Which DOAC for Which Patient?

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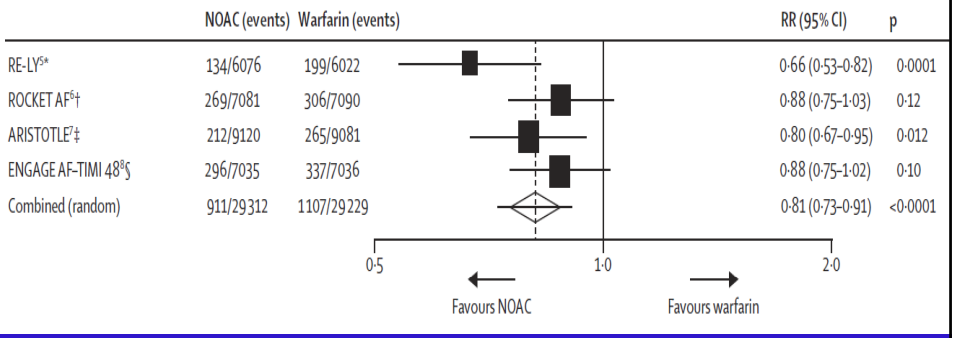
RECENT META-ANALYSIS
ALL 4 MAJOR STUDIES

- > 42,000 patients Rx with a NOAC
- > 29,000 Rx with warfarin
- RE-LY, ROCKET-AF, ARISTOTLE, ENGAGE (did not include AVERROES)
- Mean follow-up 1.8 to 2.8 years
- Median TTR 58% to 68%

Ruff et al, Lancet, Dec 2013

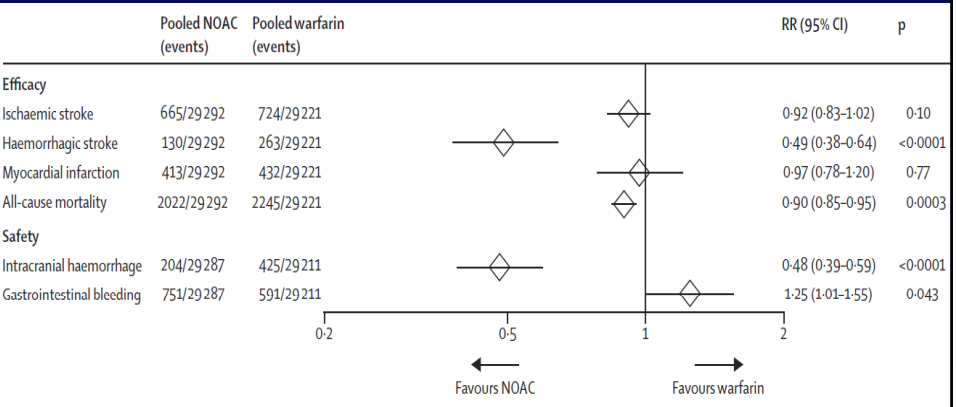
PRIMARY ENDPOINT



Data is for dabigatran 150 mg

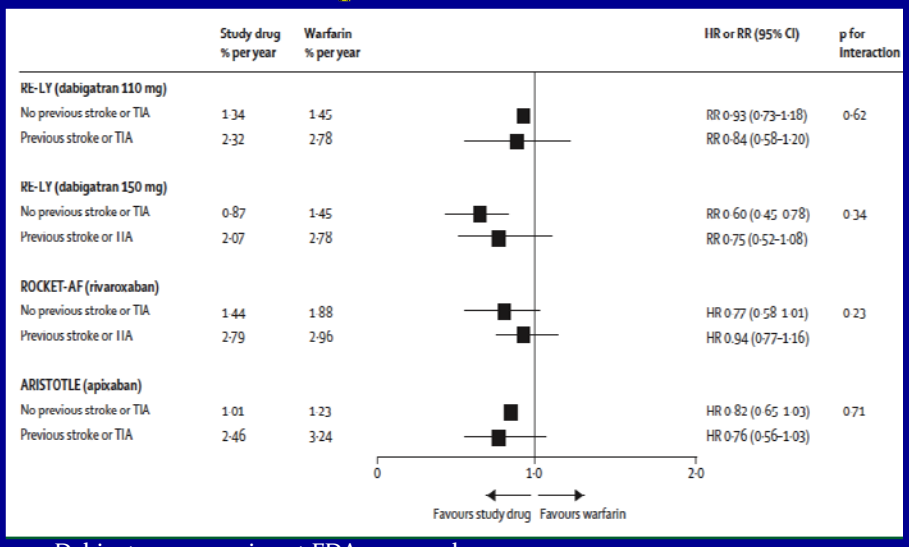
Ruff et al, Lancet, Dec 2013

SECONDARY ENDPOINTS



Ruff et al, Lancet, Dec 2013

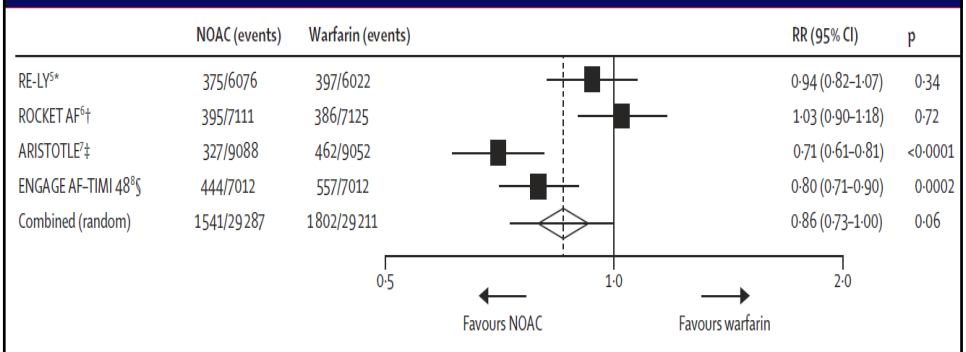
Benefits of NOACs in Primary vs Secondary Stroke Prevention



Dabigatran 110 mg is not FDA approved

Alberts et al., Lancet Neuroogy, 2012

MAJOR BLEEDING



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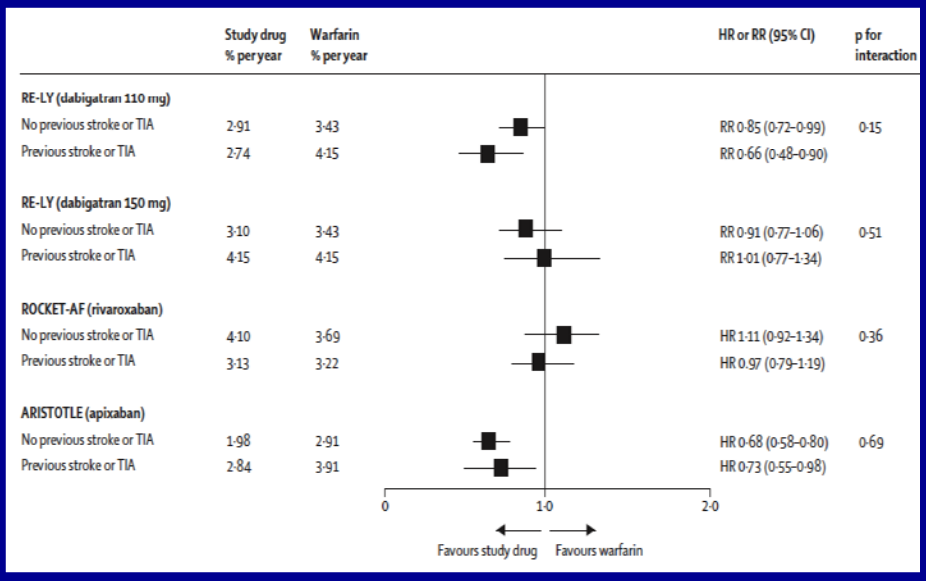
Ruff et al, Lancet, Dec 2013

Safety of NOACs – Major bleeding



Alberts et al., Lancet Neurology, 2012

Bleeding and the NOACs

- All NOACs increase the risk of bleeding compared to placebo
- All of the NOACs, EXCEPT Apixaban, had higher GI bleeding rates than warfarin
  - Especially true in elderly patients
- Apixaban and Endoxaban had lowest rates of major bleeding vs warfarin
- For CNS and fatal bleeding, only Apixaban was tested vs aspirin
  - Apixaban was as safe as aspirin in AVERROES study

EFFECTS OF THE LOW DOSE REGIMENS

- Fewer hemorrhagic strokes and SE
  - Most of the benefits were seen for CNS bleeding
  - Not as good as warfarin for ischemic stroke
  - Less all cause mortality
  - More MIs
  - Less major bleeding
  - GI bleeding about = to warfarin

NOAC SELECTION IN SPECIAL POPULATIONS

- Significant renal disease
  - Apixaban shows good safety profile
  - FDA label change shows it is now approved for dialysis patients
  - Rivaroxaban, Endoxaban good 2nd choices
  - Dabigatran NOT an option

PRIOR STROKE (ISCHEMIC)

- Consider rivaroxaban based on high % of prior stroke patients in ROCKET
  - Apixaban or Dabigatran or Endoxaban are good 2nd choice based on safety (apixaban, endoxaban) and efficacy (dabigatran)
  - But they all offer benefit
    - They at least worked as well as warfarin
    - Dabigatran superior to warfarin for preventing ischemic stroke

PRIOR STROKE (HEMORRHAGIC)

- Consider Apixaban based on overall CNS bleeding profile
  - Must determine underlying etiology of hemorrhage
  - Dabigatran or Endoxaban are good 2nd choices

CARDIAC DISEASE

- Valvular heart disease
  - Warfarin is still medication of choice (RE-ALIGN study)
  - NOACs are not approved for this indication

UNDER-APPRECIATED ISSUES WITH THESE STUDIES

- Hemorrhagic strokes are counted twice!!
  - Once in the primary endpoint (stroke and SE)
  - Again in the safety endpoint (major bleed, CNS bleed)

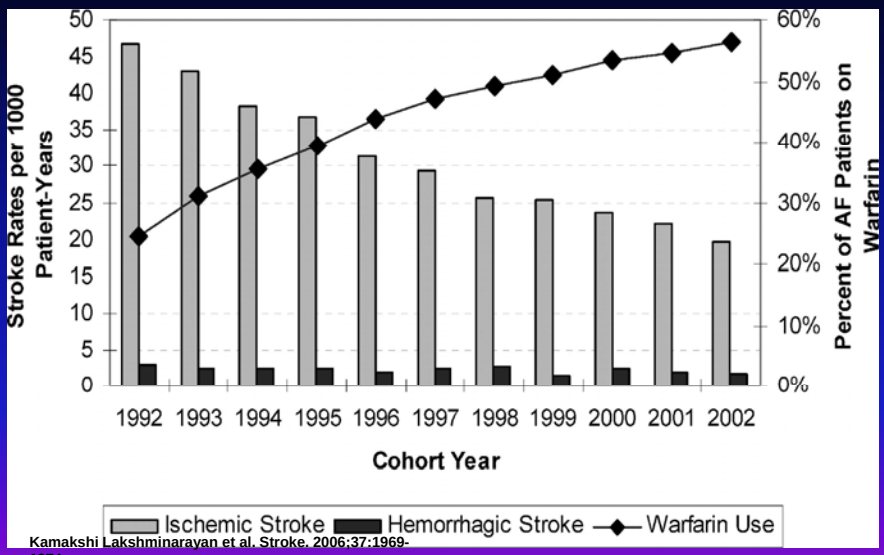
WEIGHING THE VARIOUS OUTCOMES

- In general, there are no worse outcomes than hemorrhagic stroke and death
  - ICH has a mortality of 40-50%
  - Much worse than ischemic stroke, MI, GI bleed
  - High costs are associated with cerebral hemorrhage
  - BUT…..ischemic strokes out-number hemorrhagic strokes by about 9:1 !!!

ALL OF THE NOACS STILL HAVE THE ADVANTAGES OF NOT BEING WARFARIN!!

- No need for routine monitoring
- No major food and drug interactions
- Very rapid onset of action (within 2-4 hours)
- Generally well tolerated

Warfarin, Stroke, and Afib



Kamakshi Lakshminarayan et al. Stroke. 2006;37:1969-1974

American Heart Association.

Summary Recommendations 1

- Any NOAC is preferred over no NOAC
- Apixaban and Endoxaban likely has best safety profile
  - Safe if concerned about CNS bleeding
  - Apixaban only NOAC with fewer GI bleeds than warfarin
  - As safe as aspirin for fatal bleeds
- Rivaroxaban worked well is high-risk population
  - Also once a day dosing
  - Endoxaban only other NOAC with qd dosing
- Dabigatran worked well to prevent ischemic strokes
  - Renal dosing issues
- Do not forget low-dose regimen in high-risk population
  - Direct data for Apixaban, Rivaroxaban, Endoxaban

Summary Recommendation #2

- Of more importance than which particular DOAC we use, it is more important to make sure that EVERY eligible patient is treated with A DOAC
- This has the potential to have a large public health impact