIb, A)

- Ticagrelor is preferred over clopidogrel ESC/EACTS'14 (IB), ACCF/AHA'13 (IB), CCS'12 (SR/HQ), CHEST'12 (IB)

- Longer DAPT beyond 12 months may be considered if DES ACC/AHA'16 (IIb, A), ACC/AHA'16 (IB-R), ACCF/AHA'13 (IB), CCS'12 (SR/HQ), CHEST'12 (IB)

- ASA 81mg po daily indefinitely. ESC/EACTS'14 (IA), ACCF/AHA'13 (IA) If ASA allergy or intolerance, use clopidogrel indefinitely. CCS'12 (SR/HQ)

MEDICALLY MANAGED ACS

- Ideally, DAPT with ASA 81mg po daily + clopidogrel 75mg po daily CURE, CURRENT-OASIS or ticagrelor 90mg po BID PLATO, PLATO (non-invasive management subgroup analysis) x 12 months. ACC/AHA'16 (IB-R), CCS'12 (SR/HQ), CHEST'12 (IB)

- Preference for ticagrelor over clopidogrel, ACC/AHA'16 (IIa, B-R), ACCF/AHA'13 (IB), CCS'12 (SR/HQ), COMMIT, CLARITY

- Minimum Durations with clopidogrel:
  - STEMI: 14 days to 1 month; CCS'10 (IA), CURE
  - NSTEACS: 1 month CCS'10 (IA), CURE

PERIPHERAL ARTERY DISEASE

- Symptomatic PAD: CHEST 2012 & ESC 2011 recommend against the use of DAPT for symptomatic PAD. ACCF/AHA 2011 & CCS 2010 state the combination may be considered in patients at high vascular risk with a low risk of bleeding. ACC/AHA'16 (IIb,A)
  - This is based on CHARISMA (clopidogrel + ASA vs ASA alone), in which 25% of the patients had PAD. The primary outcome was the rate of ischemic events (death, MI, stroke, urgent revascularization or hospitalization for unstable angina). Clopidogrel + ASA 6.9% vs ASA alone 7.9%, RR 0.88 (95% CI 0.77-0.998), p=0.046 (underpowered).

CARDIOVASCULAR INDICATIONS – TRIPLE THERAPY

GENERAL RECOMMENDATIONS

- Ensure there is a compelling indication for triple therapy: LV thrombus, anterior apical akinesis or dyskinesis; ACC/AHA'13 (IIb,C)

- In patients with AF, use the CHADS2 or CHA2DS2-VASc score to estimate stroke risk & the HASBLED to estimate bleed risk. ESC/EACTS'14 (IIa,C), ESC/EHRA/EAPCI/ACCA/HRS/APHRS'14 (IIb,C)

- New-generation DES are preferred over BMS, especially when HASBLED ≤ 2. ACC/AHA'13 (IC), CCS'12 (CR/LQ), ESC/EACTS'14 (IIa,C), ACCF/AHA'13 (IC), ESC/EHRA/EAPCI/ACCA/HRS/APHRS'14 (IIa,C)

- Implement strategies to reduce bleeding: aim for a TTR>70%, ESC/EACTS'14 (IA), ESC/EHRA/EAPCI/ACCA/HRS/APHRS'14 (IIa,C), AHA/ACC'14 (IC), ACCF/AHA'13 (IC)

STABLE CAD + PCI & AF

- CHA2DS2-V ASc score ≤1: consider using DAPT as an alternative to TT. ESC/EACTS'14 (IA)
  - HAS-BLED ≤2: consider using DAPT or dual therapy (OAC + clopidogrel [or ASA]), as alternatives to TT. ESC/EHA/EPACI/ACCA/HRS/APHRS'14 (IIa,C)
  - HAS-BLED >3: consider using DAPT, or dual therapy (OAC + clopidogrel [or ASA]) x 12 months, as alternatives to TT. ESC/EHA/EPACI/ACCA/HRS/APHRS'14 (IIa,C)

- CHA2DS2-V ASc score ≥2:
  - HAS-BLED ≤2: TT x 1 month, (OAC + SAPT) up to 12 months. ESC/EACTS'14 (IIa,C), ESC/EHA/EPACI/ACCA/HRS/APHRS'14 (IIa,C)
  - HAS-BLED ≥3: TT (maximum 6 months) ESC/EACTS'14 (IIa,C), ESC/EHA/EPACI/ACCA/HRS/APHRS'14 (IIa,C)

- After 1 year post-PCI, long-term OAC. ESC/EHA/EPACI/ACCA/HRS/APHRS'14 (IIa,C)

CARDIOVASCULAR INDICATIONS – TRIPLE THERAPY

STABLE CAD + PCI & AF

- CHA2DS2-V ASc score ≤1: consider using DAPT as an alternative to TT. ESC/EACTS'14 (IA)
  - HAS-BLED ≤2: consider using DAPT or dual therapy (OAC + clopidogrel [or ASA]), as alternatives to TT. ESC/EHA/EPACI/ACCA/HRS/APHRS'14 (IIa,C)
  - HAS-BLED >3: consider using DAPT, or dual therapy (OAC + clopidogrel [or ASA]) x 12 months, as alternatives to TT. ESC/EHA/EPACI/ACCA/HRS/APHRS'14 (IIa,C)

- CHA2DS2-V ASc score ≥2:
  - HAS-BLED ≤2: TT x 1 month, (OAC + SAPT) up to 12 months. ESC/EACTS'14 (IIa,C), ESC/EHA/EPACI/ACCA/HRS/APHRS'14 (IIa,C)
  - HAS-BLED ≥3: TT (maximum 6 months) ESC/EACTS'14 (IIa,C), ESC/EHA/EPACI/ACCA/HRS/APHRS'14 (IIa,C)

- After 1 year post-PCI, long-term OAC. ESC/EHA/EPACI/ACCA/HRS/APHRS'14 (IIa,C)

CARDIOVASCULAR INDICATIONS – TRIPLE THERAPY

STABLE CAD + PCI & AF

- CHA2DS2-V ASc score ≤1: consider using DAPT as an alternative to TT. ESC/EACTS'14 (IA)
  - HAS-BLED ≤2: consider using DAPT or dual therapy (OAC + clopidogrel [or ASA]), as alternatives to TT. ESC/EHA/EPACI/ACCA/HRS/APHRS'14 (IIa,C)
  - HAS-BLED >3: consider using DAPT, or dual therapy (OAC + clopidogrel [or ASA]) x 12 months, as alternatives to TT. ESC/EHA/EPACI/ACCA/HRS/APHRS'14 (IIa,C)

- CHA2DS2-V ASc score ≥2:
  - HAS-BLED ≤2: TT x 1 month, (OAC + SAPT) up to 12 months. ESC/EACTS'14 (IIa,C), ESC/EHA/EPACI/ACCA/HRS/APHRS'14 (IIa,C)
  - HAS-BLED ≥3: TT (maximum 6 months) ESC/EACTS'14 (IIa,C), ESC/EHA/EPACI/ACCA/HRS/APHRS'14 (IIa,C)

- After 1 year post-PCI, long-term OAC. ESC/EHA/EPACI/ACCA/HRS/APHRS'14 (IIa,C)

CARDIOVASCULAR INDICATIONS – TRIPLE THERAPY

STABLE CAD + PCI & AF

- CHA2DS2-V ASc score ≤1: consider using DAPT as an alternative to TT. ESC/EACTS'14 (IA)
  - HAS-BLED ≤2: consider using DAPT or dual therapy (OAC + clopidogrel [or ASA]), as alternatives to TT. ESC/EHA/EPACI/ACCA/HRS/APHRS'14 (IIa,C)
  - HAS-BLED >3: consider using DAPT, or dual therapy (OAC + clopidogrel [or ASA]) x 12 months, as alternatives to TT. ESC/EHA/EPACI/ACCA/HRS/APHRS'14 (IIa,C)

- CHA2DS2-V ASc score ≥2:
  - HAS-BLED ≤2: TT x 1 month, (OAC + SAPT) up to 12 months. ESC/EACTS'14 (IIa,C), ESC/EHA/EPACI/ACCA/HRS/APHRS'14 (IIa,C)
  - HAS-BLED ≥3: TT (maximum 6 months) ESC/EACTS'14 (IIa,C), ESC/EHA/EPACI/ACCA/HRS/APHRS'14 (IIa,C)

- After 1 year post-PCI, long-term OAC. ESC/EHA/EPACI/ACCA/HRS/APHRS'14 (IIa,C)
**CARDIOVASCULAR INDICATIONS – TRIPLE THERAPY continued**

### NSTEACS + PCI & AF
- **CHA2DS2-VASc score of 1 (in males) or 2 (in females):** consider using DAPT as an alternative to TT. ESC'15 (IIa,C)
- **HASBLED 0-2:** TT x 6 months, then dual therapy (OAC + SAPT) x 6 months, ESC/EACTS'14 (IIa,C), ESC/EHRA/EAPCI/ACCA/HRS/APHRS'14 (IIa,C) regardless of stent type.
  - **CHA2DS2-VASc ≥2:** may continue TT or dual therapy (OAC + SAPT) between 6 and 12 months. ESC/EHRA/EAPCI/ACCA/HRS/APHRS'14 (IIb,C)
  - **HASBLED ≥3:** TT x 1 month, then dual therapy (OAC + SAPT) x 11 months, regardless of stent type. May consider dual therapy (OAC + clopidogrel [or ASA]) in very selected cases e.g. stenting of left main, proximal bifurcation, recurrent MIs, etc. ESC/EHRA/EAPCI/ACCA/HRS/APHRS'14 (IIb,B)
- **After 1 year post-PCI, long-term OAC:** may use dual therapy (OAC + clopidogrel [or ASA]) x 12 months. ESC/EHRA/EAPCI/ACCA/HRS/APHRS'14 (IIb,B)
- **Medically Managed or CABG:** dual therapy (OAC + SAPT) preferred x 12 months. ESC/EHRA/EAPCI/ACCA/HRS/APHRS'14 (IIb,B)
- **Avoid TT with novel P2Y12 inhibitors:** however may consider one of these agents if the patient has a stent thrombosis while on TT with clopidogrel. ESC/EHRA/EAPCI/ACCA/HRS/APHRS'14 (IIb,C)

### STEMI + PCI & AF
- **CHA2DS2-VASc score ≥2:** may continue TT or dual therapy (OAC + SAPT) between 6 and 12 months. ESC/EHRA/EAPCI/ACCA/HRS/APHRS'14 (IIb,C)
- **HASBLED ≥3:** TT x 1 month, then dual therapy (OAC + SAPT) x 11 months, regardless of stent type. May consider dual therapy (OAC + clopidogrel [or ASA]) in very selected cases e.g. stenting of left main, proximal bifurcation, recurrent MIs, etc. ESC/EHRA/EAPCI/ACCA/HRS/APHRS'14 (IIb,B)
- **After 1 year post-PCI, long-term OAC:** may use dual therapy (OAC + clopidogrel [or ASA]) x 12 months. ESC/EHRA/EAPCI/ACCA/HRS/APHRS'14 (IIb,B)
- **Avoid TT with novel P2Y12 inhibitors:** however may consider one of these agents if the patient has a stent thrombosis while on TT with clopidogrel. ESC/EHRA/EAPCI/ACCA/HRS/APHRS'14 (IIb,C)

### Triple Therapy for Secondary Prevention
- **There are conflicting guideline considerations for the use of rivaroxaban for secondary prevention of ACS. Rivaroxaban 2.5mg BID x 1 year may be considered in select patients with a low risk of bleeding, but should not be used in preference to DAPT with a novel P2Y12 inhibitor.**
  - Note: this is not an approved indication in Canada & rivaroxaban 2.5mg is not commercially available.
  - Dabigatran & apixaban are NOT recommended for the sole indication of secondary ACS prevention. CCS'12 (SR/HQ), APPRAISE, REDEEM

### CEREBROVASCULAR INDICATIONS

#### Non-cardoembolic Ischemic Stroke
- If antiplatelet therapy is initiated within 24 hours of minor ischemic stroke/TIA, may consider DAPT x 21 days CSBPR'14 (C), AHA/ASA'14 (IIb,B), CHANCE
- Long-term DAPT started days to years after a stroke/TIA is not recommended due to the increased risk of bleeding and mortality CSBPR'14 (A), AHA/ASA'14 (IIIa), SPS3, MATCH
  - See following page for a summary of the trials that formed the basis of the guideline recommendations.

#### Intracranial Artery Stenosis
- **DAPT (ASA 325mg + clopidogrel 75mg po daily) x 90 days** for patients with recent stroke/TIA (within 30 days) due to severe stenosis (70-99%) of a major intracranial artery, with aggressive risk factor management (e.g. SBP<140mmHg or <130mmHg in DM, LDL-C < 1.81mmol/L, lifestyle modification) SAMMPRIS
- Aggressive medical management with percutaneous transluminal angioplasty and stenting (PTAS) had a NNH of 12/30 days, compared to aggressive medical management alone (rate of stroke 30 days to 1 year: NS); ARI at 30 days was 8.9% and at 3 years was 9% SAMMPRIS
### SUMMARY OF ISCHEMIC STROKE DAPT TRIALS (NON-CARDIOEMBOLIC): SECONDARY PREVENTION

<table>
<thead>
<tr>
<th>Study</th>
<th>Regimen *</th>
<th>Start of Treatment in Relation to Event</th>
<th>DAPT Duration</th>
<th>Benefit</th>
<th>Harm</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHANCE (2013, in China)</td>
<td>- Days 1-22: DAPT vs ASA  - Days 22-90: clopidogrel vs ASA 75mg daily</td>
<td>within 24 hours</td>
<td>21 days</td>
<td>↓ risk of stroke NNT=29/90 days</td>
<td>- NS for bleeding &amp; all-cause mortality</td>
</tr>
<tr>
<td>SPS3 (2012)</td>
<td>DAPT vs ASA 325mg</td>
<td>within 2 weeks to 180 days (mean 62 days)</td>
<td>3.4 years</td>
<td>NS for primary endpoint (stroke/MI)</td>
<td>↑ risk of all-cause mortality NNH=44 (or 143/year)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>↑ risk of major bleeding NNH=32 (or 100/year)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>discontinuation rates NNH=34</td>
</tr>
<tr>
<td>FASTER (2007)</td>
<td>DAPT vs ASA 81mg</td>
<td>within 24 hours</td>
<td>90 days</td>
<td>NS for primary endpoint (stroke)</td>
<td>↑ risk of symptomatic bleeding NNH=34 &amp; bruising NNH=6</td>
</tr>
<tr>
<td>MATCH (2004)</td>
<td>DAPT vs clopidogrel</td>
<td>within 3 months (mean 26 days)</td>
<td>18 months</td>
<td>NS for primary endpoint (stroke, MI, vascular death or rehospitalization for acute ischemic event)</td>
<td>↑ risk of bleeding (life-threatening NNH=50, major NNH=100)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>GI bleeds were the most common location for life-threatening (53%) &amp; major (58%) bleeds.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Kaplan-Meier curve for intracranial hemorrhage suggests no difference in risk for the first 90 days; ↑ risk with DAPT beyond 90 days.</td>
</tr>
</tbody>
</table>

* All DAPT regimens with clopidogrel 75mg daily

### ESTIMATING BLEEDING RISK for DAPT

- DAPT score calculator weighs the risk of thrombosis against the risk of bleeding... for patients who were compliant & event-free for 12 months on DAPT. As such, the DAPT score is unable to estimate the risk of bleeding in individuals whom may require less than 1 year of therapy due to bleeding risk.

- The HASBLED score was shown to have predictive value (score ≥3 indicated ↑ risk of bleeding) in Japanese patients who were on DAPT post-PCI. However, the HASBLED score has not been validated in this patient population (it has been validated in AF patients).

- The REACH registry bleeding risk score was developed & validated (CHARISMA patient population) in outpatients with/without atherothrombosis. Approximately 2/3 of the population had a history of CAD, but the authors did not report how many had undergone revascularization procedures.

- There are limitations to applying the HASBLED or REACH scores to patients who are on DAPT post-ACS; however, these tools may provide additional perspective into bleeding risk factors to consider for choice & duration of therapy.

#### HASBLED

<table>
<thead>
<tr>
<th>HASBLED RISK CRITERIA</th>
<th>POINTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension (SBP&gt;160mmHg)</td>
<td>1</td>
</tr>
<tr>
<td>Abnormal renal or liver function (1 point each)</td>
<td>1 to 2</td>
</tr>
<tr>
<td>Stroke (caused by a bleed)</td>
<td>1</td>
</tr>
<tr>
<td>Bleeding (hospitalization, Hgb &gt;20g/L, transfusion)</td>
<td>1</td>
</tr>
<tr>
<td>Labile INRs (TTR&lt;60%)</td>
<td>1</td>
</tr>
<tr>
<td>Elderly (age &gt;65 years)</td>
<td>1</td>
</tr>
<tr>
<td>Drugs (ASA/NSAID) or alcohol (≥8 drinks/week) (1 point each)</td>
<td>1 to 2</td>
</tr>
</tbody>
</table>

| TOTAL                                        |        |

HASBLED score of ≥3 indicates ↑ risk of bleeding

#### REACH

<table>
<thead>
<tr>
<th>REACH RISK FACTORS</th>
<th>POINTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: 55-64 years</td>
<td>2</td>
</tr>
<tr>
<td>65-74 years</td>
<td>4</td>
</tr>
<tr>
<td>≥75 years</td>
<td>6</td>
</tr>
<tr>
<td>Peripheral Artery Disease</td>
<td>1</td>
</tr>
<tr>
<td>Congestive Heart Failure</td>
<td>2</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>2</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2</td>
</tr>
<tr>
<td>Smoking: Former</td>
<td>1</td>
</tr>
<tr>
<td>Current</td>
<td>2</td>
</tr>
<tr>
<td>Antiplatelet agents: ASA</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
</tr>
<tr>
<td>DAPT</td>
<td>4</td>
</tr>
<tr>
<td>Oral Anticoagulants</td>
<td>4</td>
</tr>
</tbody>
</table>

| TOTAL                                      |        |

REACH score >10 indicates ↑ risk of bleeding
REFERENCES: DURATION OF DAPT & TT

CARDIOVASCULAR GUIDELINES:

CANADIAN CARDIOVASCULAR GUIDELINES


EUROPEAN CARDIOVASCULAR GUIDELINES


USA CARDIOVASCULAR GUIDELINES


**DAPT-POST PCI TRIALS (>1 year)**


**DAPLO POST PCI TRIALS**


**BARE-METAL STENTS**


**DISCONTINUATION OF THERAPY**


STENT THROMBOSIS


REVIEWS ON THE DURATION OF DAPT AFTER CORONARY STENTING

Binder R, Luscher T. Duration of DAPT after coronary artery stenting: where is the sweet spot between ischemia and bleeding? European Heart Journal. 2015; (36)1207-1211.


ASA

**CLOPIDOGREL**


Mehta SR, Yusuf S; Clopidogrel in Unstable angina to prevent Recurrent Events (CURE) Study Investigators. The Clopidogrel in Unstable angina to prevent Recurrent Events (CURE) trial programme; rationale, design and baseline characteristics including a meta-analysis of the effects of thienopyridines in vascular disease. Eur Heart J. 2000 Dec; 21(24):2033-41.


**CLOPIDOGREL: MORTALITY**


**TICAGRELOR**


**PRASUGREL**


**SWITCHING P2Y12 INHIBITORS**


**BLEEDING RISK**


**GASTROINTESTINAL BLEEDING & GASTROPROTECTION**


**DAPT + CABG**
TRIPLE THERAPY


OTHERS


CEREBROVASCULAR INDICATIONS

GUIDELINES


TRIALS


Drug Comparison Charts
10th Edition

Details That Matter
~
Objective & Evidence-based Drug Information

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Assessing Medications in Older Adults
Alternatives to explore, when less may be more

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