WHICH NOAC IS BETTER??

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WHY WE SHOULD NOT DO THIS

- Prior attempts at such indirect comparisons are almost always at least misleading, if not wrong
- Different study populations
- Different risk factors
- Different local and national treatment standards
- Different endpoint definitions

WHY WE DO IT ANYWAYS

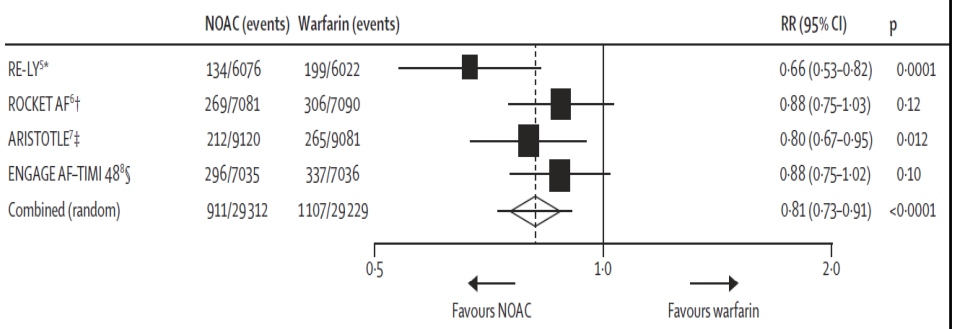
- To guide us when there are multiple choices
- We are always looking for some little advantage or difference
- Individualize therapy for each patient

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%

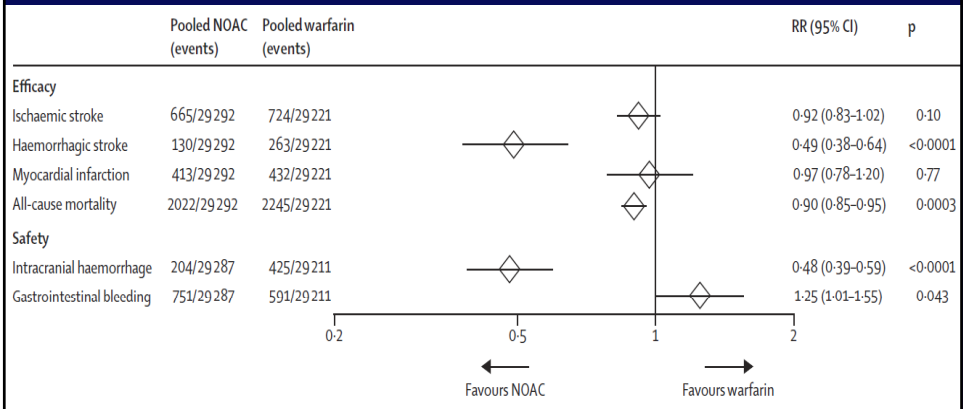
Ruff et al, Lancet, Dec 2013

PRIMARY ENDPOINT



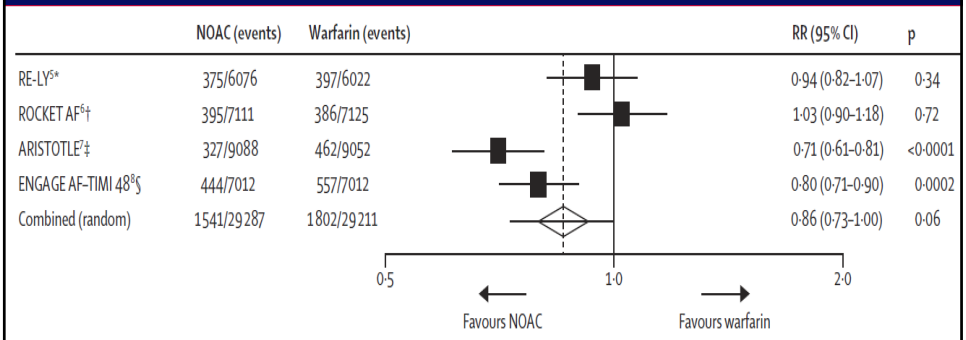
Ruff et al, Lancet, Dec 2013

SECONDARY ENDPOINTS



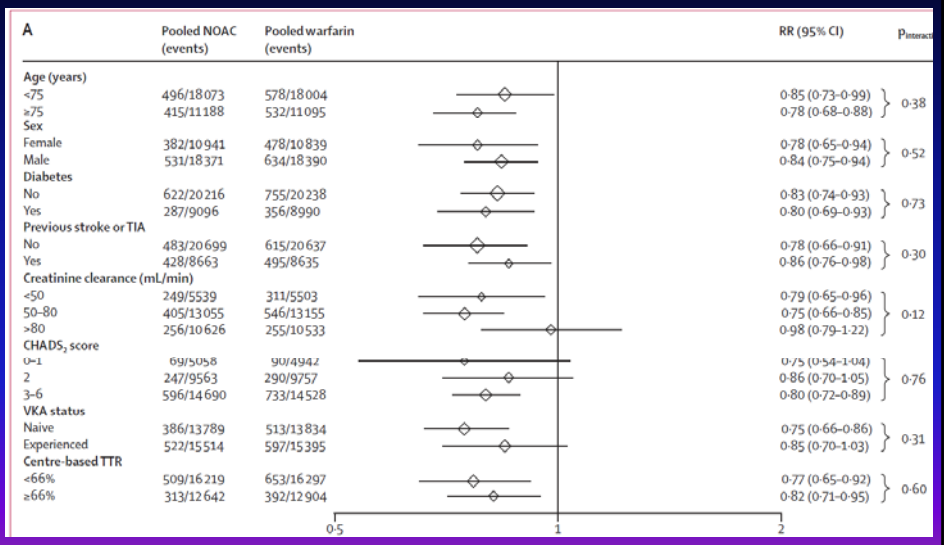
Ruff et al, Lancet, Dec 2013

MAJOR BLEEDING



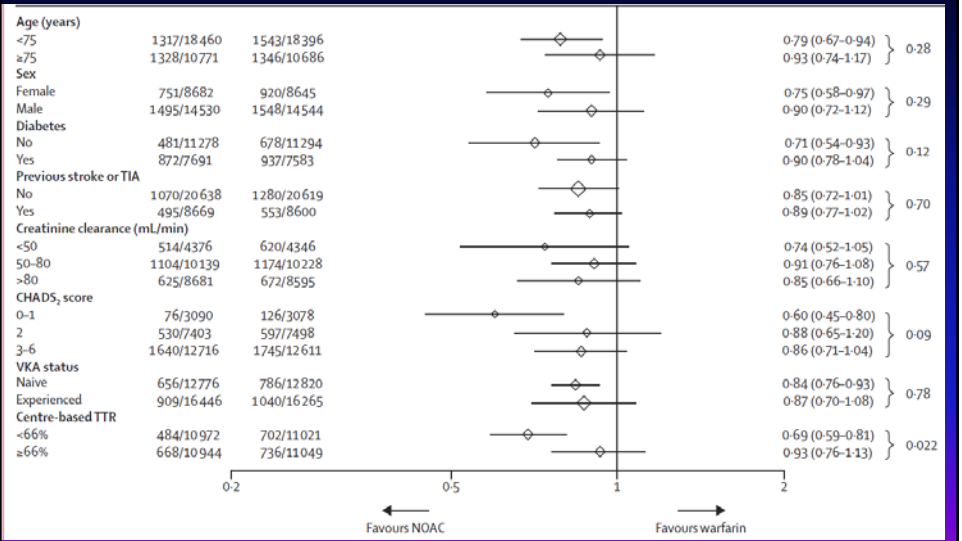
Ruff et al, Lancet, Dec 2013

PRIMARY ENDPOINT



Ruff et al, Lancet, Dec 2013

MAJOR BLEEDING



Ruff et al, Lancet, Dec 2013

EFFECTS OF THE LOW DOSE REGIMENS

- Fewer 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 great safety profile
  - FDA label change shows it is now approved for dialysis patients
  - Rivaroxaban good 2nd choice
  - Dabigatran NOT an option

PRIOR STROKE (ISCHEMIC)

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

PRIOR STROKE (HEMORRHAGIC)

- Consider apixaban based on overall CNS bleeding profile
  - Must determine underlying etiology
  - Dabigatran good 2nd choice

CARDIAC DISEASE

- Would prefer rivaraoxaban or apixaban
  - Consider dabigatran as 2nd choice
    - Further analyses failed to confirm this increased risk
  - Data are not compelling—more erring on side of caution
- Valvular disease
  - Warfarin is still medication of choice (RE-ALIGN study)

NNT TO PREVENT ICH VS WARFARIN

- 34.5 for dabigatran 150 mg BID
- 35.1 for apixaban 5 mg BID
- 59.1 for rivaroxaban 20 mg qd
- Overall risk reduction with NOACS was similar for all types of bleeds (ICH, IVH, SAH, SDH, EDH)

Chatterjee et al., JAMA Neurology, 12/13

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

IMPLICATIONS FOR THE STROKE BELT AND OUR PATIENTS

- The issue should not be which medication to use, but rather to use ANY NOAC and not just aspirin in most cases

STEPS FORWARD

- All treatments should be individualized
- Let's make a regional Stroke Belt Standard to assess risk of stroke in Afib patients
  - CHADS2 or CHADS-VASC scores
  - Calculate 5 year stroke risk
  - Use EMR to facilitate
  - Document in all patients with Afib
    - In and Out patients
  - Use data to drive more aggressive treatment and compliance paradigms

CONCLUSIONS

- Essentially all of the NOACs offer huge advantages over warfarin in terms of ease of use, which translates into efficacy and safety
- This should translate into more patients being treated
- The best way to treat stroke is to prevent stroke
- Using NOACs is a great way to prevent more strokes