Intracranial haemorrhage related to direct oral anticoagulant medications: Latest evidence for reversal strategies

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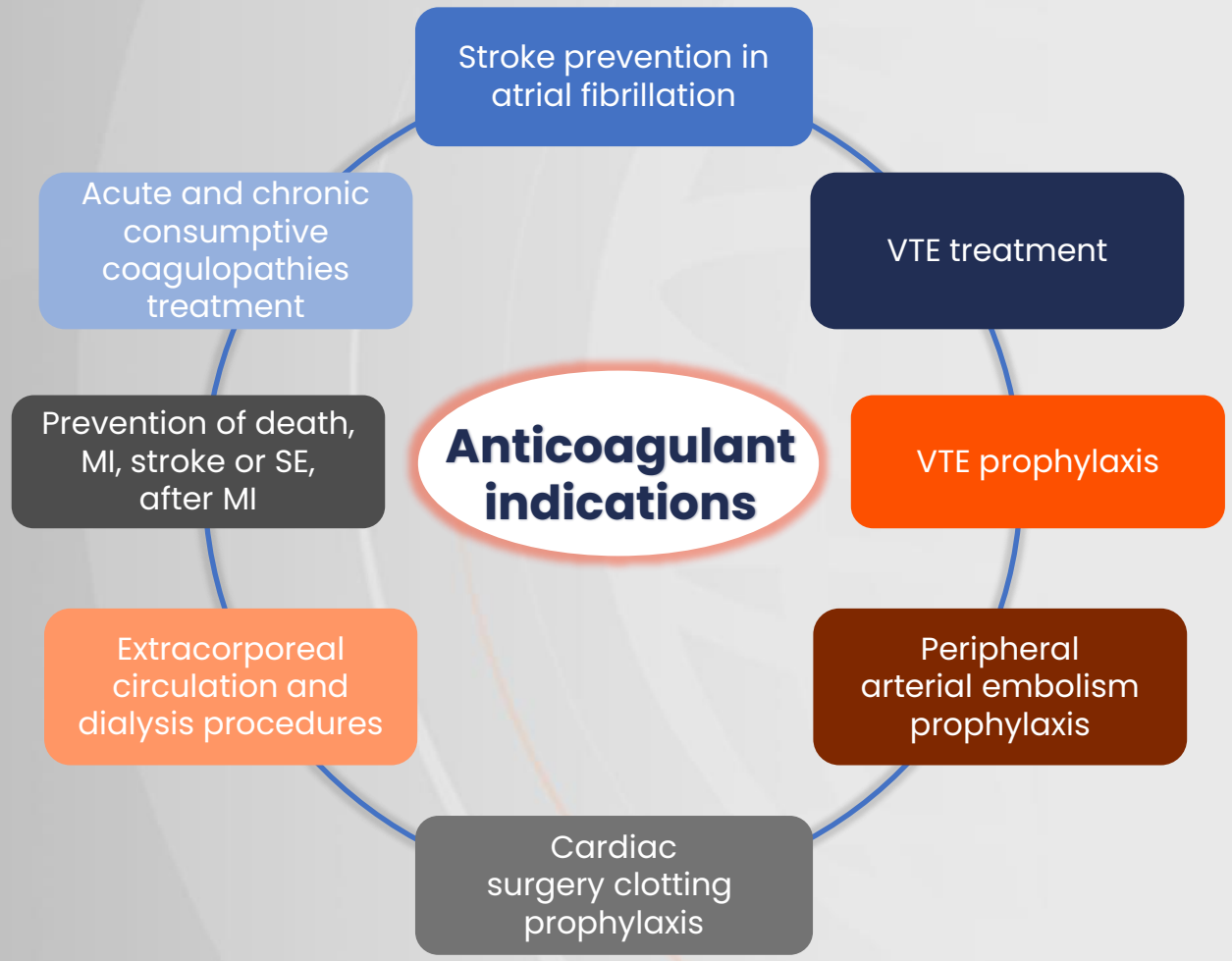
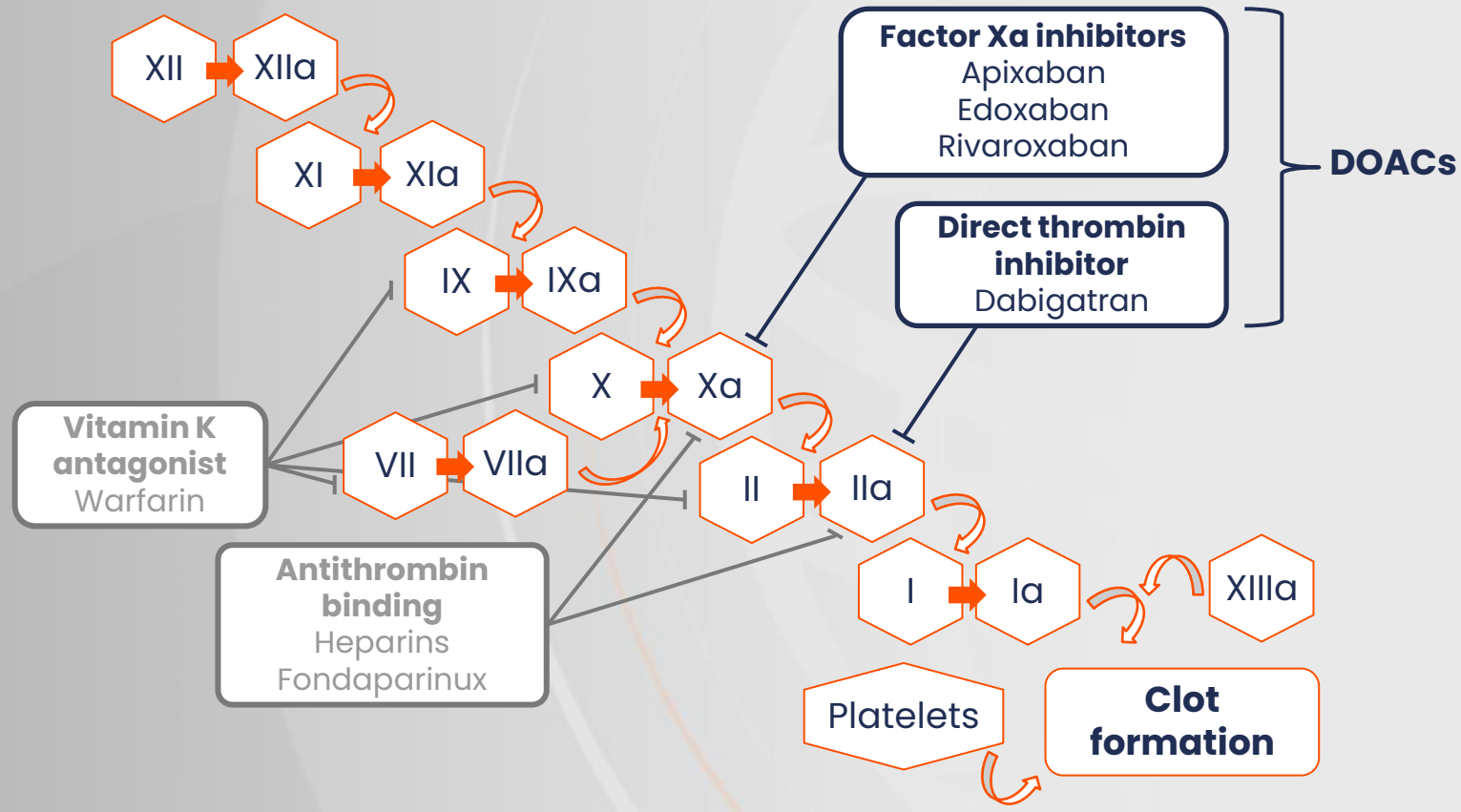
Balancing risk: DOACs in the real world

Oral and parenteral anticoagulants have a range of indications



MI, myocardial infarction; SE, systemic embolism; VTE, venous thromboembolism.
Heestermans M, et al. *Cells.* 2022;11:3214.

Anticoagulants target various components of the coagulation cascade[1,2]

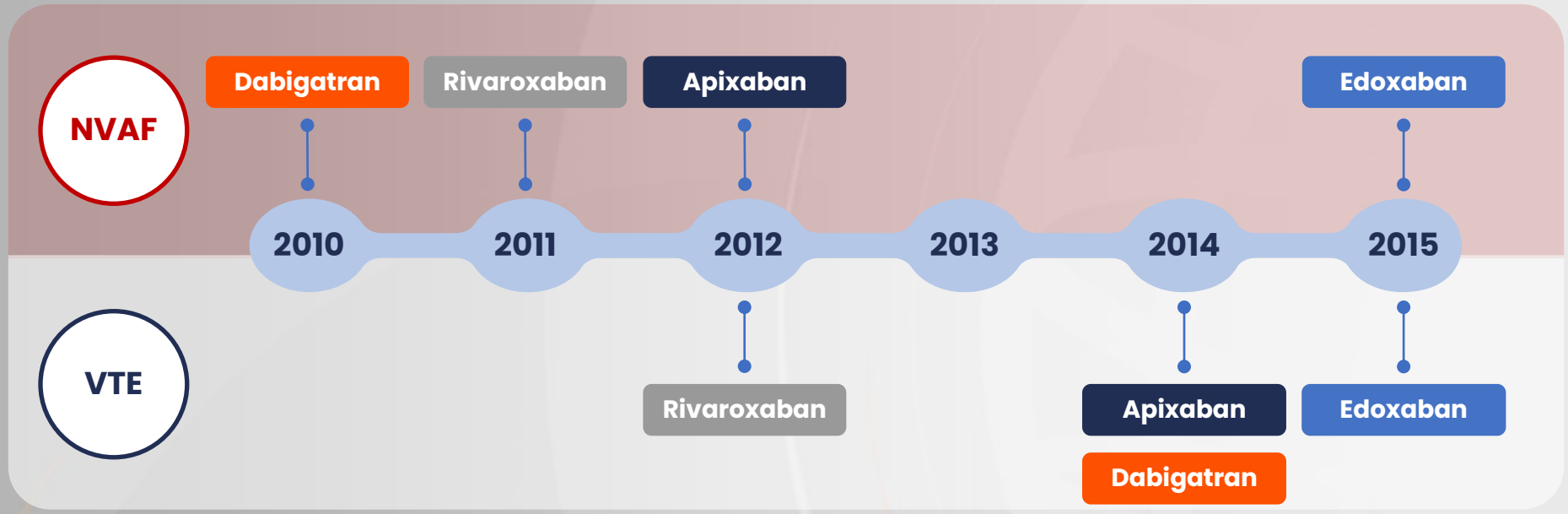


DOAC, direct oral anticoagulant.

1. Akhrass R, et al. *J Card Surg.* 2022;37:214–22; 2. Heestermans M, et al. *Cells.* 2022;11:3214.

DOACs have been widely approved for multiple indications

Timeline of key FDA approvals for DOAC indications[1]



Other approved indications:[2–4]

- DVT prophylaxis after hip and/or knee surgery: apixaban, dabigatran, rivaroxaban
- CV risk reduction in patients with CAD: rivaroxaban
- Paediatric VTE treatment and secondary prophylaxis: dabigatran, rivaroxaban

CAD, coronary artery disease; CV, cardiovascular; DOAC, direct oral anticoagulant; DVT, deep vein thrombosis; FDA, US Food and Drug Administration; NVAF, non-valvular atrial fibrillation; VTE, venous thromboembolism.

1. Arora P, et al. *Res Social Adm Pharm*. 2023;19:1424–31; 2. FDA. Apixaban PI. 2021. Available at: www.accessdata.fda.gov/drugsatfda_docs/label/2021/202155s034lbl.pdf (accessed 3 May 2024); 3. FDA. Dabigatran PI. 2023. Available at: www.accessdata.fda.gov/drugsatfda_docs/label/2024/022512s047lbl.pdf (accessed 3 May 2024); 4. FDA. Rivaroxaban PI. 2023. Available at: www.accessdata.fda.gov/drugsatfda_docs/label/2023/022406s041lbl.pdf (accessed 3 May 2024).

DOACs have a range of benefits compared with other anticoagulants

DOACs are more effective in reducing the risk of stroke/SEE, mortality and recurrent VTE vs VKA therapy

AF population[1]

Composite stroke/SEE*

15%

N=77,011
OR 0.85
(95% CI 0.75–0.98)

All-cause mortality*

14%

N=77,011
OR 0.86
(95% CI 0.82–0.91)

VTE population[2]

Recurrent VTE or death**

12%

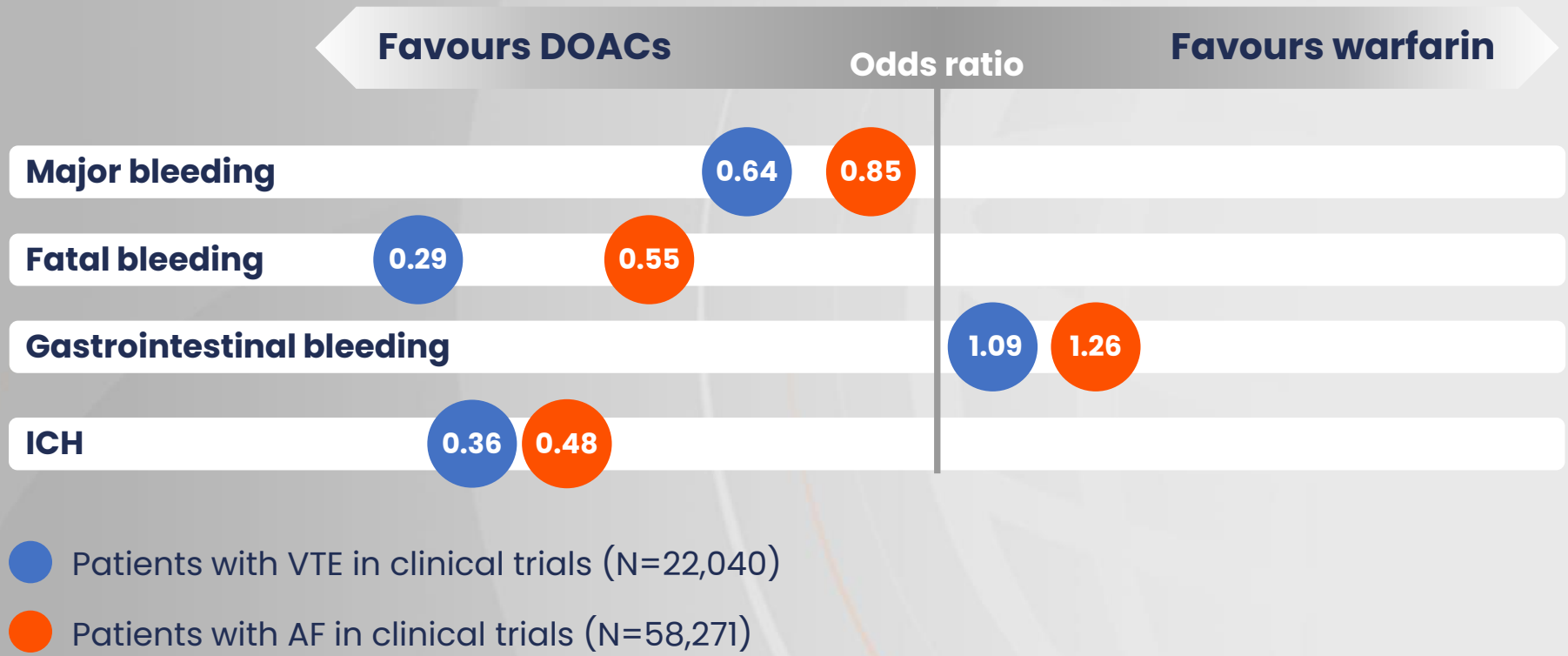
N=22,040
OR 0.88
(95% CI 0.75–1.03)

Practical advantages of DOACs over warfarin and other VKAs[3]

- Fixed dosing
- No need for routine anticoagulation-level monitoring
- Rapid onset and short half-life
- Fewer drug-drug and drug-food interactions

*Meta-analysis data from 12 studies in patients with AF. **Meta-analysis data from 5 studies in patients with acute VTE.
AF, atrial fibrillation; CI, confidence interval; DOAC, direct oral anticoagulant; OR, odds ratio; SEE, systemic embolic event; VKA, vitamin K antagonist; VTE, venous thromboembolism.
1. Hicks T, et al. *Open Heart.* 2016;3:e000279; 2. Makam RCP, et al. *PLoS One.* 2018;13:e0197583; 3. Julia S, James U. *Eur Cardiol.* 2017;12:40–5.

Bleeding rates with DOACs are generally lower than with warfarin

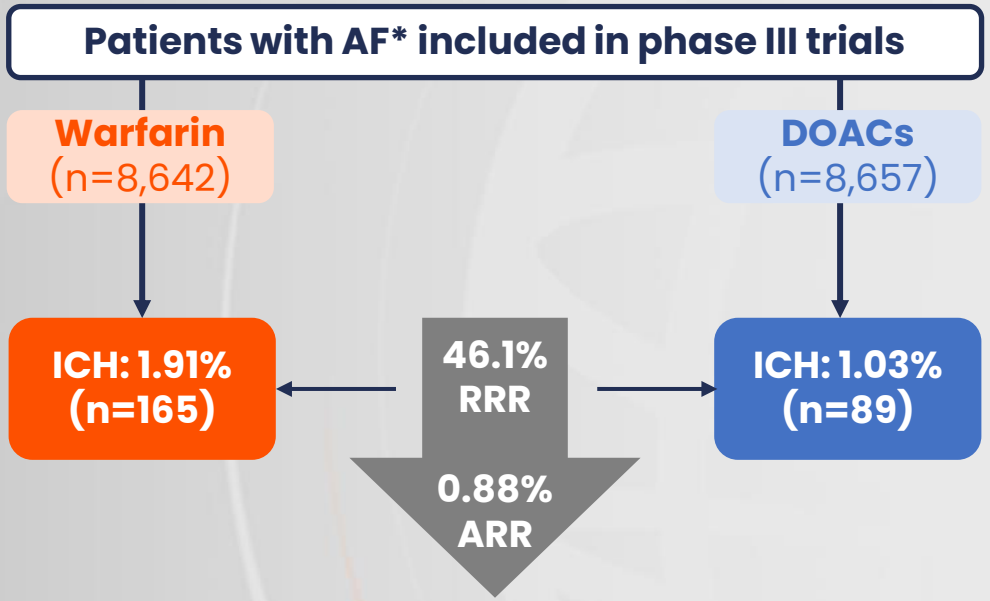


AF, atrial fibrillation; DOAC, direct oral anticoagulant; ICH, intracranial haemorrhage; VTE, venous thromboembolism.

Makam RCP, et al. *PLoS One.* 2018;13:e0197583.

ICH is an important complication in patients treated with DOACs

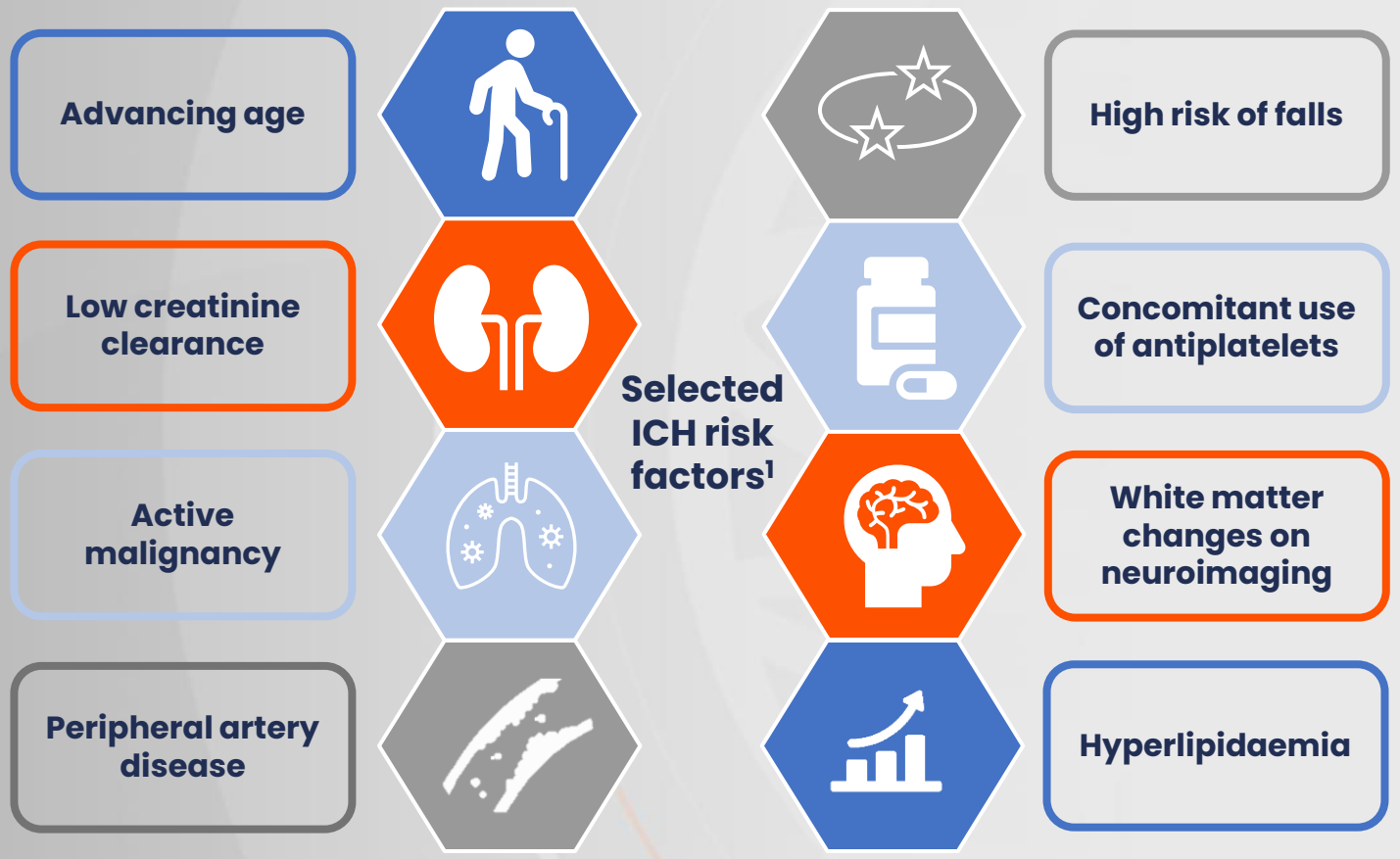
DOACs are associated with a lower incidence of ICH vs warfarin[1]



- Although the risk of ICH is lower with DOACs compared with warfarin therapy,[2] this remains an important potential complication
- Incidence of ICH is likely to increase given the rise in use of DOACs and the ageing population[3]

*Patients with AF and a history of stroke/transient ischaemic attack.
AF, atrial fibrillation; ARR, absolute risk reduction; DOAC, direct oral anticoagulant; ICH, intracranial haemorrhage; RRR, relative risk reduction.
1. Ntaios G, et al. *Int J Stroke.* 2017;12:589–96; 2. Wolfe Z, et al. *J Thromb Haemost.* 2018;16:1296–306; 3. Christensen H, et al. *Eur Stroke J*. 2019;4:294–306.

Several factors predict ICH risk in patients treated with DOACs



- Tools such as the HAS-BLED bleeding risk assessment evaluate some of these risk factors and may have value in predicting ICH risk[2]

DOAC, direct oral anticoagulant; HAS-BLED, Hypertension, Abnormal kidney and liver function, Stroke, Bleeding, Labile international normalized ratios, Elderly, Drugs and alcohol; ICH, intracranial haemorrhage.

1. Paciaroni M, et al. *Stroke.* 2021;52:1450–4; 2. Guo Y, et al. *Am J Med.* 2018;131:185–92.

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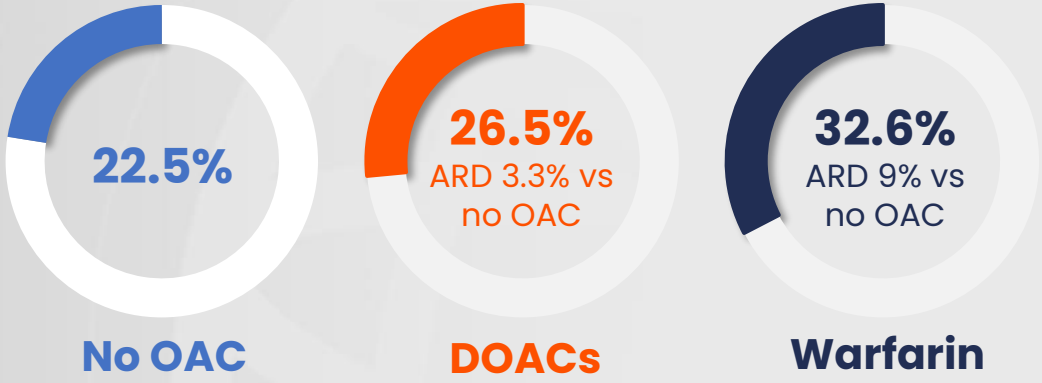
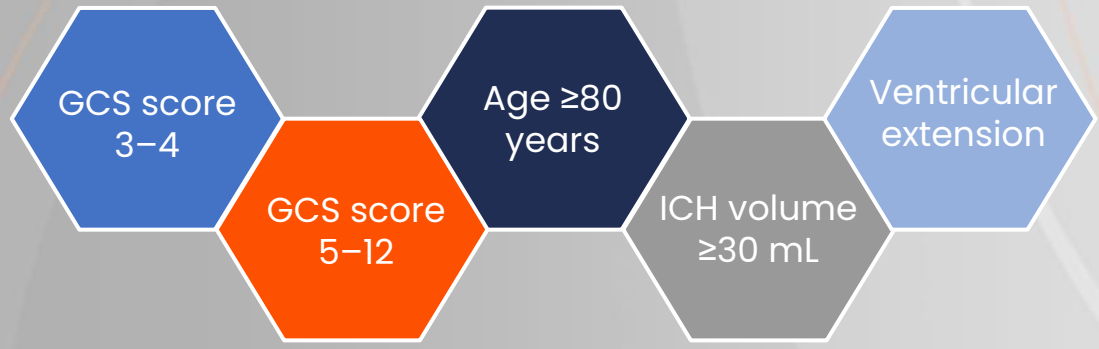
Risk factors should be considered to reduce DOAC-ICH mortality

In-hospital mortality following ICH is lower with DOACs vs warfarin but remains high[1]

- Registry-based retrospective cohort study
- Patients presenting with ICH (N=141,311)
- Analysis based on exposure to OACs within 7 days prior to presentation



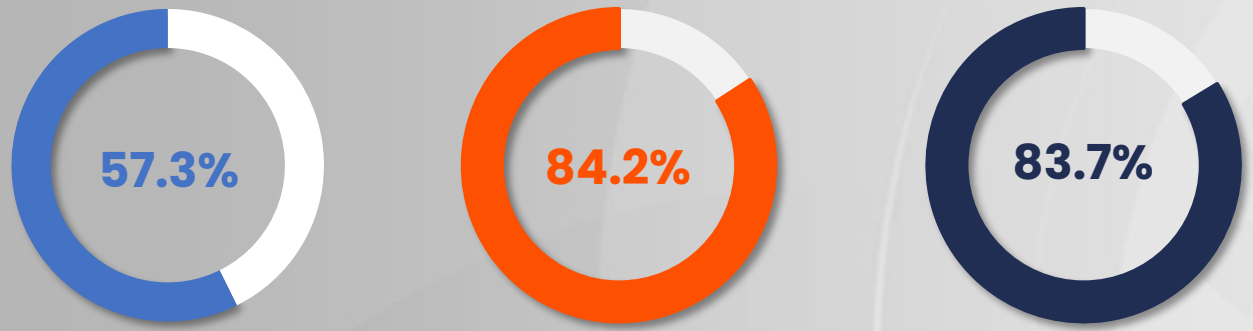
Risk factors for 30-day mortality in patients with ICH using OACs have been identified[2]



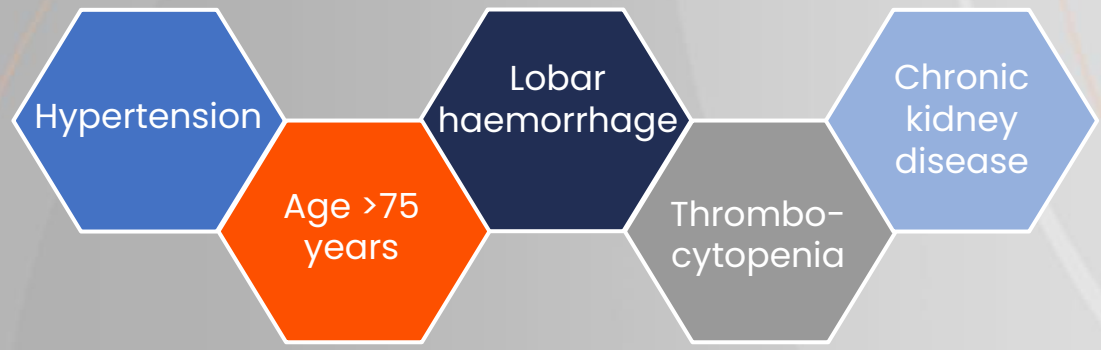
ARD, adjusted risk difference; DOAC, direct oral anticoagulant; GCS, Glasgow Coma Scale; ICH, intracranial haemorrhage; OAC, oral anticoagulant.
1. Inohara T, et al. *JAMA.* 2018;319:463–73; 2. Fakiri MO, et al. *Eur J Neurol.* 2020;27:2006–13.

Risk factors should be considered to reduce morbidity in DOAC-ICH

Proportion of patients with poor functional outcomes following ICH, by anticoagulant status (N=916)[1*]



Risk factors for recurrence of ICH have been identified, including:[2]



*Poor functional outcomes were defined as modified Rankin scale score 4–6[1] (moderately severe disability or greater, including death).
DOAC, direct oral anticoagulant; ICH, intracranial haemorrhage; VKA, vitamin K antagonist.

1. Baharoglu MI, et al. *Front Neurol*. 2021;12:684476; 2. Grainger BT, et al. *J Thromb Haemost.* 2024;22:594–603.

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Evidence for DOAC reversal agents for the management of ICH

Case study in DOAC-ICH

- A 76-year-old man presents to the ED at 8 am with **suspected ischaemic stroke**, having **developed symptoms in the last 2.5 hours.** He was well and without symptoms the evening before
- He has a **history of AF** and **blood pressure upon arrival is 190/120 mmHg**

His wife explained to the paramedic that he is taking a **twice-daily anticoagulant tablet; she is not sure which one** and **he has not taken his morning dose**

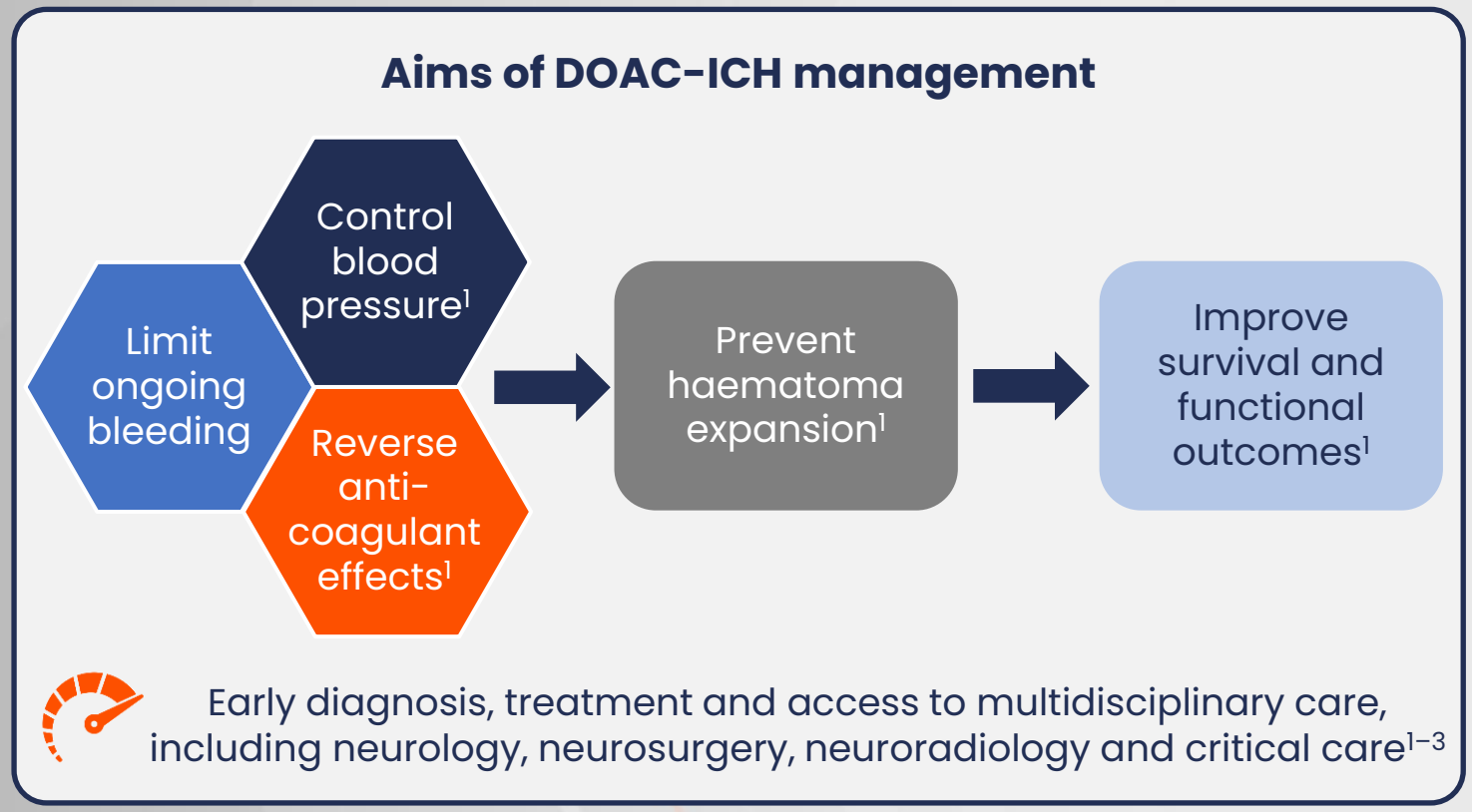
What next steps should the ED physician take?

Consider the following:

- Lower blood pressure
- Verify anticoagulant taken
- CT scan
- Establish ischaemic vs haemorrhagic stroke

AF, atrial fibrillation; CT, computed tomography; DOAC, direct oral anticoagulant; ED, emergency department; ICH, intracranial haemorrhage.

A rapid response and early targeted therapy are crucial in DOAC-ICH



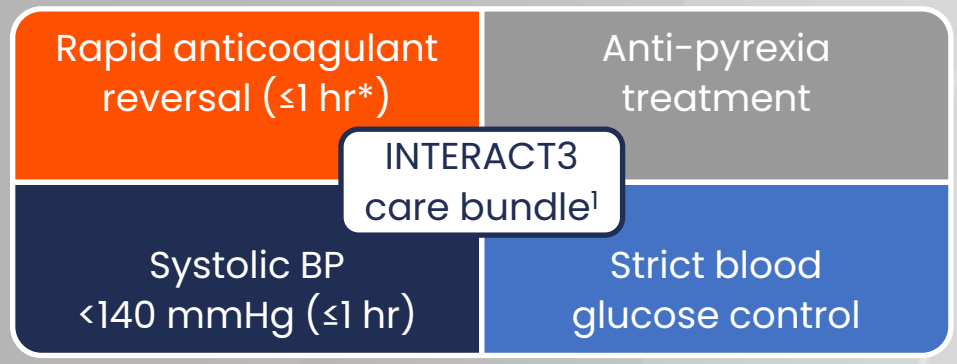
- Delays in identification and management of ICH are associated with poor prognosis[4]

DOAC, direct oral anticoagulant; ICH, intracranial haemorrhage.

1. Greenberg SM, et al. *Stroke.* 2022;53:e282–361; 2. Kim JY, Bae HJ. *J Stroke*. 2017;19:28–39; 3. Luca F, et al. *Front Cardiovasc Med.* 2023;10:1061618; 4. Han HJ, et al. *Yonsei Med J.* 2021;62:911–7.

Care bundles can reduce morbidity and mortality in DOAC-ICH

Care bundles combining treatment strategies can improve outcomes in ICH[1,2]



In a RCT that included **6,255 patients with ICH** in 121 hospitals, use of the **INTERACT3 care bundle** vs usual care led to a **14% reduction in poor functional outcomes** (p=0.015)[1]

ABC-ICH care bundle[2]

- Systolic BP 130–140 mmHg (≤1 hr)
- Rapid anticoagulant reversal (≤90 mins)
- Prompt neurosurgical referral

Implementation of **ABC-ICH** in **patients with ICH** led to a **38% reduction in 30-day mortality** vs pre-implementation levels (p=0.03)†[2]

*Target INR <1.5. †266 patients in the group admitted to hospital during the ABC-ICH implementation period; 353 patients in the group admitted before implementation.
BP, blood pressure; DOAC, direct oral anticoagulant; hr, hour; ICH, intracranial haemorrhage; INR, international normalized ratio; RCT, randomized controlled trial.
1. Ma L, et al. *Lancet.* 2023;402:27–40; 2. Parry-Jones AR, et al. *Ann Neurol.* 2019;86:495–503.

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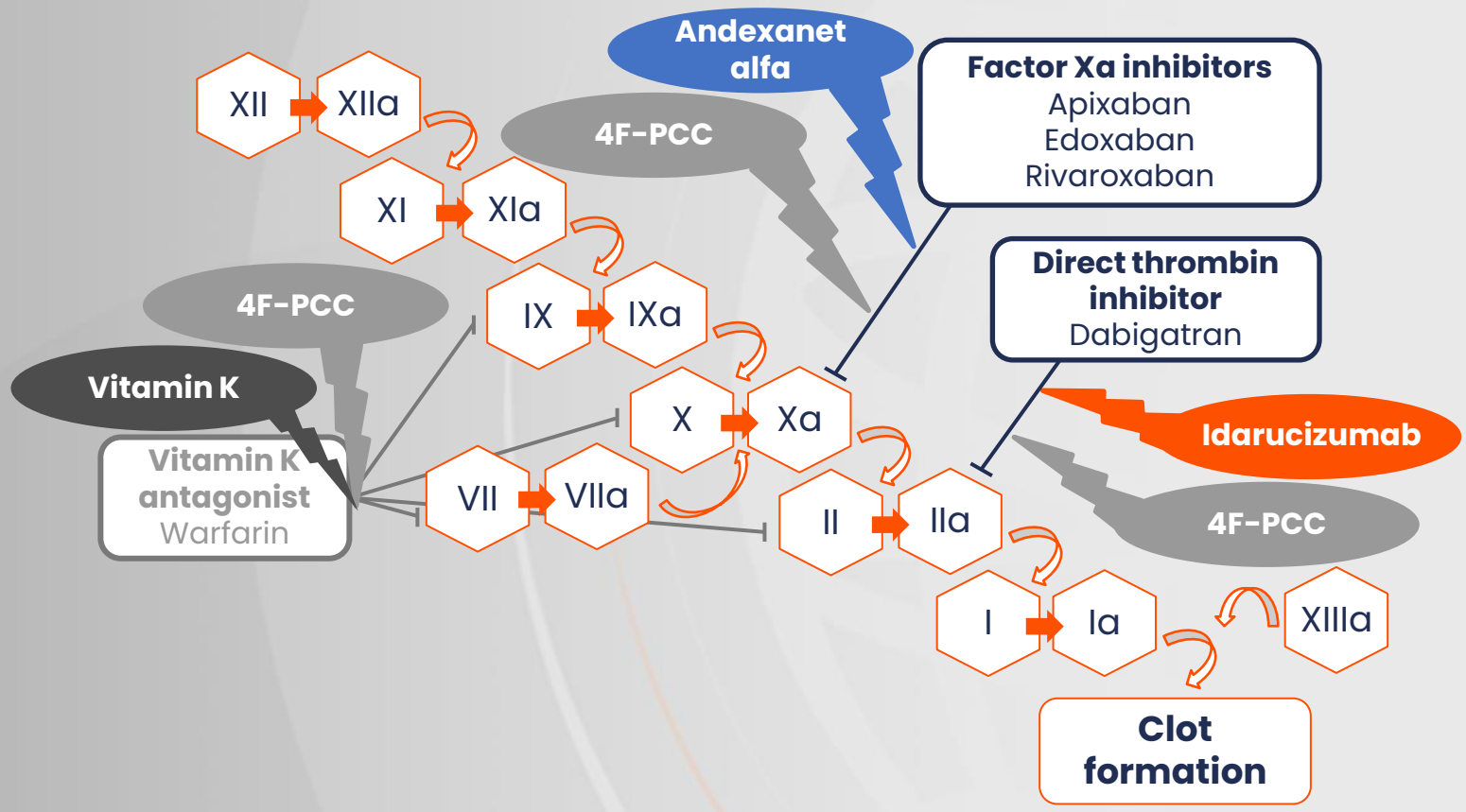
Reversal agents have been developed that target oral anticoagulants



4F-PCC, four-factor prothrombin complex concentrate.
Akhrass R, et al. *J Card Surg.* 2022;37:214–22.

DOAC-ICH reversal agents show unique characteristics

	PCC	Idarucizumab	Andexanet alfa
DOACs targeted[1,2]	Non-specific	Dabigatran	Apixaban Rivaroxaban Edoxaban*
Approval status[1] (DOAC related)	Not approved for DOAC reversal	Approved	Approved*
Indications	Life-threatening or uncontrolled bleeding *(if specific reversal agents are not available)*[1,3]	Life-threatening or uncontrolled bleeding; emergency surgery or urgent procedures[4]	Life-threatening or uncontrolled bleeding[5]
Mechanism of action	Non-specific; raises factor levels and 'overwhelms' DOAC[1,2]	Rapid, specific binding to dabigatran (<5 mins)[2,6]	Rapid, specific binding to factor Xa inhibitors (2–5 mins)[2,7]
Terminal half-life[2]	Elevated clotting factors likely persist for at least 24 hr	4–8 hr	5–7 hr
Contraindications	Refer to local summary of product characteristics/prescribing information		

*Andexanet alfa is not approved for edoxaban-treated patients outside of Japan.[5,8,9] DOAC, direct oral anticoagulant; FDA, US Food and Drug Administration; hr, hour; ICH, intracranial haemorrhage; PCC, prothrombin complex concentrate.

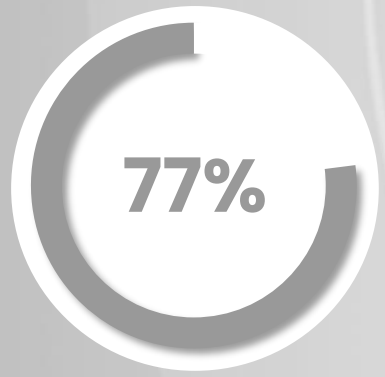
1. White K, et al. *Br J Cardiol.* 2022;29:1; 2. Cuker A, et al. *Am J Hematol.* 2019;94:697–709; 3. Hoffman M, et al. *Int J Emerg Med.* 2018;11:55; 4. FDA. Idarucizumab PI. 2015. Available at: www.accessdata.fda.gov/drugsatfda_docs/label/2015/761025lbl.pdf (accessed 16 May 2024); 5. FDA. Coagulation factor Xa (recombinant) PI. 2024. Available at: www.fda.gov/media/113279/download (accessed 16 May 2024); 6. Schiele F, et al. *Blood.* 2013;121:3554–62; 7. Heo YA. *Drugs Ther Perspect.* 2018;34:507–12; 8. Yajima T, et al. *Nihon Yakurigaku Zasshi.* 2023;158:89–100; 9. EMA. Andexanet alfa SmPC. 2023. Available at: https://bit.ly/3WFrRJH (accessed 16 May 2024).

Meta-analysis data support use of PCCs in managing DOAC-ICH

Meta-analysis of studies in 967 adults with DOAC-ICH

23 studies (21 retrospective, 2 prospective)

4F-PCC



Anticoagulation reversal rate

4F-PCC, four-factor prothrombin complex concentrate; DOAC, direct oral anticoagulant; ICH, intracranial haemorrhage.
Chaudhary R, et al. *JAMA Netw Open*. 2022;5:e2240145.

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Idarucizumab effectively reverses dabigatran anticoagulation

RE-VERSE AD trial[1]

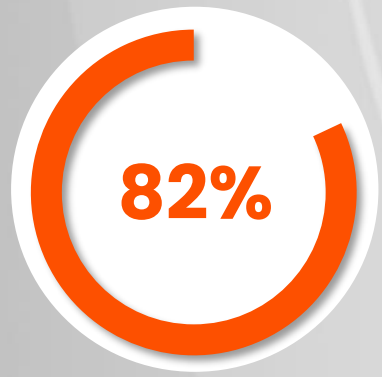
Multicentre, prospective, open-label study

- Patients on dabigatran with uncontrolled bleeding (n=301), or due an urgent procedure (n=202)
- In those with **uncontrolled bleeding, 33% presented with DOAC-ICH**

Idarucizumab 5 g IV

100% Median maximum percentage reversal of dabigatran within 4 hr*

Meta-analysis data in 340 patients with DOAC-ICH[2]



Anticoagulation reversal rate

*Result for the 461 patients included in the primary efficacy analysis.
DOAC, direct oral anticoagulant; hr, hours; ICH, intracranial haemorrhage; IV, intravenous.
1. Pollack CV Jr, et al. *N Engl J Med*. 2017;377:431–41; 2. Chaudhary R, et al. *JAMA Netw Open*. 2022;5:e2240145.

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Andexanet alfa effectively reverses FXa inhibitor anticoagulation

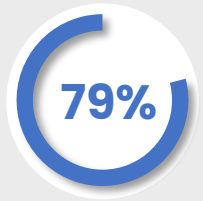
ANNEXA-4 trial[1]

Multicentre, prospective, phase IIIb/IV cohort study

Patients with acute major bleeding within 18 hr of FXa inhibitor administration (n=349*)

Low- or high-dose andexanet alfa

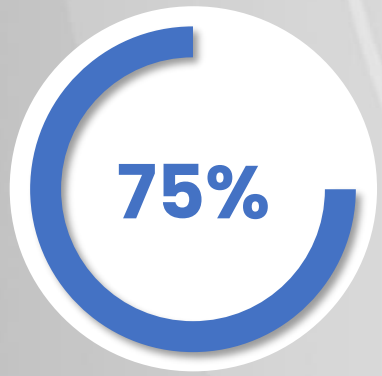
ICH cohort (n=246)



Anticoagulation reversal rate

ANNEXA-I trial data support these findings in DOAC-ICH; at prespecified interim analysis after 450 patients had been randomized, the DSMB recommended termination of the study for superior efficacy[2]

Meta-analysis data in 525 patients with DOAC-ICH[3]



Anticoagulation reversal rate

*Efficacy population.
DOAC, direct oral anticoagulant; DSMB, Data and Safety Monitoring Board; FXa, factor Xa; hr, hours; ICH, intracranial haemorrhage.
1. Milling TJ Jr, et al. *Circulation*. 2023;147:1026–38; 2. Connolly S. *Int J Stroke*. 2023;18(Suppl. 3):422. LBO004/#2806; 3. Chaudhary R, et al. *JAMA Netw Open*. 2022;5:e2240145.

Adverse events should be considered with DOAC-ICH reversal agents

Meta-analysis data: All-cause mortality and TE events[1*]

4F-PCC

In pts with ICH:

18 studies, N=784

All-cause mortality: 26%

17 studies, N=615

TE event rate: 8%

Andexanet alfa

In pts with ICH:

13 studies, N=506

All-cause mortality: 24%

11 studies, N=445

TE event rate: 14%

Idarucizumab

In pts with ICH:

5 studies, N=340

All-cause mortality: 11%

4 studies, N=300

TE event rate: 5%

Serious adverse events include:

4F-PCC[2]
Stroke, DVT, thrombosis, venous insufficiency

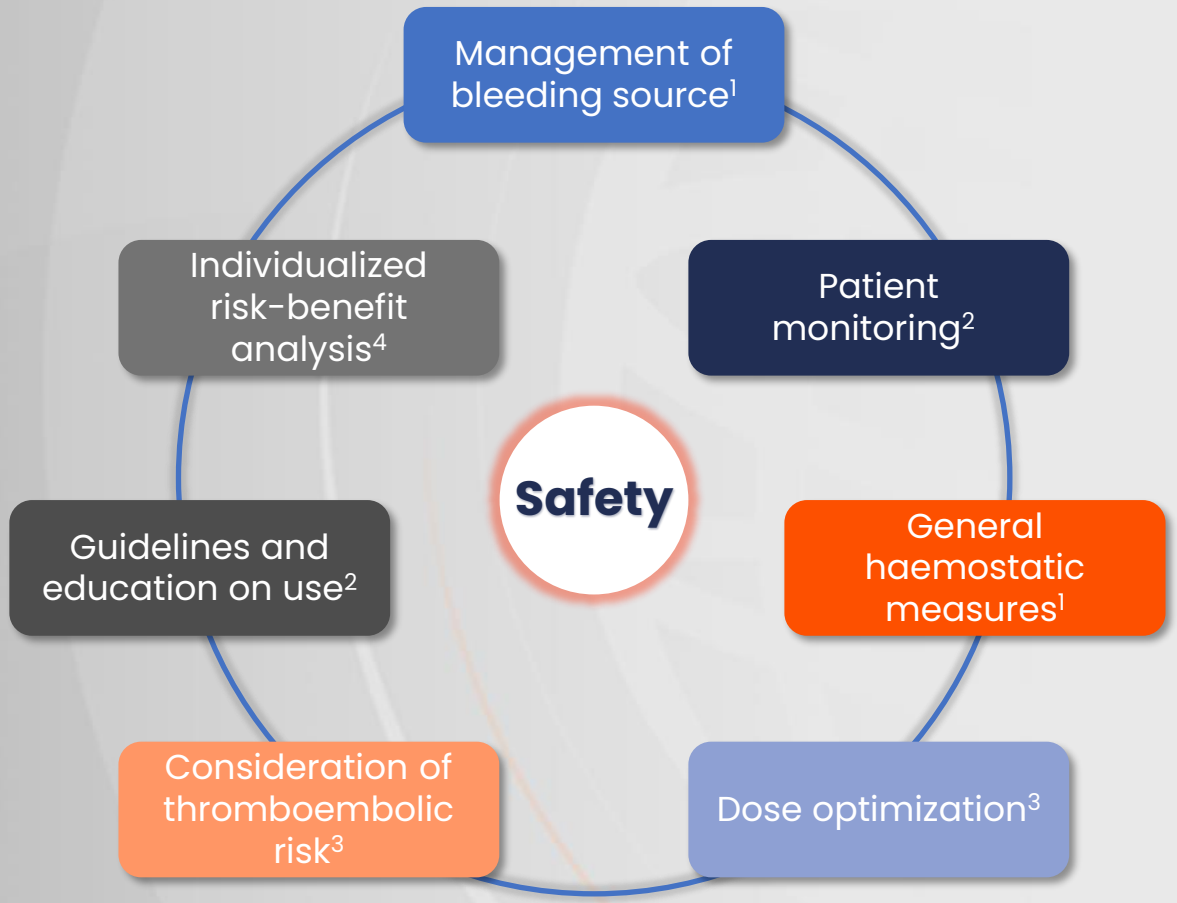
Andexanet alfa[3]
Thromboembolic events, ischaemic events, cardiac arrest, sudden death

Idarucizumab[4]
Delirium, cardiac arrest, sepsis, septic shock

*Data based on meta-analysis, using different timeframes for outcome assessments; comparisons between agents are indirect and may be prone to bias due to differences in study designs and populations. 4F-PCC, four-factor prothrombin complex concentrate; DOAC, direct oral anticoagulant; DVT, deep-vein thrombosis; ICH, intracranial haemorrhage; pts, patients; TE, thromboembolic.

1. Chaudhary R, et al. *JAMA Netw Open*. 2022;5:e2240145; 2. FDA. Prothrombin complex concentrate (human) PI. 2023. Available at: www.fda.gov/media/85512/download (accessed 7 April 2024); 3. Heo YA. *Drugs Ther Perspect.* 2018;34:507–12; 4. Pollack CV Jr, et al. *N Engl J Med*. 2017;377:431–41.

Multiple factors influence the safe and effective use of DOAC reversal agents



DOAC, direct oral anticoagulant.

1. White K, et al. *Br J Cardiol.* 2022;29:1; 2. Cuker A, et al. *Am J Hematol*. 2019;94:697–709; 3. Greenberg SM, et al. *Stroke.* 2022;53:e282–361; 4. Milling TJ, Pollack CV. *Am J Emerg Med*. 2020;38:1890–903.

Multiple factors influence the safe and effective use of DOAC reversal agents

- Patients experiencing DOAC-associated bleeding are also at **increased risk** of developing **subsequent thrombotic events**, with those experiencing ICH being most at risk[1]
- Reversing DOAC therapy exposes patients to the **thrombotic risk of their underlying disease**[1–3]

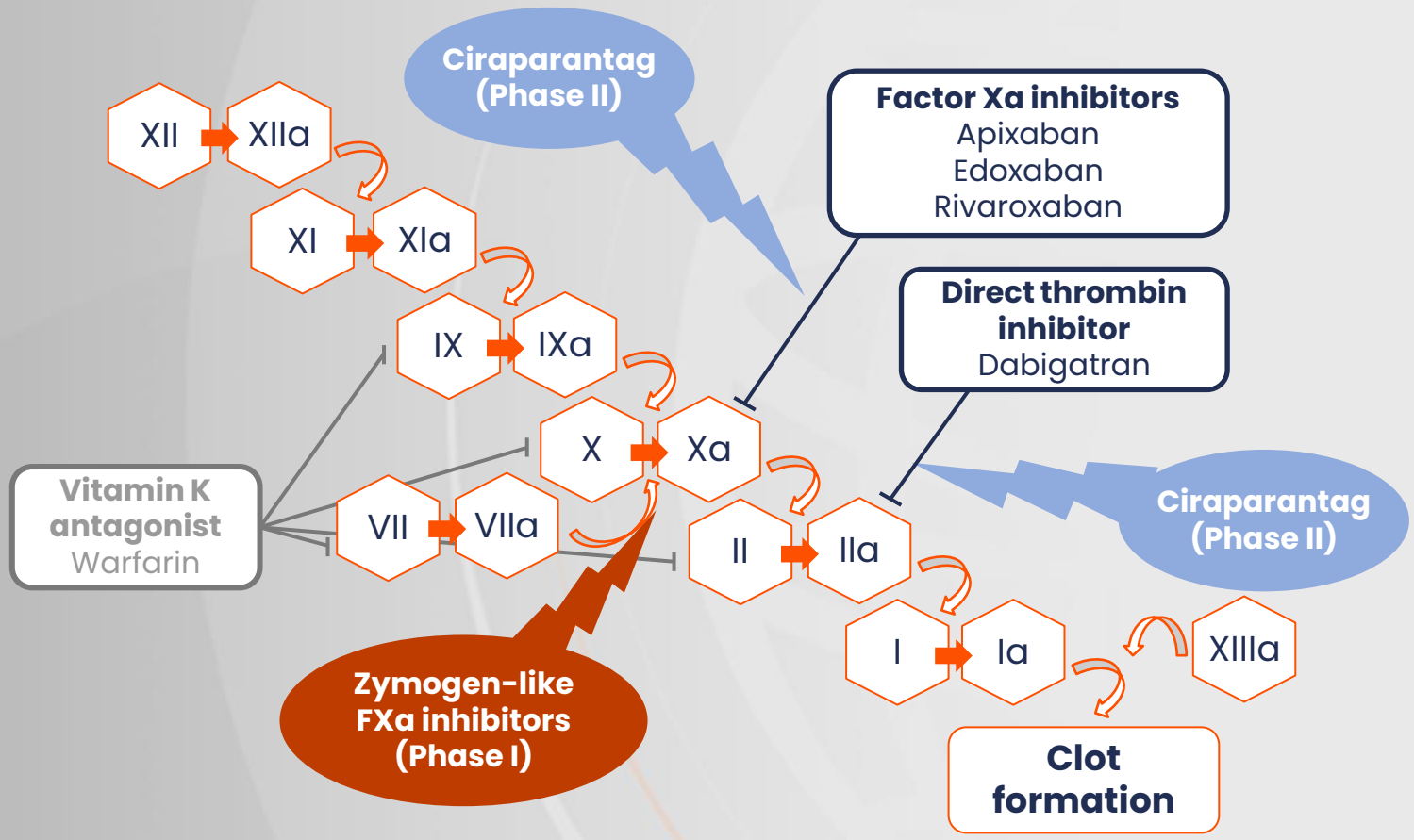
There is a need to implement strategies to reduce risk and identify patients at greatest risk of thromboembolism[4]

Consideration of thromboembolic risk[3]

DOAC, direct oral anticoagulant; ICH, intracranial haemorrhage.

1. White K, et al. *Br J Cardiol*. 2022;29:1; 2. FDA. Coagulation factor Xa (recombinant) PI. 2024. Available at: www.fda.gov/media/113279/download (accessed 13 May 2024);
3. FDA. Idarucizumab PI. 2015. Available at: www.accessdata.fda.gov/drugsatfda_docs/label/2015/761025lbl.pdf (accessed 16 May 2024);
4. Greenberg SM, et al. *Stroke*. 2022;53:e282–361.

Emerging reversal agents are in clinical development[1,2]



FXa, factor Xa.

1. van Es N, et al. *Eur Heart J.* 2023;44:1795–806; 2. ClinicalTrials.gov. Available at: www.clinicaltrials.gov (accessed 14 May 2024).

Trials are ongoing with current and new DOAC reversal agents

Currently used agents

4F-PCC

- Evaluation in DOAC-ICH (NCT06096051)
- Phase III trial of low- and high-doses in patients with acute major bleeding on DOAC therapy (NCT04867837)

Andexanet alfa

- ASTRO-DE: Non-interventional study of impact on ICH volume in patients taking apixaban or rivaroxaban (NCT05127941)
- Retrospective, real-world study of outcomes in hospitalized patients (NCT05898412)

Idarucizumab

- No ongoing trials identified

Emerging agents

Ciraparantag

- Phase I/II data demonstrate restoration of coagulation in DOAC-treated healthy volunteers[1,2]
- Well tolerated in healthy elderly subjects[2]
- Phase II trial ongoing in healthy adults (NCT04593784)

Others

- Most are in early clinical development[3]
- Data needed in DOAC reversal contexts

4F-PCC, four-factor prothrombin complex concentrate; DOAC, direct oral anticoagulant; ICH, intracranial haemorrhage.
Trial information by NCT identifiers available at: www.clinicaltrials.gov (accessed 7 May 2024).
1. Ansell JE, *N Engl J Med.* 2014;371:2141–2; 2. Ansell J, et al. *Eur Heart J.* 2022;43:985–92; 3. van Es N, et al. *Eur Heart J.* 2023;44:1795–806.

Managing DOAC-ICH: What do the guidelines say?

Guidelines on DOAC-ICH are diverse and potentially outdated

ASA/AHA 2022[1]

USA focus
Recommendations on the management of patients with spontaneous ICH

APSC 2021[2]

Asia-Pacific focus
Consensus recommendations on thrombotic and bleeding risk management in patients with AF on DOACs

ACC 2020[3]

USA focus
Expert consensus decision pathway on management of bleeding in patients on oral anticoagulants

ESO 2019[4]

European focus
Recommendations on reversal of VKA and DOACs in patients with acute ICH

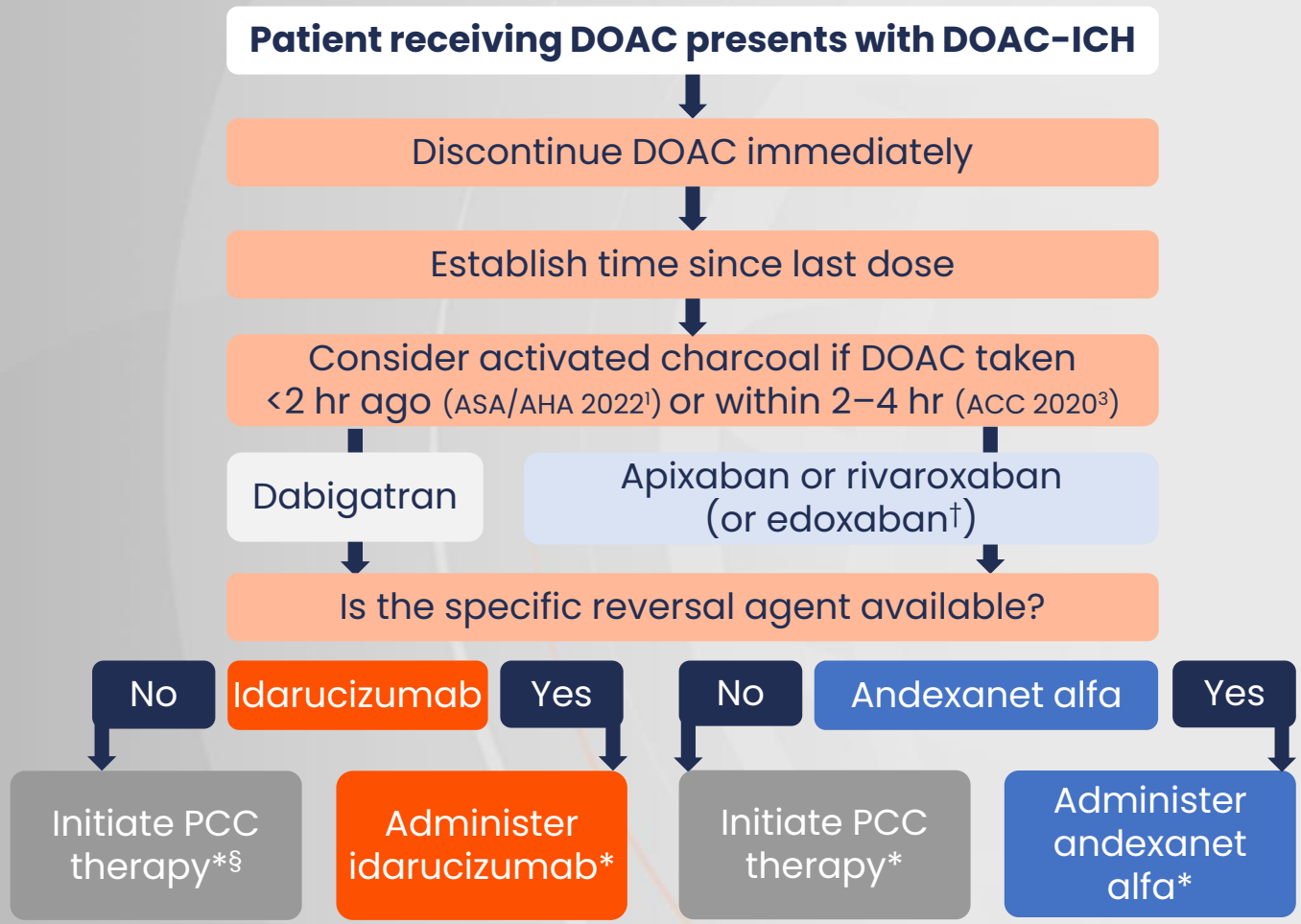
Guidelines from other regions and organizations are available, but are potentially outdated or lack a focus on DOAC-ICH:

- Japanese Circulation Society (2020)[5]
- National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand (2018)[6]
- Brazilian Society of Cardiology (2016)[7]

ACC, American College of Cardiology; AF, atrial fibrillation; AHA, American Heart Association; APSC, Asian Pacific Society of Cardiology; ASA, American Stroke Association; DOAC, direct oral anticoagulant; ESO, European Stroke Association; ICH, intracranial haemorrhage; VKA, vitamin K antagonist.

1. Greenberg SM, et al. *Stroke.* 2022;53:e282–361; 2. Chong DT, et al. *Eur Cardiol.* 2021;16:e23; 3. Tomaselli GF, et al. *J Am Coll Cardiol.* 2020;76:594–622; 4. Christensen H, et al. *Eur Stroke J.* 2019;4:294–306; 5. Nakamura M, et al. *Circ J.* 2020;84:831–65; 6. Brieger D, et al. *Heart Lung Circ.* 2018;27:1209–66; 7. Magalhães LP, et al. *Arq Bras Cardiol.* 2016;107:501–8.

Specific reversal agents are recommended in DOAC-ICH when available[1–4]



*Treatment recommendations are common across ASA/AHA 2022[1], APSC 2021[2], ACC 2020[3] and ESO 2019[4] guidelines

†Andexanet alfa is not approved for edoxaban-treated patients outside of Japan.[5,6,7] §ASA/AHA 2022: renal replacement therapy may be considered to reduce dabigatran concentration.[1]

ACC, American College of Cardiology; AHA, American Heart Association; APSC, Asian Pacific Society of Cardiology; ASA, American Stroke Association; DOAC, direct oral anticoagulant; ESO, European Stroke Association; hr; hours; ICH, intracranial haemorrhage; PCC, prothrombin complex concentrate. 1. Greenberg SM, et al. *Stroke.* 2022;53:e282–361; 2. Chong DT, et al. *Eur Cardiol.* 2021;16:e23; 3. Tomaselli GF, et al. *J Am Coll Cardiol.* 2020;76:594–622; 4. Christensen H, et al. *Eur Stroke J.* 2019;4:294–306; 5. Yajima T, et al. *Nihon Yakurigaku Zasshi.* 2023;158:89–100; 6. FDA. Coagulation factor Xa (recombinant) PI. 2024. Available at: www.fda.gov/media/113279/download (accessed 13 May 2024); 7. EMA. Andexanet alfa SmPC. 2023. Available at: https://bit.ly/3WFrRJH (accessed 13 May 2024).

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There are key factors to consider when using guidelines on anticoagulant reversal in DOAC-ICH

1st

Current guidelines are consistent in advocating first-line use of andexanet alfa or idarucizumab, where available[1–4]

Specific reversal agents should be used promptly in patients with DOAC-ICH[1]

The strength of recommendations varies due to lack of inclusion of recent trials in some guidelines[1–7]

In recent years, **data have become available which may not yet be incorporated into guidelines,** e.g. ANNEXA-I[8] and ANNEXA-4[9] trial data for andexanet alfa

DOAC, direct oral anticoagulant; ICH, intracranial haemorrhage.

1. Greenberg SM, et al. *Stroke.* 2022;53:e282–361; 2. Chong DT, et al. *Eur Cardiol.* 2021;16:e23; 3. Tomaselli GF, et al. *J Am Coll Cardiol.* 2020;76:594–622; 4. Christensen H, et al. *Eur Stroke J.* 2019;4:294–306; 5. Nakamura M, et al. *Circ J.* 2020;84:831–65; 6. Brieger D, et al. *Heart Lung Circ.* 2018;27:1209–66; 7. Magalhães LP, et al. *Arq Bras Cardiol.* 2016;107:501–8; 8. Connolly S. *Int J Stroke.* 2023;18(Suppl. 3):422. LBO004/#2806; 9. Milling TJ Jr, et al. *Circulation.* 2023;147:1026–38.

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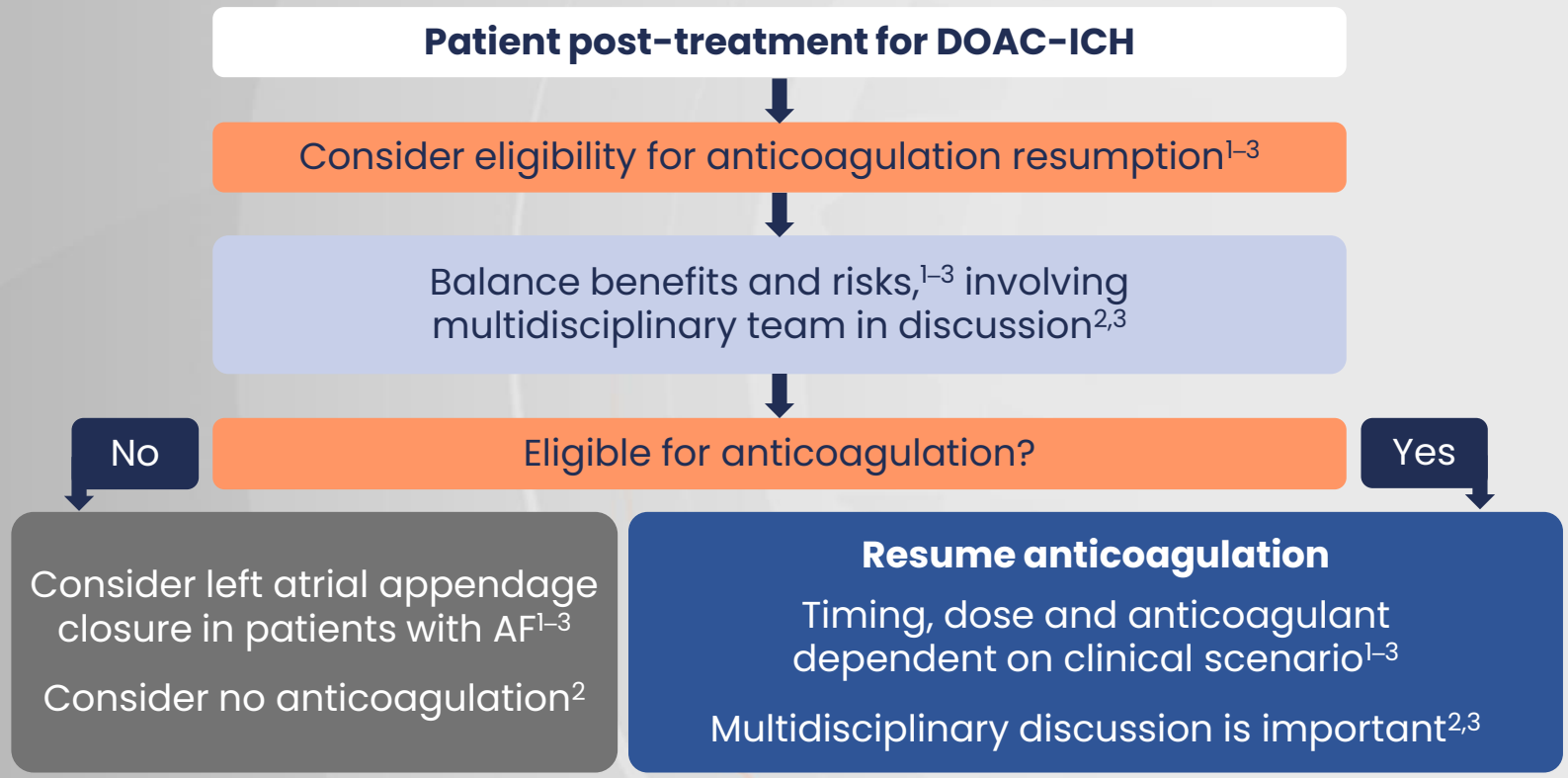
Guidelines vary for anticoagulation resumption following DOAC-ICH, but have some common principles

Based on recommendations in the **ASA/AHA**,[1] **APSC**[2] and **ACC**[3] guidelines:

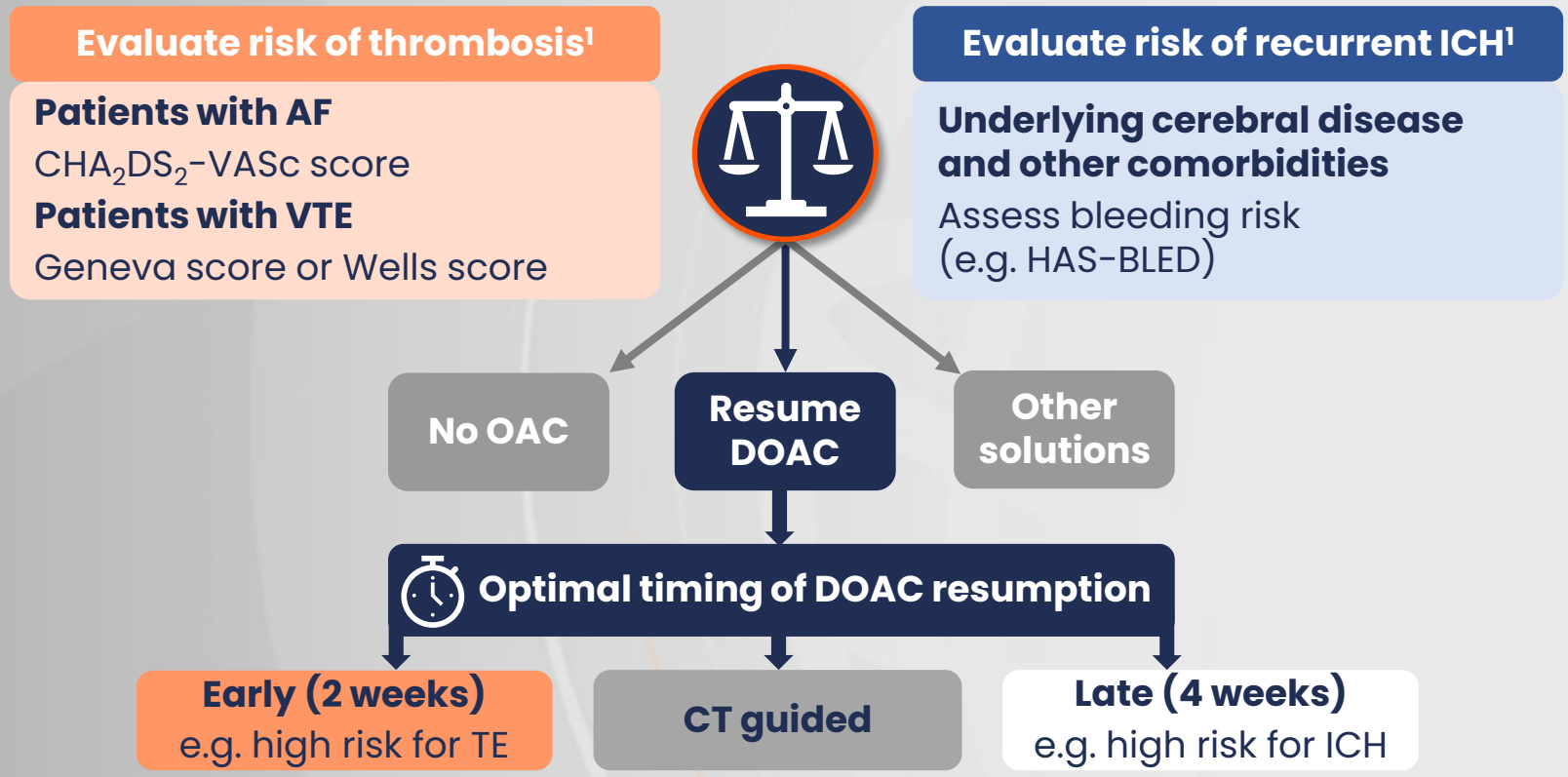


There are no recommendations on resuming anticoagulation in the 2019 ESO guidelines[4]

ACC, American College of Cardiology; AF, atrial fibrillation; AHA, American Heart Association; APSC, Asian Pacific Society of Cardiology; ASA, American Stroke Association; DOAC, direct oral anticoagulant; ESO, European Stroke Association; ICH, intracranial haemorrhage.

1. Greenberg SM, et al. *Stroke.* 2022;53:e282–361; 2. Chong DT, et al. *Eur Cardiol.* 2021;16:e23; 3. Tomaselli GF, et al. *J Am Coll Cardiol.* 2020;76:594–622; 4. Christensen H, et al. *Eur Stroke J.* 2019;4:294–306.

Anticoagulation resumption after DOAC-ICH requires risk assessment



- Address modifiable risk factors at every patient contact[1,2]
- Schedule more regular review and follow-up for high-risk patients[1]

AF, atrial fibrillation; CHA_2DS_2-VASc, Congestive heart failure or left ventricular dysfunction, Hypertension, Age ≥75 (doubled), Diabetes, Stroke (doubled)-Vascular disease, Age 65–74, Sex category; CT, computed tomography; DOAC, direct oral anticoagulant; HAS-BLED, Hypertension, Abnormal kidney and liver function, Stroke, Bleeding, Labile international normalized ratios, Elderly, Drugs and alcohol; ICH, intracranial haemorrhage; OAC, oral anticoagulant; TE, thromboembolism; VTE, venous thromboembolism.

1. Li YG, Lip GYH. *Curr Atheroscler Rep.* 2018;20:32; 2. Lucà F, et al. *Front Cardiovasc Med.* 2023;10:1061618.

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Case study in DOAC-ICH

- A 76-year-old man presents to the ED at 8 am with **suspected ischaemic stroke**, having **developed symptoms in the last 2.5 hours.** He was well and without symptoms the evening before
- He has a **history of AF** and **blood pressure upon arrival is 190/120 mmHg**

His wife explained to the paramedic that he is taking a **twice-daily anticoagulant tablet; she is not sure which one** and **he has not taken his morning dose**

- CT **confirmed ICH**
- **Apixaban identified** as the anticoagulant (twice-daily tablet)
- **Anti-factor Xa** level was **112 ng/mL**

- Low-dose **andexanet alfa** commenced
- Blood pressure lowered
- **After 7 days, discharged** to neurorehabilitation unit for management of residual impairments
- **Decision** to be made **on whether to restart anticoagulation**

AF, atrial fibrillation; CT, computed tomography; DOAC, direct oral anticoagulant; ED, emergency department; ICH, intracranial haemorrhage.

Summary

Although DOACs are generally associated with lower bleeding rates and are increasingly used in preference to VKA therapy, they are also associated with a risk of ICH

Specific reversal agents are effective, with an acceptable safety profile, in DOAC-ICH management

Guidelines agree on the use of specific reversal agents, where available

DOAC, direct oral anticoagulant; ICH, intracranial haemorrhage; VKA, vitamin K antagonist.