ESCP Workshop
DOAC: what the FAQ?
Silas Rydant (Bel) & Aris Prins (Ned)
FAQ 1: who is Aris

• 2004 – 2007 hospital pharmacist, Dundee (Scotland)

• 2007 – present community pharmacist in Poeldijk (the Netherlands)

• Specialties: renal impairment and anticoagulation
FAQ 2: who is Silas

• 2010 – present : flying pharmacist

• 2013 – present : coordination pharmaceutical care projects@KAVA

• 2016 – present : development of GP/pharmacist training programs
FAQ 2: why us?

• Special interest in the safe & rational use of (oral) anticoagulation

• Involved in the development and implementation of (inter)national guidelines, consensus meetings, training programs...

• We love Belgian Beer
Disclosures Aris Prins

Conflict of interest for this workshop: none

Has been paid and given lectures for:

- Novartis
- Boehringer Ingelheim
- Novo Nordisk,
- Bristol-Myers Squibb
- Pfizer
- Bayer
- Astra Zeneca
- Sanofi
Conflict of interest for this workshop: none

Has been paid and given lectures for:

- Bayer
- GlaxoSmithKline
- Abbvie
- Amgen
FAQ 3: who are you and what do you expect to take away from this workshop?
LET'S GET STARTED
FAQ 4: NOAC or DOAC?
NOAC: NON-VKA Oral AntiCoagulant
DOAC: Direct Oral AntiCoagulants

*DOH!
FAQ

Who prescribes it?
Who continues it?
Who is responsible?
Who can patients turn to?
What do we expect regarding trouble / advantages
Do we need regional protocols?
What is the pharmacist role?
What do the insurance companies think?
Optimal care
Optimal care
Reality
Our FAQ’s

1. When why what DOAC?
2. Finding the right dose
3. Lets interact (or not?)!
4. How to manage double and triple therapy
5. Why should(ut) we screen?
Does anyone still receive Acetylsalicylic acid (aspirin) for AF?
Effecacy and safety of aspirin vs apixaban

Ng KN et al. Age and Ageing 2016; 45: 77–83
Francis

Francis is 76 years old is diagnosed with AF. No renal problems, only a previous GI haemorrhage.

He also takes

*Simvastatine 40 mg OD evening*

*Ibuprofen (OTC) – when backpain*

*Omeprazole 40 mg – OD morning*

What considerations do you make when anticoagulation needs to be initiated?
### Apixaban age

<table>
<thead>
<tr>
<th></th>
<th>HR (95% CI)</th>
<th>P value for interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke / SE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65 yrs</td>
<td>1,16 (0,77–1,73)</td>
<td>0,11</td>
</tr>
<tr>
<td>65–74 yrs</td>
<td>0,72 (0,54–0,96)</td>
<td></td>
</tr>
<tr>
<td>≥75 yrs</td>
<td>0,71 (0,53–0,95)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Major Bleeding</th>
<th>HR (95% CI)</th>
<th>P value for interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;65 yrs</td>
<td>0,78 (0,55–1,11)</td>
<td></td>
</tr>
<tr>
<td>65–74 yrs</td>
<td>0,71 (0,56–0,89)</td>
<td></td>
</tr>
<tr>
<td>≥75 yrs</td>
<td>0,64 (0,52–0,79)</td>
<td></td>
</tr>
</tbody>
</table>

HR, hazard ratio, SE. Systemic embolism

Adapted from Halvorsen S. Eur Heart J 2014;35:1864–1872
# Edoxaban age

<table>
<thead>
<tr>
<th>Stroke / SE</th>
<th>HR (95% CI)</th>
<th>P value for interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;65 yrs</td>
<td>0.94 (0.65–1.37)</td>
<td>0.84</td>
</tr>
<tr>
<td>65–74 yrs</td>
<td>0.89 (0.68–1.16)</td>
<td></td>
</tr>
<tr>
<td>≥75 yrs</td>
<td>0.71 (0.66–1.04)</td>
<td></td>
</tr>
</tbody>
</table>

HR, hazard ratio, SE. Systemic embolism

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HR, hazard ratio, SE. Systemic embolism

Adapted from Kato ET. J Am Heart Assoc. 2016 May 20;5(5)
Rivaroxaban age

HR, hazard ratio, SE. systemic embolism

Adapted from Halperin JL. Circulation 2014;130:138-146
### Dabigatran age

<table>
<thead>
<tr>
<th></th>
<th>HR (95% CI)</th>
<th>P value for interaction</th>
<th>HR (95% CI)</th>
<th>P value for interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stroke / SE</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dabigatran 110 mg</td>
<td>0.81</td>
<td></td>
<td>Dabigatran 150 mg</td>
<td>0.81</td>
</tr>
<tr>
<td><strong>Age &lt;75 yrs</strong></td>
<td>0.93 (0.70–1.22)</td>
<td></td>
<td>0.63 (0.46–0.86)</td>
<td></td>
</tr>
<tr>
<td><strong>Age ≥75 yrs</strong></td>
<td>0.88 (0.66–1.17)</td>
<td></td>
<td>0.67 (0.49–0.90)</td>
<td></td>
</tr>
</tbody>
</table>

**HR, hazard ratio, SE. systemic embolism**

Adapted from Eikelboom JW. Circulation 2011;123:2363-2372
### Table 1  Selected indications and contraindications for non-vitamin K antagonist oral anticoagulant therapy in atrial fibrillation patients

<table>
<thead>
<tr>
<th>Condition</th>
<th>Eligibility for NOAC therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanical prosthetic valve</td>
<td>Contraindicated</td>
</tr>
<tr>
<td>Moderate to severe mitral stenosis (usually of rheumatic origin)</td>
<td>Contraindicated</td>
</tr>
<tr>
<td>Mild to moderate other native valvular disease (e.g., mild-moderate aortic stenosis or regurgitation, degenerative mitral regurgitation etc.)</td>
<td>Included in NOAC trials</td>
</tr>
<tr>
<td>Severe aortic stenosis</td>
<td>Limited data (excluded in RE-LY); Most will undergo intervention</td>
</tr>
<tr>
<td>Bioprosthesis valve (after &gt; 3 months post operatively)</td>
<td>Not advised if for rheumatic mitral stenosis</td>
</tr>
<tr>
<td>Mitral valve repair (after &gt; 3 months post operatively)</td>
<td>Acceptable if for degenerative mitral regurgitation or in the aortic position</td>
</tr>
<tr>
<td>PTAV and TAVI</td>
<td>No prospective data yet; May require combination with single or dual antiplatelet therapy</td>
</tr>
<tr>
<td>Hypertrophic cardiomyopathy</td>
<td>Few data, but patients may be eligible for NOACs</td>
</tr>
</tbody>
</table>

Hatched—limited data.

PTAV, percutaneous transluminal aortic valvuloplasty; TAVI, transcatheater aortic valve implantation.
Amount of first prescriptions (in the Netherlands)
Evolution of VKA/DOAC (Belgium)

Aantallen patiënten

Jaar


Totaal

Vitamine K antagonisten

Directe orale anticoagulantia
When why what DOAC?
Is adherence something to consider when initiating DOAC?
Reasons for discontinuation of NOAC’s in Sweden

### Reasons for Discontinuation of NOACs

<table>
<thead>
<tr>
<th>NOAC</th>
<th>Side Effects</th>
<th>Bleeding</th>
<th>Various</th>
<th>Patient Decision</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran</td>
<td>4%</td>
<td>16%</td>
<td>17%</td>
<td>63%</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>7%</td>
<td>9%</td>
<td>38%</td>
<td>46%</td>
</tr>
<tr>
<td>Apixaban</td>
<td>4%</td>
<td>27%</td>
<td>46%</td>
<td>23%</td>
</tr>
</tbody>
</table>

### Outcomes of NOAC Discontinuation

- **Change to another NOAC**: 58%
- **Change to VKA**: 27%
- **Withdrawal of Anticoagulation**: 15%
- **Various**: 4%

  * Various conditions, which warrant withdrawal as determined by the patients physician, like risks for interaction with concomitant medication, cardiac intervention, cancer, new onset of cardiac ischemia, cerebral ischemic stroke, and worsened renal function.
Adherence of DOAC’s in the Nederlands amongst 560 pharmacist

DOI 10.1186/s12959-017-0156-y

RESEARCH Open Access

NOACs replace VKA as preferred oral anticoagulant among new patients: a drug utilization study in 560 pharmacies in The Netherlands

J. M. van den Heuvel¹,², A. M. Hövels¹, H. R. Büller³, A. K. Mantel-Teeuwisse¹, A. de Boer¹ and A. H. Maitland-van der Zee¹,²*

<table>
<thead>
<tr>
<th>Table 2 Percentage of adherent patients per NOAC</th>
<th>Pct of patients</th>
<th>Nr of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apixaban</td>
<td>92%</td>
<td>7094</td>
</tr>
<tr>
<td>Dabigatran</td>
<td>88%</td>
<td>11,782</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>88%</td>
<td>13,975</td>
</tr>
<tr>
<td>Total</td>
<td>89%</td>
<td>32,851</td>
</tr>
</tbody>
</table>
Side-effects

• Is bleeding a reason not to initiate DOAC?
Risk of strokes and bleeds per age

Adapted from Van Walraven C et al. Stroke 2009;40:1410-1416
when, why, what DOAC?

Individual patient groups and characteristics

- Asian patients
- Elderly patients
- Renal impairment
- Previous GI haemorrhage
- High bleeding risk (HAS-BLED ≥3)
- Recurrent stroke despite well-managed VKA
- Preference for low pill burden
- Patient less likely to do well on VKA (SAmET2R2 score >2)

Consider:
- Agents with reduced risk of ICH and major haemorrhage in Asian populations
- Co-morbidities and agents with lower extracranial haemorrhage amongst elderly (age >75)
- Consider agents with lower haemorrhagic complications in moderate-severe renal impairment
- Consider agents with no increased risk of GI haemorrhage
- Consider agents with lower incidence of extracranial haemorrhage
- Consider agent with demonstrable benefit in reducing both ischaemic AND haemorrhagic stroke
- Consider once-daily formulations
- Avoid ‘trial of warfarin’ and consider NOAC upfront when deciding on OAC in newly diagnosed patient

NOACs with characteristics beneficial to target group

- Apixaban
- Dabigatran
- Edoxaban
- Apixaban
- Apixaban 110 mg
- Dabigatran 110 mg
- Edoxaban
- Edoxaban 150 mg
- Rivaroxaban

Any NOAC, but consider patient characteristics when choosing agent

Mary

Mary is 76 years old and takes warfarin (Marevan®).

What could potentially interfere with warfarin?
A. *co-trimoxazol*
B. *Levothyroxine*
C. *Rosuvastatin*
Enter a drug, OTC or herbal supplement:

warfarin

Serious - Use Alternative

Enter a drug, OTC or herbal supplement:

levothyrionine

1 Interaction Found

Monitor Closely

rosuvastatin + warfarin

rosuvastatin increases effects of warfarin by unspecified interaction mechanism. Use Caution/Monitor.
Mary

What could be an alternative and how will you manage this?
Switch from VKA to DOAC

Guideline: stop VKA, start DOAC if INR ≤ 2

Prescribing

• What role do you have (or potentially see) when initiating or switching of anticoagulation?
Our FAQ’s

1. When why what DOAC?

2. Finding the right dose

3. Lets interact (or not?)!

4. How to manage double and triple therapy

5. Why should(nt) we screen?
<table>
<thead>
<tr>
<th>Indication</th>
<th>Dabigatran (Pradaxa®)</th>
<th>Rivaroxaban (Xarelto®)</th>
<th>Apixaban (Eliquis®)</th>
<th>Edoxaban (Lixiana®)</th>
<th>Treatment duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary prevention VTE Knee/hip replacement</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trombo-embolic prevention (AF)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment DVT &amp; PE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secundary prevention DVT &amp; PE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Normal dosage NOAC’s

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dabigatran (Pradaxa®)</th>
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<th>Apixaban (Eliquis®)</th>
<th>Edoxaban (Lixiana®)</th>
<th>Treatment duration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary prevention VTE Knee/hip replacement</strong></td>
<td>220 mg 1x/day (10d/35d)</td>
<td>10 mg 1x/day (2w / max 5 w)</td>
<td>2,5 mg 2x/day (14d/38d)</td>
<td>X</td>
<td>Afh. van GM Knie: 10-14d Heup: 32-38d</td>
</tr>
<tr>
<td><strong>Trombo-embolische preventie (VKF)</strong></td>
<td>150 mg 2x/dag</td>
<td>20 mg 1x/dag</td>
<td>5 mg 2x/dag</td>
<td>60 mg 1x/dag</td>
<td>In principe levenslang</td>
</tr>
<tr>
<td><strong>Behandeling acute DVT en PE</strong></td>
<td>150 mg 2x/dag (na LMGH min 5d)</td>
<td>15 mg 2x/dag (21d) =&gt; 20 mg 1x/dag</td>
<td>10 mg 2x/dag (7d) =&gt; 5 mg 2x/d</td>
<td>60 mg 1x/dag (na LMGH min 5d)</td>
<td>Minstens 3 maand, overleg met specialist</td>
</tr>
<tr>
<td><strong>Secundaire preventie DVT en PE</strong></td>
<td>150 mg 2x/dag</td>
<td>20 mg 1x/dag (6m) =&gt; 10mg 1x/dag</td>
<td>2,5 mg 2x/dag</td>
<td>60 mg 1x/dag</td>
<td>Individuele afweging</td>
</tr>
</tbody>
</table>

Preventie atherotrombotische events na ACS: Pradaxa®, Eliquis®, Lixiana®: geen indicatie; Xarelto®: geen TB in België
Factors that influence the dose

• What factors can impact the ‘right’ dose?
Factors that influence the dose

- What factors can impact the ‘right’ dose?

- Serum creatinine
- Indication
## Factors

<table>
<thead>
<tr>
<th>Factor</th>
<th>Dabigatran (Pradaxa®)</th>
<th>Rivaroxaban (Xarelto®)</th>
<th>Apixaban (Eliquis®)</th>
<th>Edoxaban (Lixiana®)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indication</td>
<td>V</td>
<td>V</td>
<td>V</td>
<td>V</td>
</tr>
<tr>
<td>Age</td>
<td>V</td>
<td></td>
<td>V</td>
<td>V</td>
</tr>
<tr>
<td>Weight</td>
<td></td>
<td>V</td>
<td>V</td>
<td>V</td>
</tr>
<tr>
<td>Comedication</td>
<td>V</td>
<td></td>
<td></td>
<td>V</td>
</tr>
<tr>
<td>Renal impairment</td>
<td>V</td>
<td>V</td>
<td>V</td>
<td>V</td>
</tr>
<tr>
<td>Risk for bleeding*</td>
<td>V</td>
<td>V</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*To consider if risk of bleeding is high and risk of TE low*
John

John, 85 years old and has the following medication:

R/ Bisoprolol 5mg
R/ Allopurinol 100 mg
R/ Rivaroxaban 20 mg (AF)
R/ Sitagliptine 50 mg
R/ metformine BID 500 mg

What potential problem do you see?
John

Based on the medication, John probably has mild renal impairment

Sitagliptine 50 mg => GFR between 30 – 45
Metformine 1000 mg daily => GFR 30 – 45
Allopurinol 100 mg => GFR >20

What about Rivaroxaban?
Rivaroxaban is cleared by the kidney (up to 35%) and T½ is around 13h in elderly

⇒ *Renal impairment could lead to higher risk for bleedings*

⇒ *John has a eGFR of 38 mL/min*

⇒ *Dose reduction? What sources do you use?*
SmPC: Mild (30-49mL/min) or severe (15 - 29 ml/min) 15 mg OD
Stephanie

Stephanie is taking Apixaban 2,5 mg. What can/will you check before dispensing?

- Indication
- Age
- Weight
- Renal
- Comedication
Stephanie

- **Indication**: Atrial fibrillation
- **Age**: 72 year
- **Weight**: 78
- **CrCl**: 45 mL/min
- **Serum**: 110 mmol

⇒ What dose is appropriate for Stephanie?

A. 2.5 mg twice daily
B. 2.5 mg once daily
C. 5 mg twice daily
D. 5 mg once daily
Stephanie – apixaban

When lower the dose?

15-30 ml/min

OR

≥80 år

≤60 kg

≥133 µmol/l

2 / 3 factors
Stephanie

- **Indication:** Atrial fibrillation
- **Age:** 72 year
- **Weight:** 78
- **CrCl:** 45 mL/min
- **Serum:** 110 mmol

⇒ What dose is appropriate for Stephanie?

A. 2,5 mg twice daily
B. 2,5 mg once daily
C. 5 mg twice daily
D. 5 mg once daily
Dosisaanpassingen DOACs bij AF

**Serum creatinine**

<table>
<thead>
<tr>
<th>DOAC</th>
<th>Dosering</th>
<th>Beperkingen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apixaban</td>
<td>Naar 2,5 mg BID</td>
<td>15-30ml/min</td>
</tr>
<tr>
<td>Edoxaban</td>
<td>Naar 30 mg OD</td>
<td>15-50ml/min</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>Naar 15 mg OD</td>
<td>15-50ml/min</td>
</tr>
<tr>
<td>Dabigatran</td>
<td>Naar 110 mg BID</td>
<td>30-50ml/min</td>
</tr>
</tbody>
</table>

* dronedarone, erythromycine, ketokonazol, ciclosporine

**Bronnen:** Farmacotherapeutisch kompas en vigerende SmPCs van apixaban, dabigatran, edoxaban en rivaroxaban
Question

What is the possible clinical impact of over- and under dosing?

*Is it a problem in real life?*
Mogelijke gevaren van onder- en overdosering
Effects of under-dosage in day to day practice

Effectiveness and safety of reduced dose non-vitamin K antagonist oral anticoagulants and warfarin in patients with atrial fibrillation: propensity weighted nationwide cohort study

The administration of a lower dose than should be given according to the patient profile can influence clinical outcomes.


Nielsen et al. BMJ 2017
Overdosing DOAC

Renal impairment and indication for dose reduction

43% is potentially overdosed

Higher risk of bleeding (geen verschil in beroerte)

Non–Vitamin K Antagonist Oral Anticoagulant Dosing in Patients With Atrial Fibrillation and Renal Dysfunction; Yao 2017
Underdosing DOAC

- No renal impairment
- 13% potentially underdosed
- Higher risk of stroke (geen verschil in bloeding)

Non–Vitamin K Antagonist Oral Anticoagulant Dosing in Patients With Atrial Fibrillation and Renal Dysfunction; Yao 2017
Renal impairment & the right dose

How do you tackle these problems in your setting?
Renal impairment & the right dose

How do you tackle these problems in your setting?

Who knows the app ‘NOACs easy’?
Medical Pharmaceutical Consultation

• Local meeting GP ⇔ community pharmacists (small groups)

• Projects around the use of medication can be funded by the NIHDI(€ 2500 / project)

• Projects DOAC / CKD : 13 / 23
Welkom op onze website!

De *huisartsenvereniging Domus Medica* en de *Koninklijke Apothekers Vereniging Antwerpen* (KAVA) geloven sterk in de meerwaarde van het Medisch Farmaceutisch Overleg (MFO). Om hun leden beter te informeren over de mogelijkheden van het MFO en de kwaliteit hiervan te verbeteren werd deze website ontwikkeld.
Medical Pharmaceutical Consultation

- Preparation (GP/pharmacist)
- Local meeting
- Case discussion
- Decisions & conclusions
- Actionpoints
- Evaluation
Medical Pharmaceutical Consultation

• Discussed cases
  • A correct prescription (dosing)
  • How and when to switch
  • How to tackle interactions
  • Gastro-protection
  • Bridging or stop?

⇒% patients with a dose cf guideline/SKP

⇒% patients with DOAC + NSAID + PPI
Medical Pharmaceutical Consultation

• How do you measure ‘quality’?
Key messages

• Different factors can impact the right dose

• Under-and overdosing is a clinical problem

• Common training (GP/pharmacist) is necessary

• There are tools/guidelines/schedules available
Our FAQ’s

1. When why what DOAC?
2. Finding the right dose
3. Lets interact (or not?)!
4. How to manage double and triple therapy
5. Why should(nt) we screen?
Pharmacists role

• What sources do you use to find interactions? Who takes responsibility?
## Food

**DOAC with or without food?**

<table>
<thead>
<tr>
<th>Indicatie</th>
<th>Dabigatran (Pradaxa®)</th>
<th>Rivaroxaban (Xarelto®)</th>
<th>Apixaban (Eliquis®)</th>
<th>Edoxaban (Lixiana®)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bio availability</td>
<td>3-7%</td>
<td>66% - 100%</td>
<td>50%</td>
<td>62%</td>
</tr>
<tr>
<td>Clearance</td>
<td>80% renaal</td>
<td>35% renaal</td>
<td>27% renaal</td>
<td>50% renaal</td>
</tr>
<tr>
<td>T 1/2</td>
<td>12-17u (tot 13u bij ouderen)</td>
<td>5-9u</td>
<td>12u</td>
<td>10-14u</td>
</tr>
<tr>
<td>CYP3A4</td>
<td>Neen</td>
<td>Ja</td>
<td>Ja</td>
<td>Ja</td>
</tr>
<tr>
<td>ATTENTION</td>
<td>DO NOT OPEN</td>
<td>15-20mg with FOOD</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
José

• José is taking rivaroxaban OD 20 mg for AF

Atenolol 100 mg OD
Atorstatine 40 mg OD
Metformine 850 mg 2/day
Bumetanide 1 mg OD
Itraconazol 200 mg OD

What potential interaction do you see? How will you act?
Itraconazole increases levels of rivaroxaban by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor. Avoid concomitant use of rivaroxaban and combined Pgp and strong CYP3A4 Inhibitors. Combination may lead to significant increases in rivaroxaban levels and increase bleeding risk.
José

• Change itraconazol with fluconazole
**Figure 3** NOAC selection based on drug–drug interactions and/or risk of bleeding. Use of plasma level measurements to guide dosing is generally discouraged and should only be used in rare cases of potentially substantial interactions or special situations, and only in centres with great experience in the performance and interpretation of such assays as well as the care of NOAC-treated patients.
Bridging

• Mia needs to undergo a kidney biopsy. She’s taking dabigatran.

• How will you manage her medication during her stay?

• What are the guidelines in your setting?
Preoperative bridging with LMWH or heparin is not recommended in NOAC-treated patients since the predictable waning of the anticoagulation effect allows properly timed short-term cessation of NOAC therapy before surgery. On the contrary, the mixing of two anticoagulants (although with similar pharmaco-dynamics and -kinetics) has been associated with an increased bleeding risk. As demonstrated in the BRIDGE trial for VKA, bridging with heparin/LMWH was associated with a significantly higher risk of major bleeding during cessation of oral anticoagulation but did not reduce cardiovascular events.
Bridging

• What consideration you make to stop a DOAC upfront?
  • Type intervention (bleeding risk)
  • Renal clearance
  • Age
  • History of bleeding
  • Comedication
## Bridging

### Table 11: Timing of last non-vitamin K antagonist oral anticoagulant intake before start of an elective intervention

<table>
<thead>
<tr>
<th></th>
<th><strong>Dabigatran</strong></th>
<th><strong>Apixaban – Edoxaban – Rivaroxaban</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No important bleeding risk and/or adequate local haemostasis possible: perform at trough level (i.e. 12 h or 24 h after last intake)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Low risk</strong></td>
<td><strong>High risk</strong></td>
<td><strong>Low risk</strong></td>
</tr>
<tr>
<td>CrCl ≥80 mL/min</td>
<td>≥24h</td>
<td>≥48h</td>
</tr>
<tr>
<td>CrCl 50–79 mL/min</td>
<td>≥36h</td>
<td>≥72h</td>
</tr>
<tr>
<td>CrCl 30–49 mL/min</td>
<td>≥48h</td>
<td>≥96h</td>
</tr>
<tr>
<td>CrCl 15–29 mL/min</td>
<td>Not indicated</td>
<td>Not indicated</td>
</tr>
<tr>
<td>CrCl &lt;15 mL/min</td>
<td>No official indication for use</td>
<td></td>
</tr>
</tbody>
</table>

**No bridging with LMWH/UFH**
Bridging

• What is the guideline for dental interventions?

*Dental surgery*

Dental surgery is generally considered a procedure with minor bleeding risk and with the possibility for adequate local haemostasis. Most professional statements on dental surgery advise not to suspend NOAC treatment and avoid the use of NSAIDs.\(^{274}\) However, recommendations are often based on a low quality of evidence and mainly rely on available pharmacological information.\(^ {275}\) Dental extractions can generally be performed safely in an outpatient facility by applying
Our FAQ’s

1. When why what DOAC?
2. Finding the right dose
3. Lets interact (or not?)!
4. How to manage double and triple therapy
5. Why should(nt) we screen?
What is your role with double /triple therapie?

• How often do you see triple anticoagulation therapies?
• What do you do?
• Is there a guideline in your country?
• Who do you contact?
• What do you need fo safe dispensing?
ESC richtlijnen AF + PCI

AF patient in need of OAC after elective PCI with stent

Bleeding risk low compared to risk for ACS or stent thrombosis

Bleeding risk high compared to risk for ACS or stent thrombosis

Time from PCI

0
1 month
3 months
6 months
12 months
lifelong

Triple therapy (IIaB)

Dual therapy (IIaC)

OAC monotherapy (IB)

OAC
Aspirin 75–100 mg daily
Clopidogrel 75 mg daily

ACS = acute coronary syndrome; AF = atrial fibrillation; OAC = oral anticoagulation (using vitamin K antagonists or non-vitamin K antagonist oral anticoagulants); PCI = percutaneous coronary intervention.

aDual therapy with OAC and aspirin or clopidogrel may be considered in selected patients.

bOAC plus single antiplatelet.

cDual therapy with OAC and an antiplatelet agent (aspirin or clopidogrel) may be considered in patients at high risk of coronary events.

ESC richtlijnen AF + ACS

AF patient in need of OAC after an ACS

Bleeding risk low compared to risk for ACS or stent thrombosis

Bleeding risk high compared to risk for ACS or stent thrombosis

Time from ACS
0
1 month
3 months
6 months
12 months
lifelong

Triple therapy² (IIaB)

OAC monotherapy³ (IB)

Dual therapy¹ (IIaC)

OAC monotherapy³ (IB)

OAC
Aspirin 75–100 mg daily
Clopidogrel 75 mg daily

ACS = acute coronary syndrome; AF = atrial fibrillation; OAC = oral anticoagulation (using vitamin K antagonists or non-vitamin K antagonist oral anticoagulants); PCI = percutaneous coronary intervention.

²Dual therapy with OAC and aspirin or clopidogrel may be considered in selected patients, especially those not receiving a stent or patients at a longer time from the index event.

³OAC plus single antiplatelet.

⁴Dual therapy with OAC and an antiplatelet agent (aspirin or clopidogrel) may be considered in patients at high risk of coronary events.

Do you see a role for pharmacists to screen for AF?
Screening for AF
MyDiagnostick

1 min with automatic classification

Connection via USB, measurements easily visible

No extra equipment required

No need to undress

Just hold while seated and without speaking

Validated instrument

Tieleman et al. 2014
Screenen for AF in a geriatric surgery

Inclusion clinic and + daycare patients

Total of 459 patients, average age 78 ± 7 jaar

• 53% female
• Morbidity 5 ± 2 years, polypharmacie 58%
• Walking disorder 24%, repeatative falls 32%
• High risk of malnutrition 21%
• Milde cognitive disorders 35%, dementia 23%
Screenen for AF in a geriatric surgery

Resultaten of screening

Known AF: 89 (19.4%) patiënten

New AF at first visit: 4 (0.9%) patients

New AF at follow up visits: 14 (3.1%) patients

Total AF: 107 (23.3%) patients

AF de novo: 18 (3.9%) patients
Risk-benefit of anticoagulation treatment of AF in fragile elderly

Thromboembolic Risk, Bleeding Outcomes and Effect of Different Antithrombotic Strategies in Very Elderly Patients With Atrial Fibrillation: A Sub-Analysis From the PREFER in AF (PREvention of Thromboembolic Events–European Registry in Atrial Fibrillation)

Giuseppe Patti, MD; Markus Lucerna, PhD; Ladislav Pecen, PhD; Jolanta M. Siller-Matula, MD; Ilaria Cavallari, MD; Paulus Kirchhof, MD; Raffaele De Caterina, MD, PhD
Risk-benefit of anticoagulation treatment of AF in fragile elderly

– Big European cohort study
– 6412 patients with AF (2012-2014) of which 505 above the age of 85 years
– Comparison of risk of bleeding/stroke with or without anticoagulation therapy
Risk-benefit of anticoagulation treatment of AF in fragile elderly

Figure 3. Incidence of thromboembolic events (stroke/TIA/SEE) in patients aged <85 and ≥85 years receiving OAC or no OAC (antiplatelet therapy only or no antithrombotic drug).

Patti et al, J AM Heart Assoc 2017
Risk-benefit of anticoagulation treatment of AF in fragile elderly

Figure 4. Incidence of major bleeding in patients aged <85 and ≥85 years receiving OAC or no OAC (antiplatelet therapy only or no antithrombotic drug).

Patti et al, J AM Heart Assoc 2017
Net clinical benefit bij ouderen

Bloedingen

Patti et al. J Am Heart Assoc 2017
Casus?