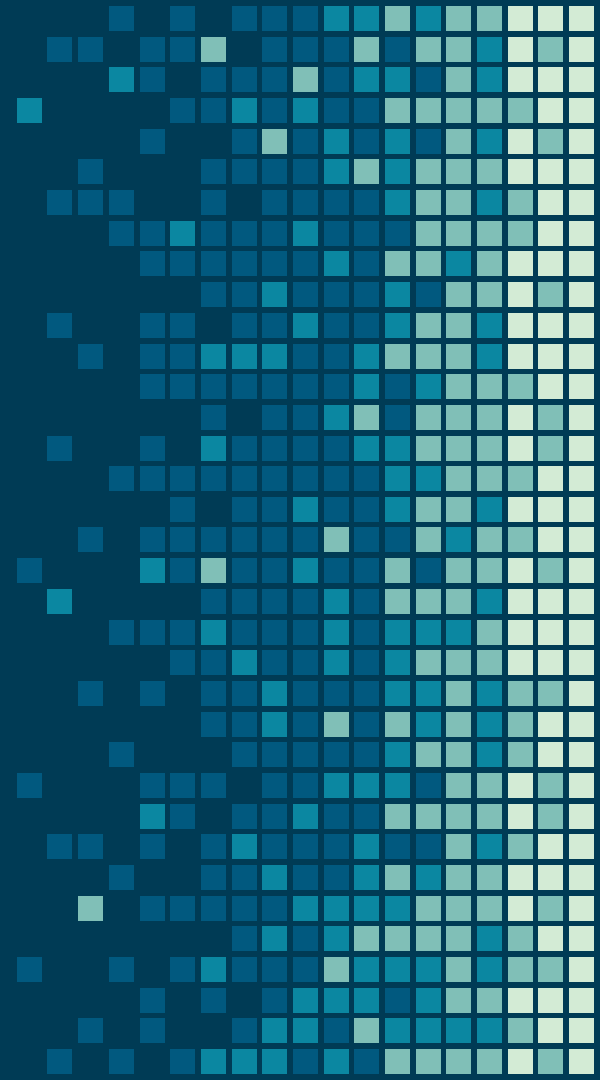


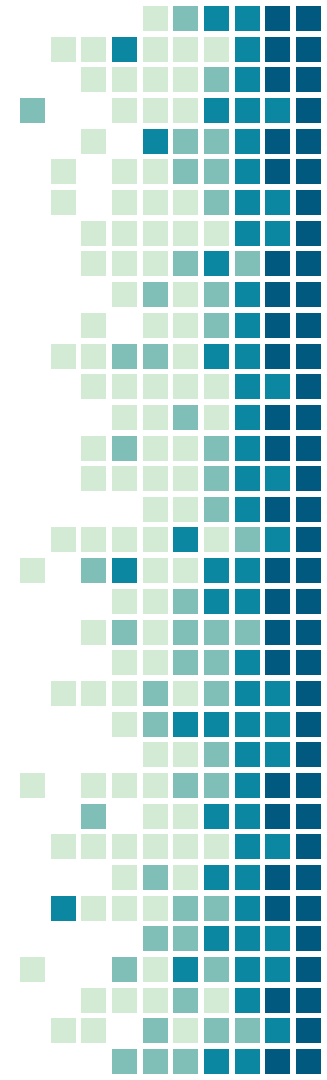
Challenges in the Use of DOACs in the Elderly

Krish Raina, Divyanka Kavdikar, Rohit Dandavate



Introduction

- DOACs (Direct Oral Anticoagulants) are needed in the elderly to manage several conditions such as non-valvular atrial fibrillation and stroke prophylaxis.
- DOACs have been reported to significantly reduce the risk of stroke and systemic thromboembolism in older patients, without increasing the risk of major bleeding (even more than in younger patients) and have a more favorable risk profile.
- Although DOACs are the antithrombotic treatment of choice, irrespective of age, certain factors may limit their use.



Introduction, contd.

- Prescribing and maintaining FDA-recommended doses of DOACs in the elderly is very challenging due to multiple factors.
- Fluctuations in renal function, comorbidities, and concomitant antiplatelet use may necessitate more individualized dosing strategies with these agents.
- We have reviewed the use of DOACs especially as they relate to the use in the elderly, and have tried to comment on the various challenges during the use of DOACs in the elderly.

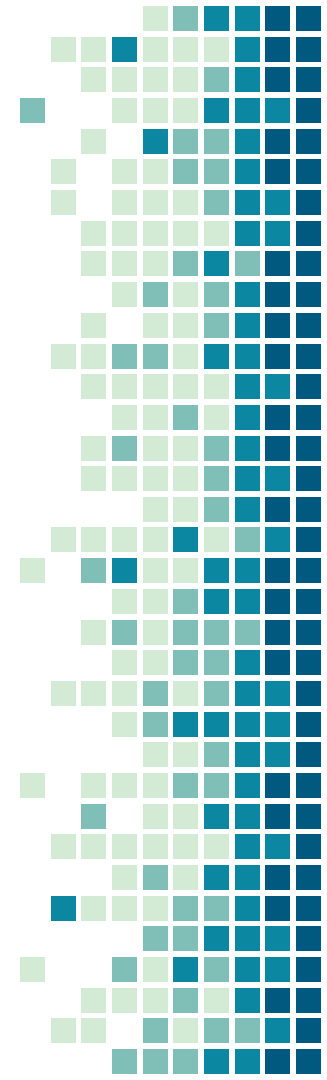
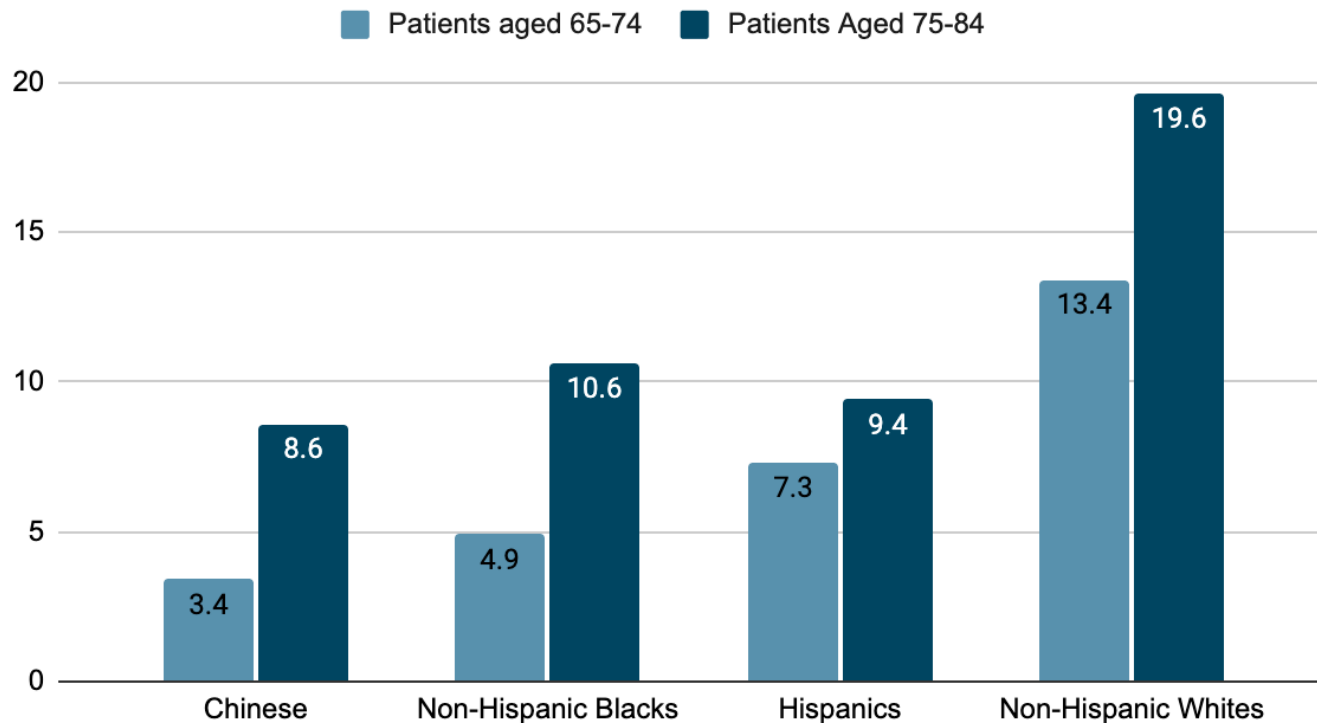


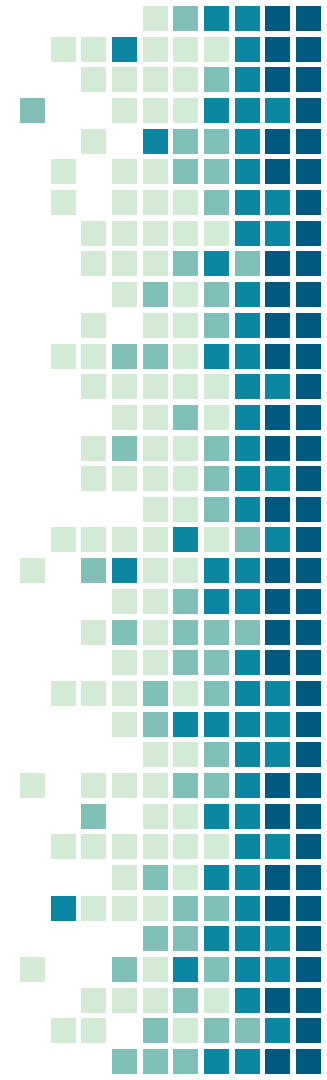
Figure 1 (Based upon the MESA Study)

Incidence of AF in Elderly Patients (%)



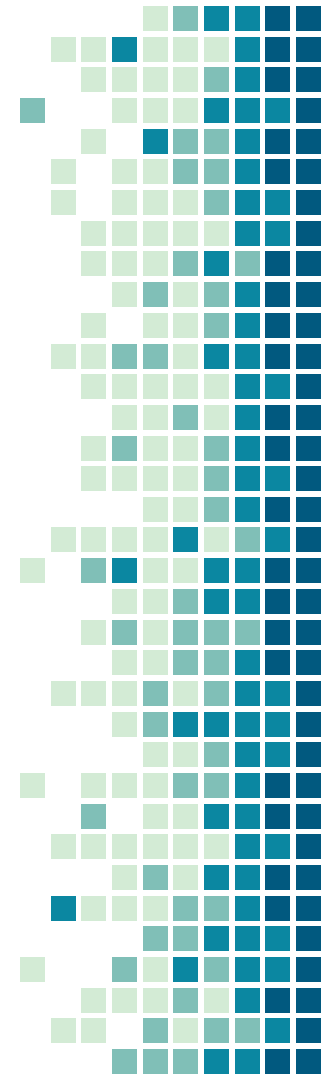
Age and Incidence of AF

- The prevalence of AF increases with age, and two-thirds of patients with AF are the elderly (aged ≥ 75 years).
- The Framingham Heart Study group had shown age to be the greatest risk factor for AF, surpassing other risk factors, including male sex, obesity, diabetes, smoking, hypertension, heart failure, and coronary artery disease.



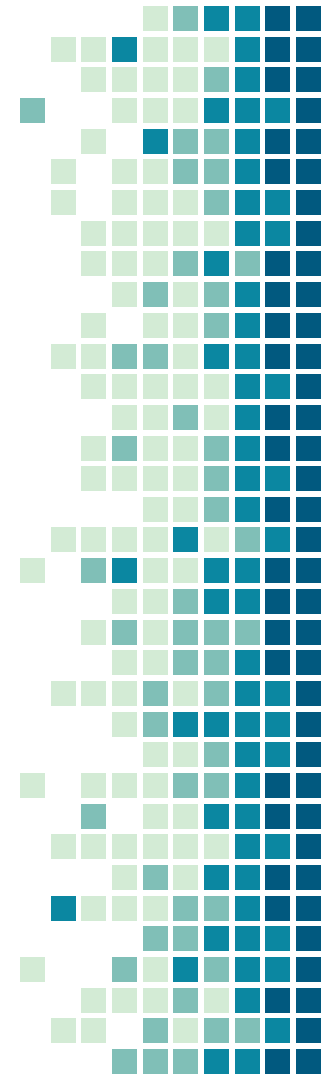
Age and Incidence of AF

- The quality of life is poor, with larger number of hospitalizations, and more cardiovascular events in elderly patients with AF, compared to patients younger than 75 years old.
- In addition, older age is a known factor that can increase the risk of stroke/systemic embolism, which is one of the most common complications of AF; thus, the occurrence of comorbidities is frequent in the elderly.



What is a DOAC

- DOAC (Direct Oral AntiCoagulant), is an anticoagulant that works differently from warfarin at specific sites in the coagulation cascade while achieving similar anticoagulation effects.
- DOACs are used for the prevention of thrombosis in several cardiovascular thrombotic conditions.
- The first DOAC approved by the FDA in 2010 was dabigatran.



Types of DOACs (Figure 2)

Factor Xa Inhibitors:

- Rivaroxaban (Xarelto)
- Apixaban (Eliquis)
- Edoxaban (Savaysa)

Direct Thrombin Inhibitor (DTI):

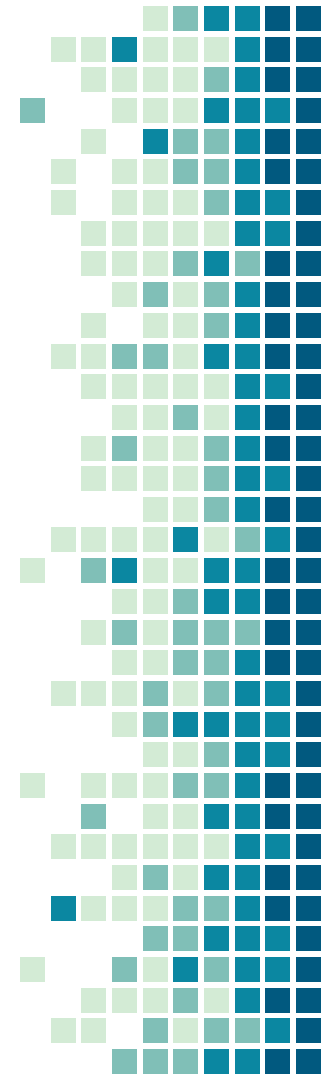
- Dabigatran (Pradaxa)



Figure 2: DOACs

Mechanism of Action of DOACs

- Clotting factors are proteins produced by the liver.
- Several clotting factors work together in a “cascade” effect at the injured site and form a blood clot.
- Apixaban, Rivaroxaban and Edoxaban inhibit Factor Xa
- Dabigatran inhibits Factor IIA.
- The onset of action of DOACs is about 1-3 hours and the half life is between 10-14 hours.



Mechanism of Action of DOACs Contd. (Figure 3)

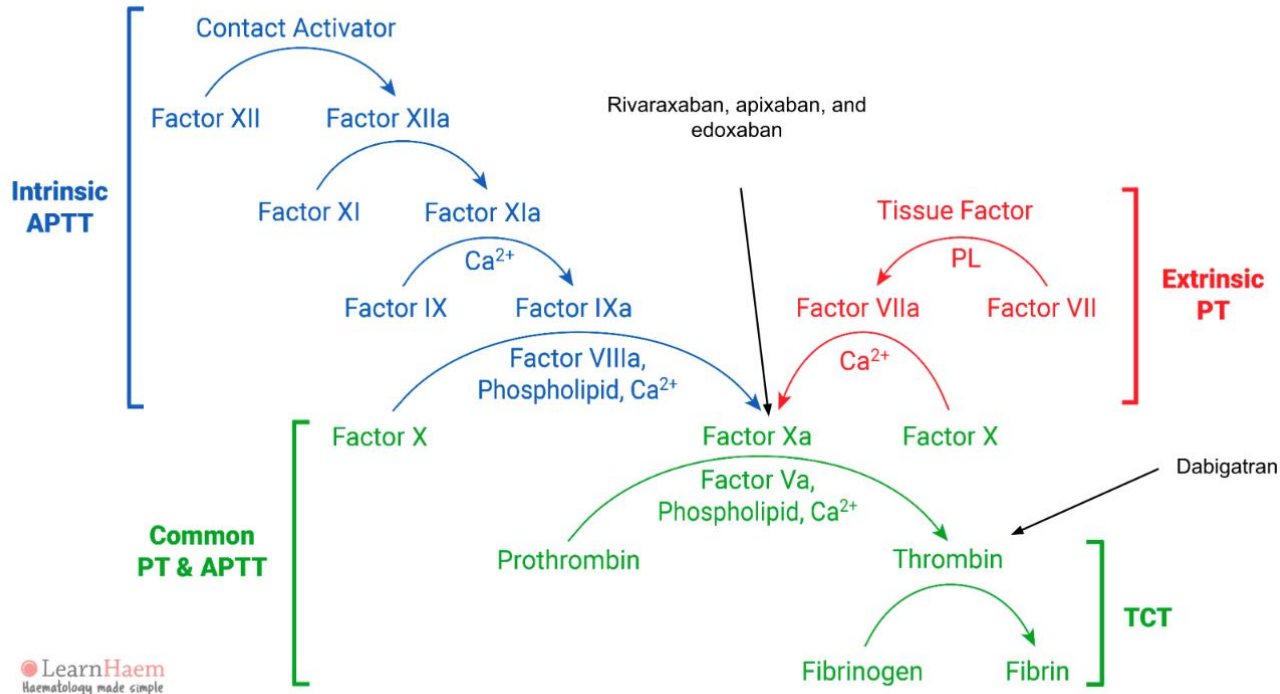
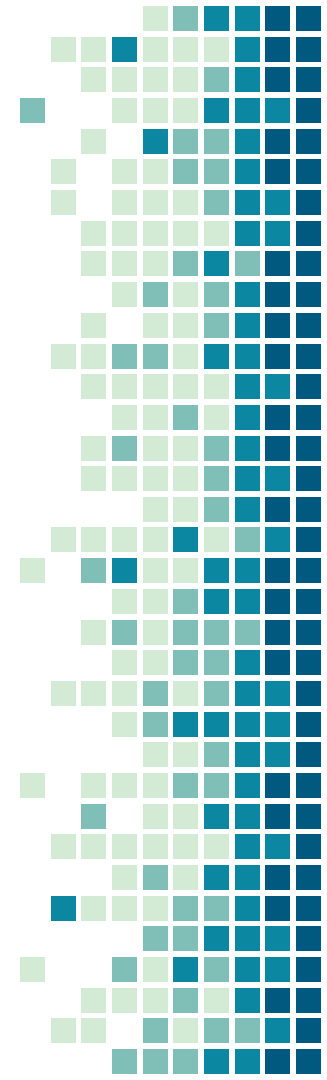


Figure 3: DOACs Mechanism of Action

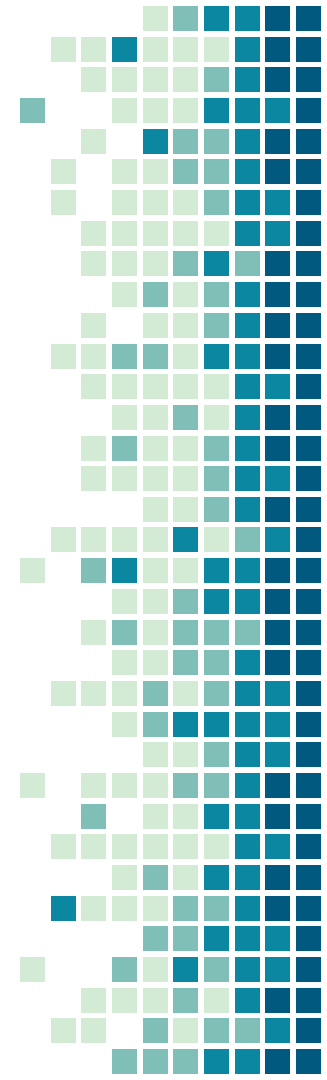
Indications of DOACs

- Prevention and treatment of thrombosis in cardiovascular conditions including DVT and PE, atrial fibrillation, and recurrent thrombotic stroke.
- DOACs provide both clinicians and patients safer, more effective, and convenient therapeutic alternatives in thromboembolic conditions.



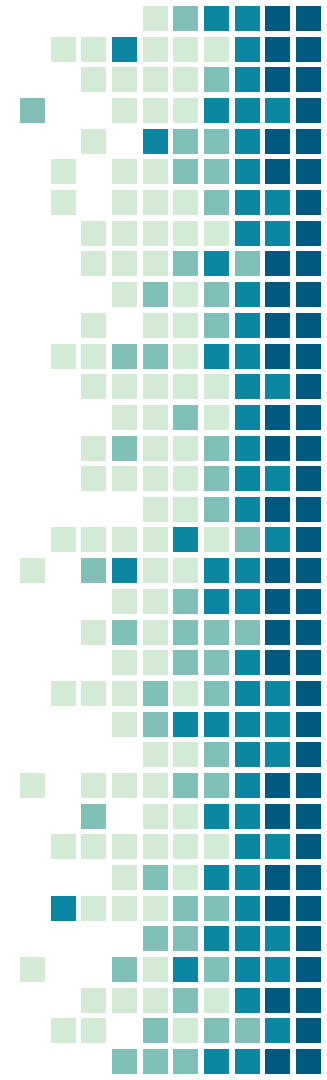
When Should DOACs be Avoided?

- Patients with severe hepatic disease in which warfarin is the only recommended anticoagulant.
- Dabigatran, apixaban, and edoxaban are viable options in patients with moderate hepatic impairment and do not require dose adjustments.



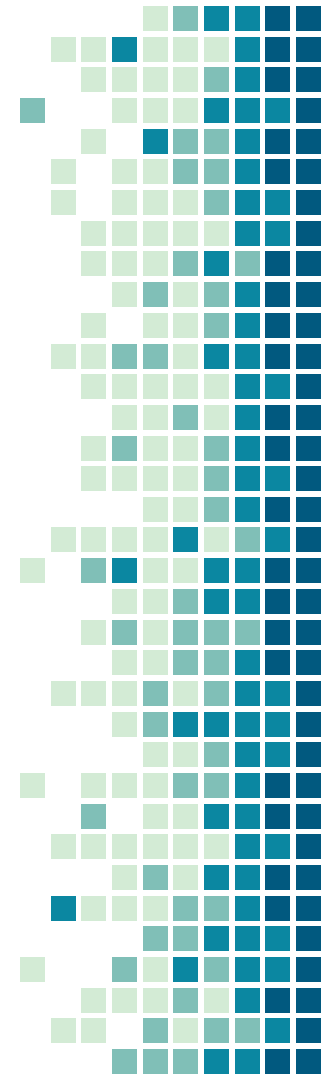
Challenges for the use of DOACs in the elderly (75 + yrs)

- Memory Issues/Dementia: Elderly patients often forget to take their medications consistently which can affect drug levels and efficacy.
- Accidental overdose of anticoagulants can cause an excessive risk of bleeding. This can occur due to memory and visual difficulties.
- Polypharmacy & Drug Interaction: Elderly people usually take multiple medications, which may alter the effects of anticoagulants



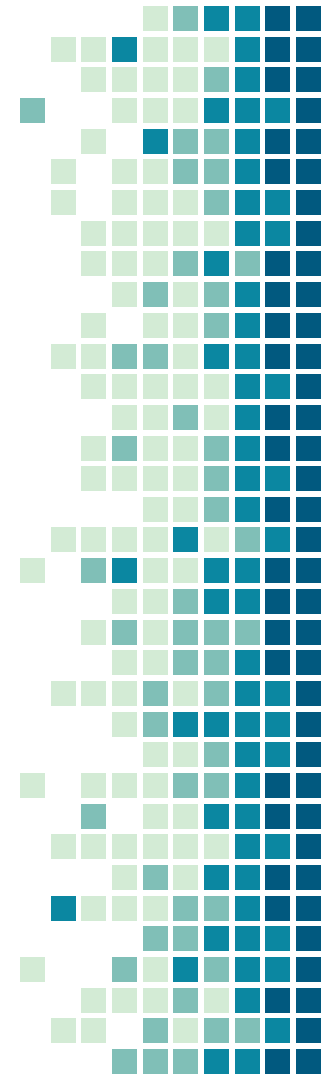
Challenges for the use of DOACs in the elderly (75 + yrs), contd.

- Altered Pharmacokinetics: Renal function typically declines with age, thereby affecting excretion of anticoagulants. This may cause a longer half life and elevated bleeding risk
- Falls: Elderly patients tend to have an elevated risk of falls due to multiple reasons including stroke, imbalance, visual difficulties, arthritis, and frailty. This leads to increased risk of intracranial and musculoskeletal bleeding.



Advantages of using DOACS vs warfarin in the elderly

- No need for regular blood tests (INR)
- No dietary restrictions
- Stable and predictable dosage
- Rapid onset and offset of action
- Fewer drug interactions



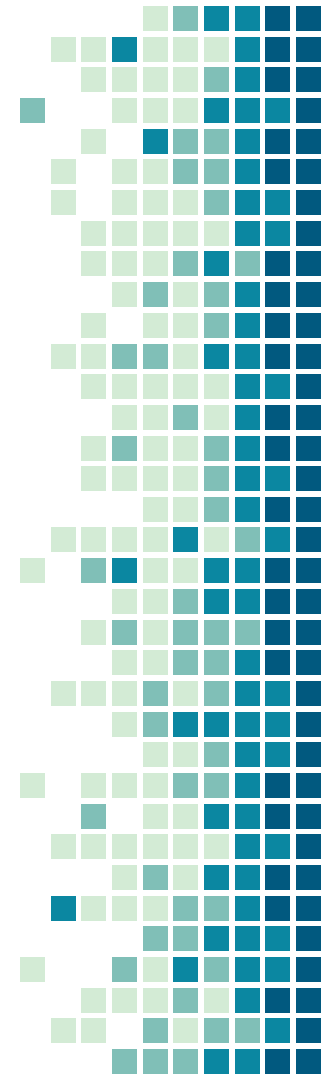
Disadvantages of DOACs vs warfarin in the elderly

- High cost
- Absence of tests to measure drug levels or effect
- Lack of universal reversal agents/antidotes:
 - Warfarin (Vitamin K & Fresh Frozen Plasma)
 - Dabigatran (idarucizumab)
 - Apixaban and Rivaroxaban (andexanet Alfa)
 - Edoxaban (none)



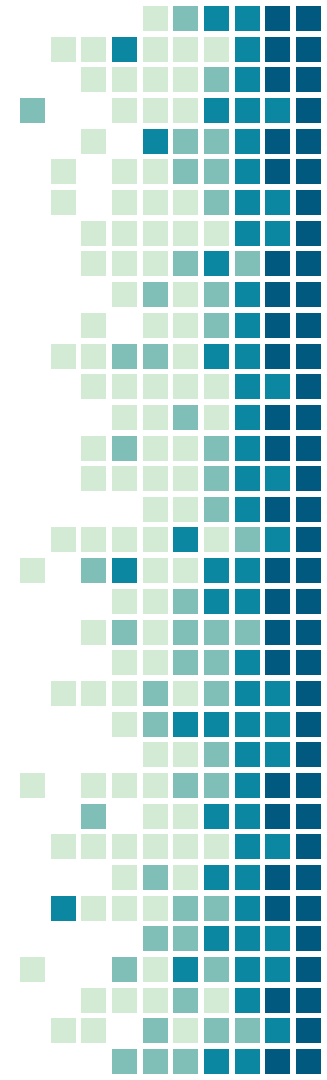
Are DOACs as effective and safe as warfarin in the elderly?

- DOACs are equally effective as warfarin, and show a lower incidence of stroke/systemic embolism and major bleeding compared with warfarin in antithrombotic therapy in the elderly patients with apixaban being the best of all DOACs.



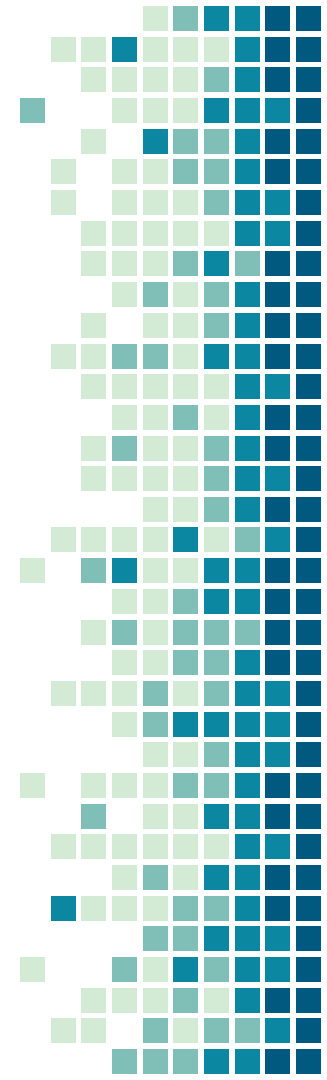
Conclusions

- Elderly people face unique challenges when using DOACs including memory issues, kidney dysfunction, falls, and polypharmacy
- Advanced age should not be the single limiting factor when prescribing DOACs, and the decision should be made based on net clinical benefit and a comprehensive geriatric assessment.
- DOACs significantly reduce the risk of stroke and systemic thromboembolism in elder patients, without increasing the risk of major bleeding. DOACs are safe and effective for use in the elderly, but should be used with great caution.
- DOACs offer various practical advantages over warfarin in the elderly.
- Apixaban, followed by edoxaban, was considered the most appropriate treatment in the various complex clinical situations examined.



Acknowledgments

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