DUR as *decision support* when designing outcome studies

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”The report is purely descriptive, and it is unclear **what the information teaches us**”

”This reviewer does not understand **the scientific importance of such information**”


DUR

Non-vitamin K antagonists oral anticoagulants (NOACs)

Atrial fibrillation (AF) and venous thromboembolism (VTE)

Dabigatran – Rivaroxaban – Apixaban – Edoxaban

No direct RCT comparison – assumed similar efficacy

GI-bleeding risk: Dabigatran > Rivaroxaban & Edoxaban > Apixaban

Comparative effectiveness and safety of NOAC A vs. NOAC B

Cohort study

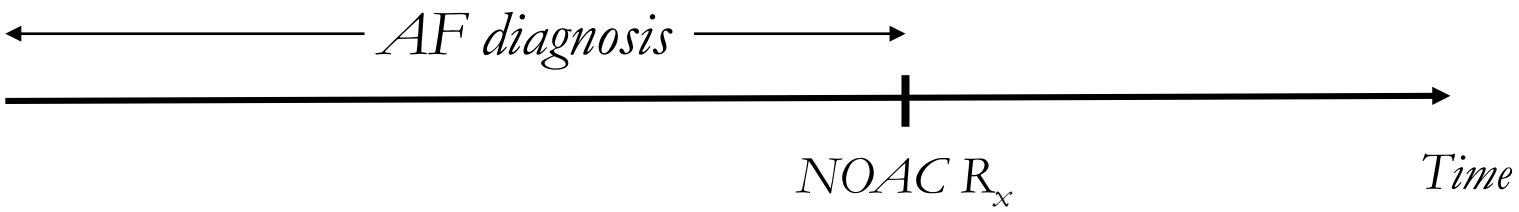
NOAC use for AF

Effectiveness outcome: ischemic stroke

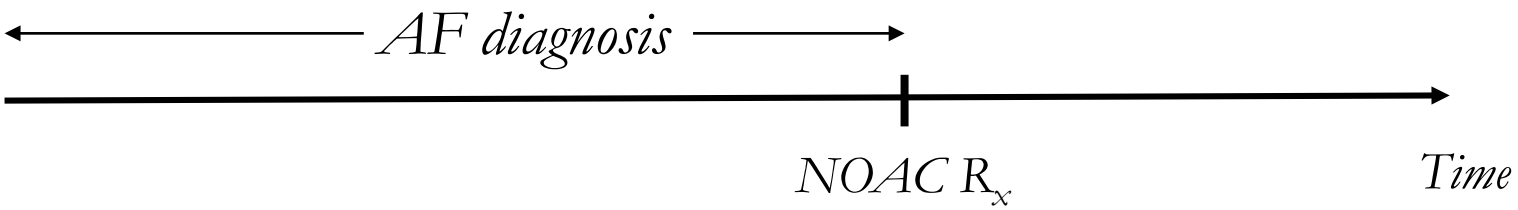
Safety outcome: bleeding

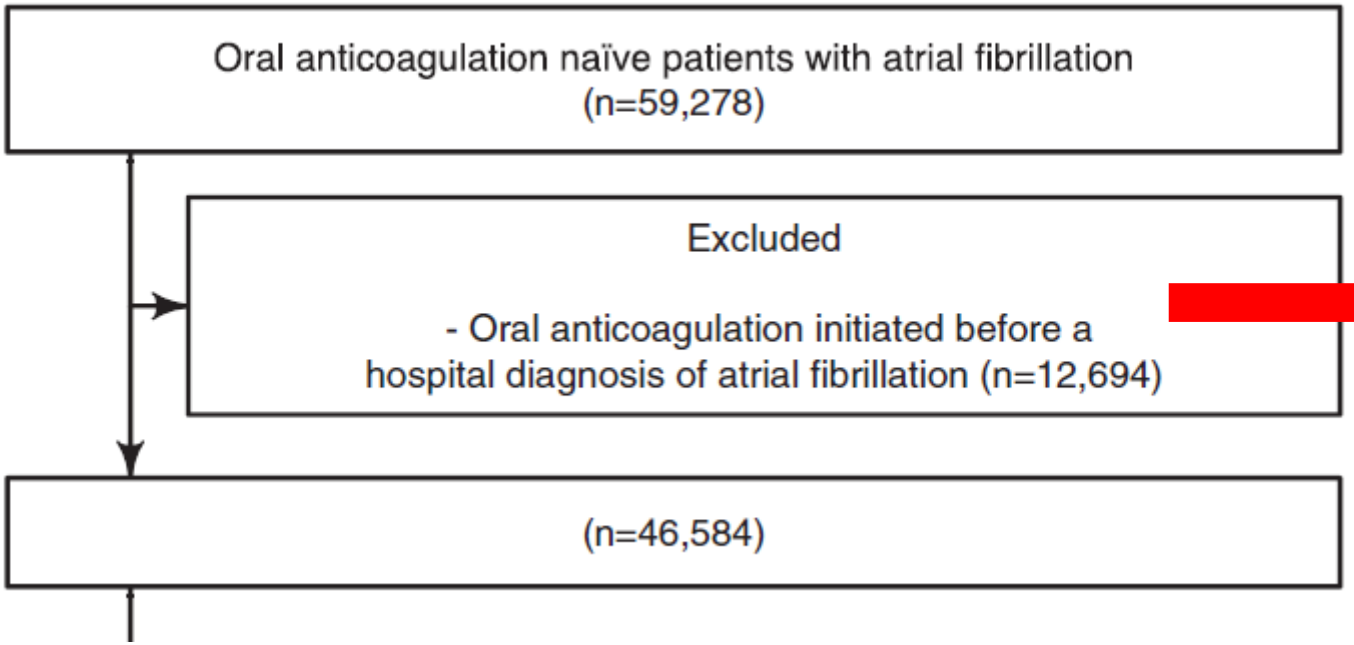
Q1: Cohort identification

The study cohort should consist of all Danes using NOAC A or NOAC B for AF (= population-based)



Will this approach capture all relevant users?





21%

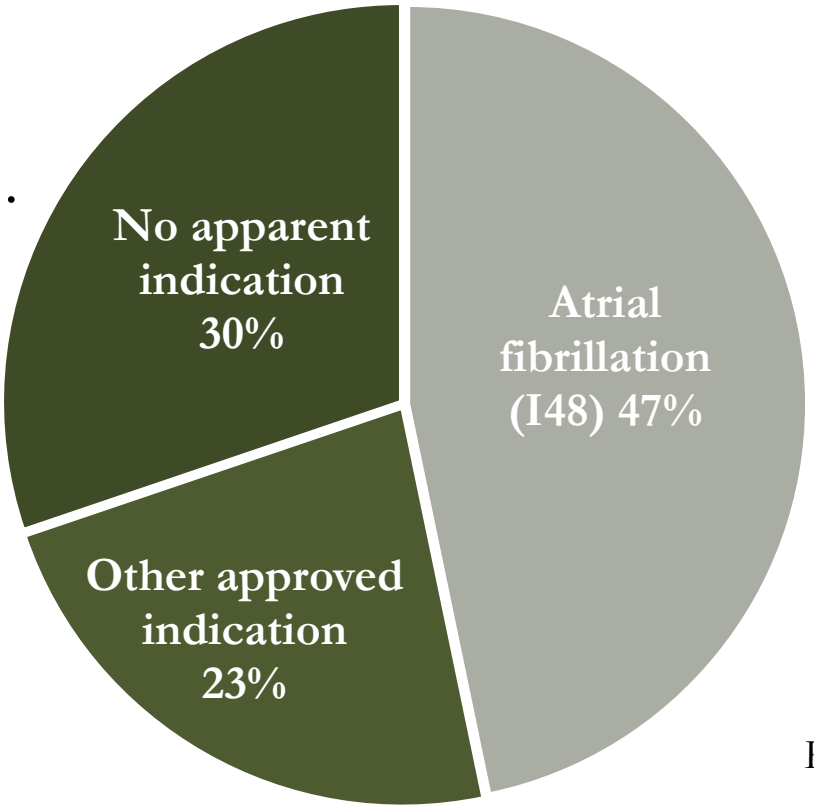
NOAC prescription → AF diagnosis
Median: 69 days (IQR 24-244)

Stærk et al. Scientific Reports. 2014

Do we get them all then?

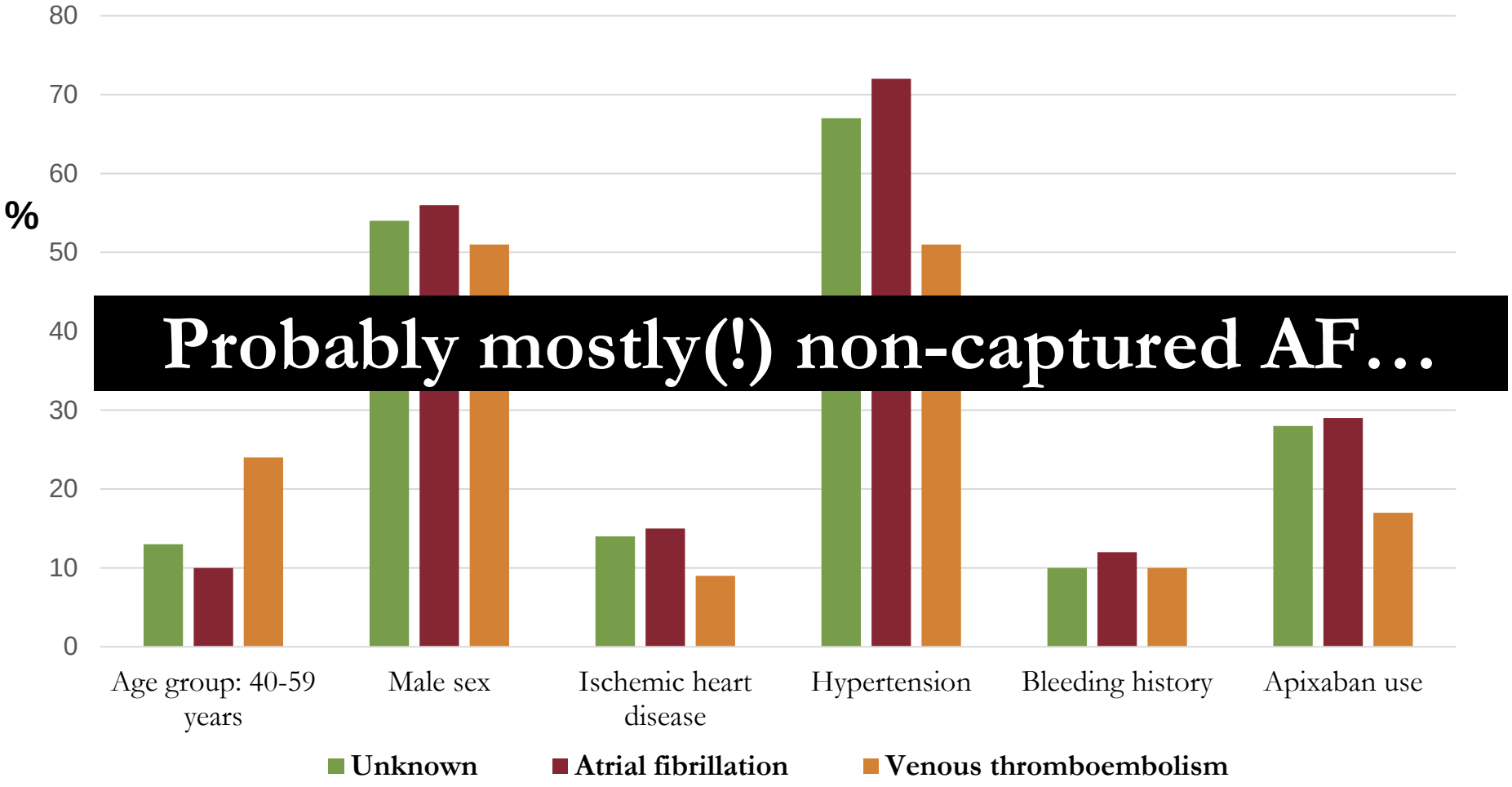
New NOAC users 08/2011-06/2017: 133,588

> 40,000…



Haastrup et al. BCPT. 2018

Who are they?
And should they be included in my study?



Probably mostly(!) non-captured AF…

Haastrup et al. BCPT. 2018

Cohort identification

NOAC prescription

+

No non-AF NOAC indication at time of redemption

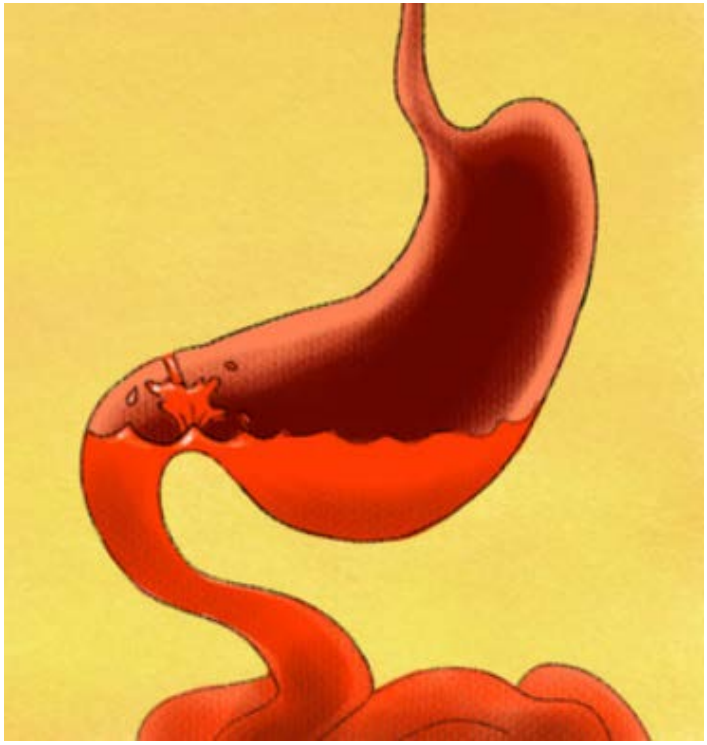
Supplementary analysis: require AF diagnosis

Q2: Appropriate comparison?

Rivaroxaban vs. apixaban and risk of GI-bleeding

RCT-based hypothesis:

Rivaroxaban > apixaban




Low-risk drug
High-risk drug
High-risk patient

Review | Journal of INTERNAL MEDICINE

doi: 10.1111/joim.12360

Choosing the right drug to fit the patient when selecting oral anticoagulation for stroke prevention in atrial fibrillation

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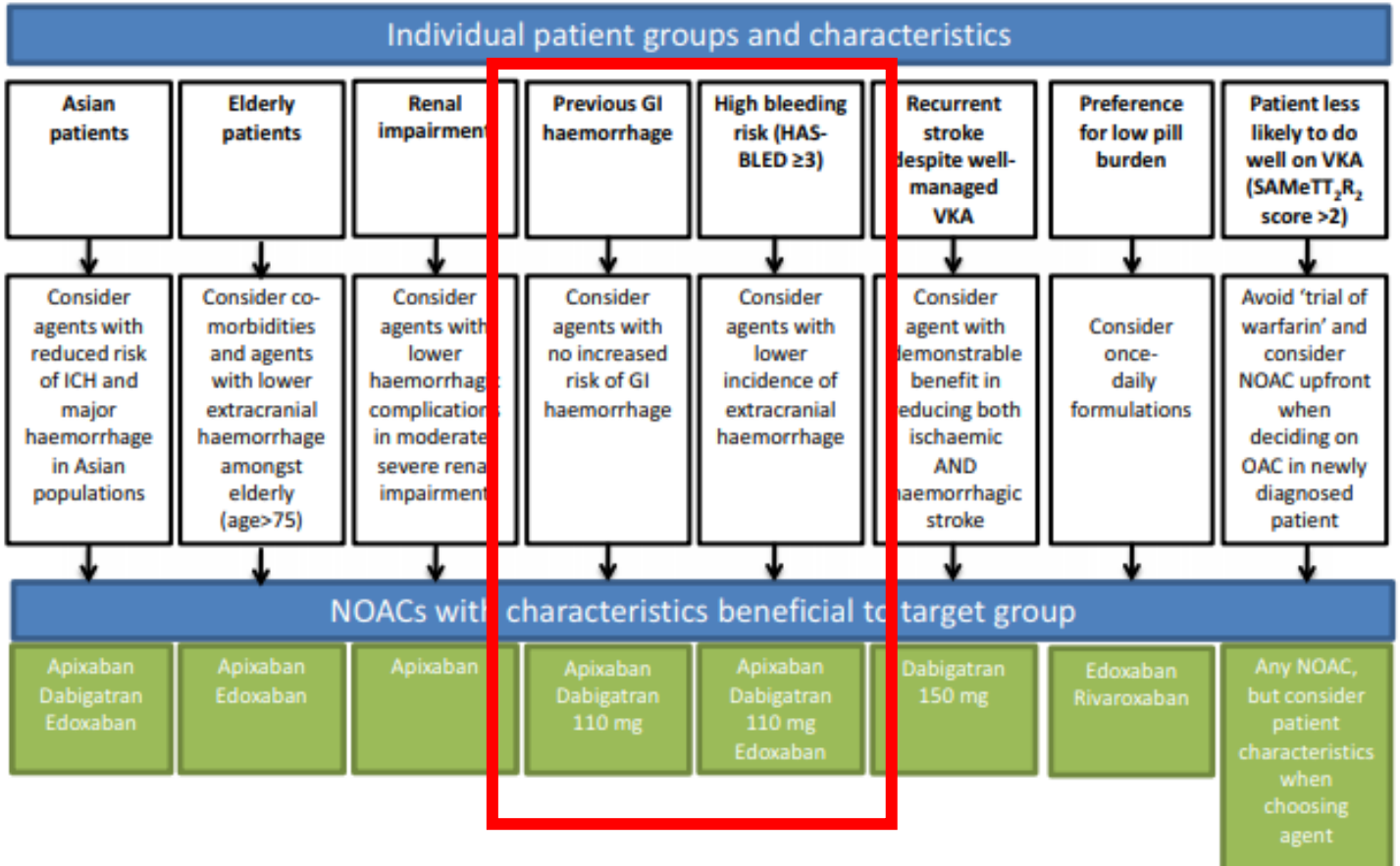
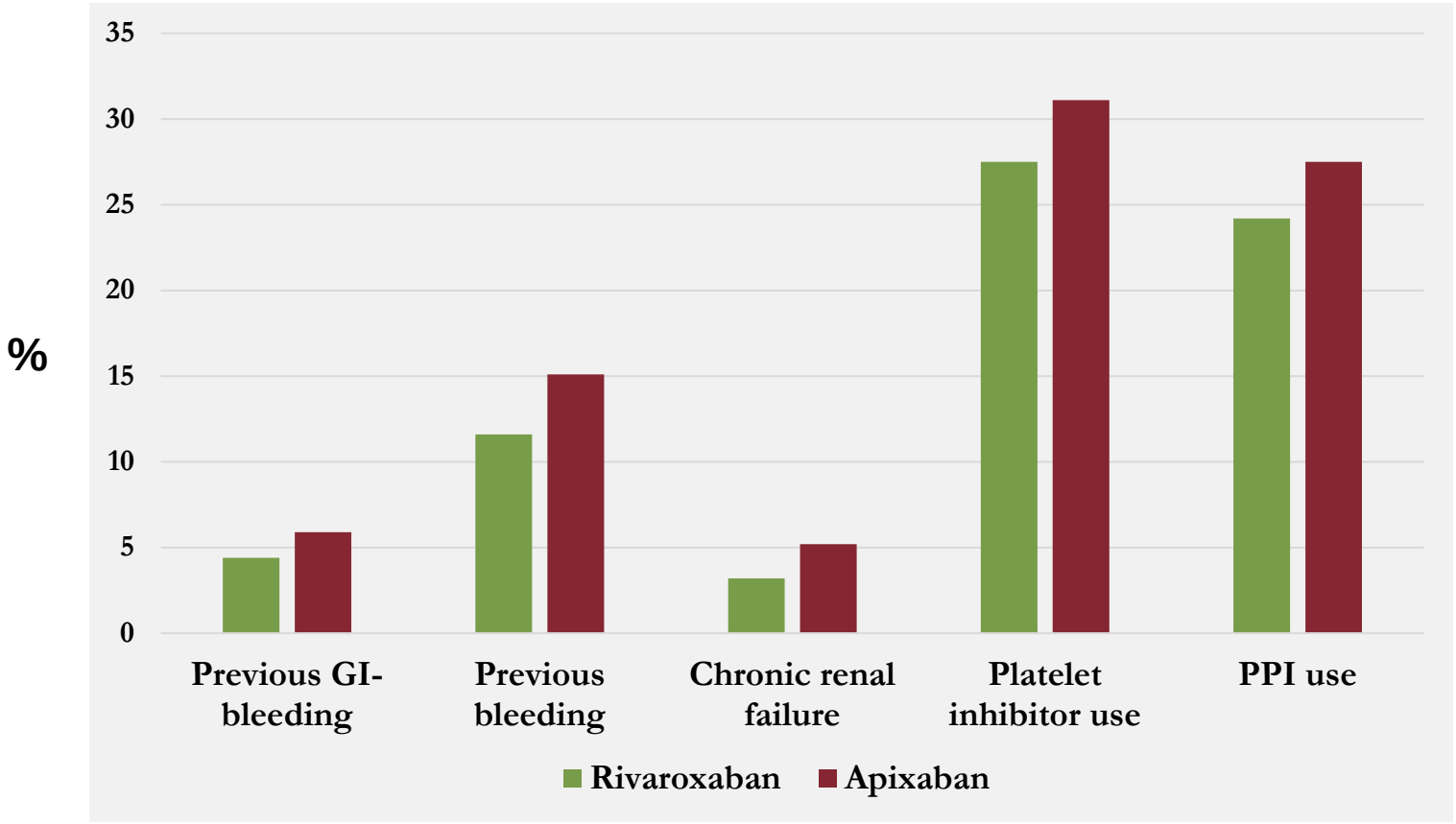



Low-risk drug
High-risk drug
Selective/preferential prescribing
Channeling bias
Confounding by indication
High-risk patient



Hellfritzsch et al. BCPT 2017

In case of likely selective prescribing

Do your best to adjust

AND

Acknowlegde that this probably isn't enough…

Conclude very carefully on your findings!

Q3: ITT-like approach appropriate if follow-up is up to 2 years?

Entry at NOAC initiation

Censoring at outcome/death/study end

Assumption: continuous use/no switching/no stop

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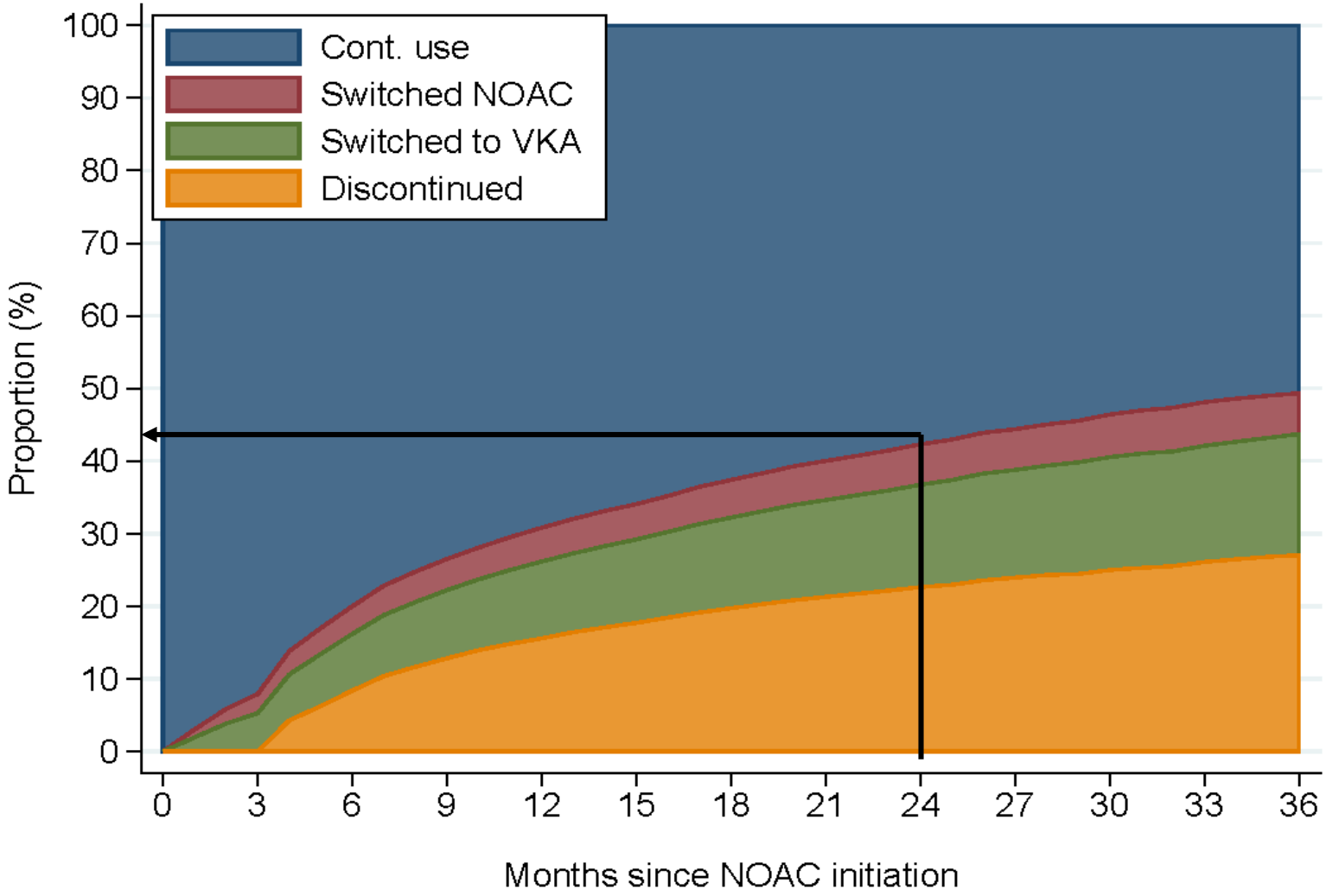
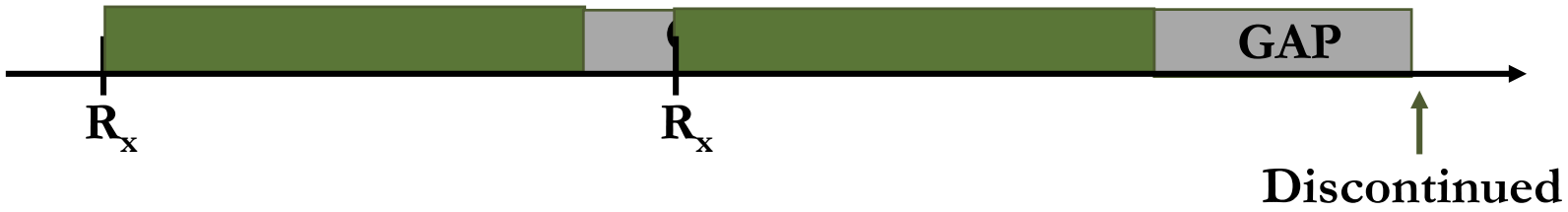


>40% exposure misclassification with ITT-approach…

Hellfritzsch et al. BCPT 2017

Ok - censoring at discontinuation

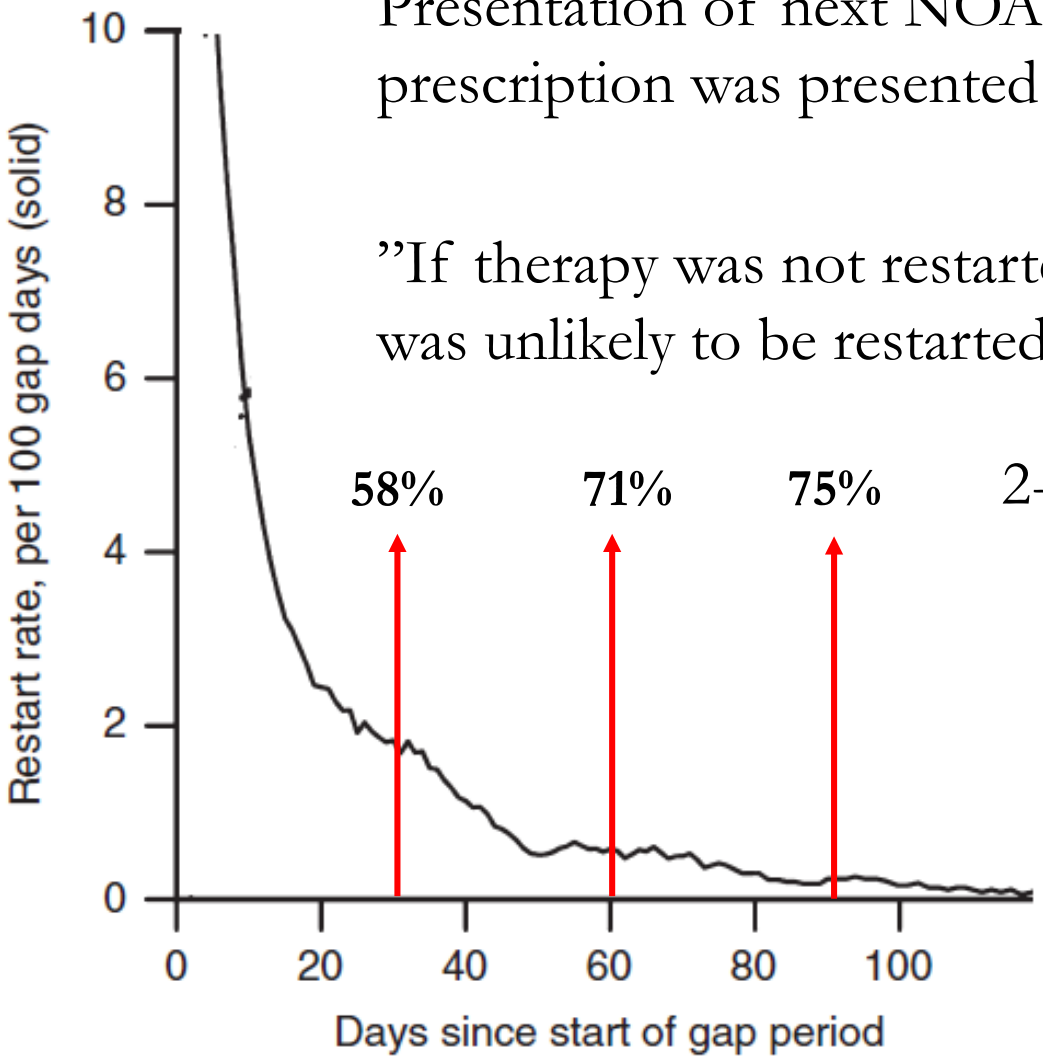


Q4: Allowed gap?

No matter what: do sensitivity analyses…

Presentation of next NOAC prescription if no prescription was presented during covarage by the last

”If therapy was not restarted within 60 days, it was unlikely to be restarted at all”



2-year persistence rates

Gorst-Rasmussen et al. JTH. 2018
Haastrup et al. BCPT. 2018

Conclusions

Designing studies is all about decisions!

Preceeding drug utilization research can help you qualify these decision and thereby increase the validity of your outcome study

Thank you!

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