



Universitäres Herzzentrum
Hamburg

Ein Unternehmen des UKE



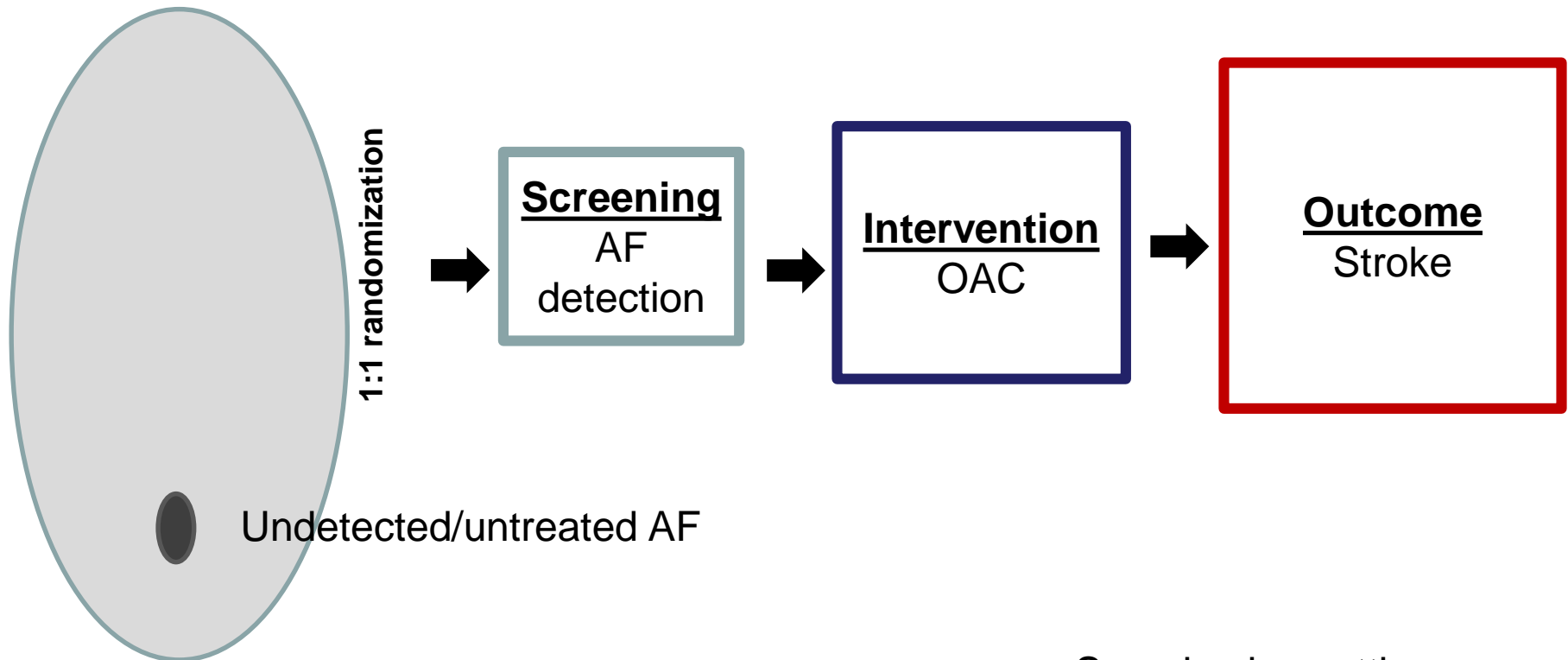
What Size of Study is Required to Impact Guidelines

AF-Screen International Collaboration Meeting

Renate B. Schnabel

Rome, August 26, 2016

Screening population

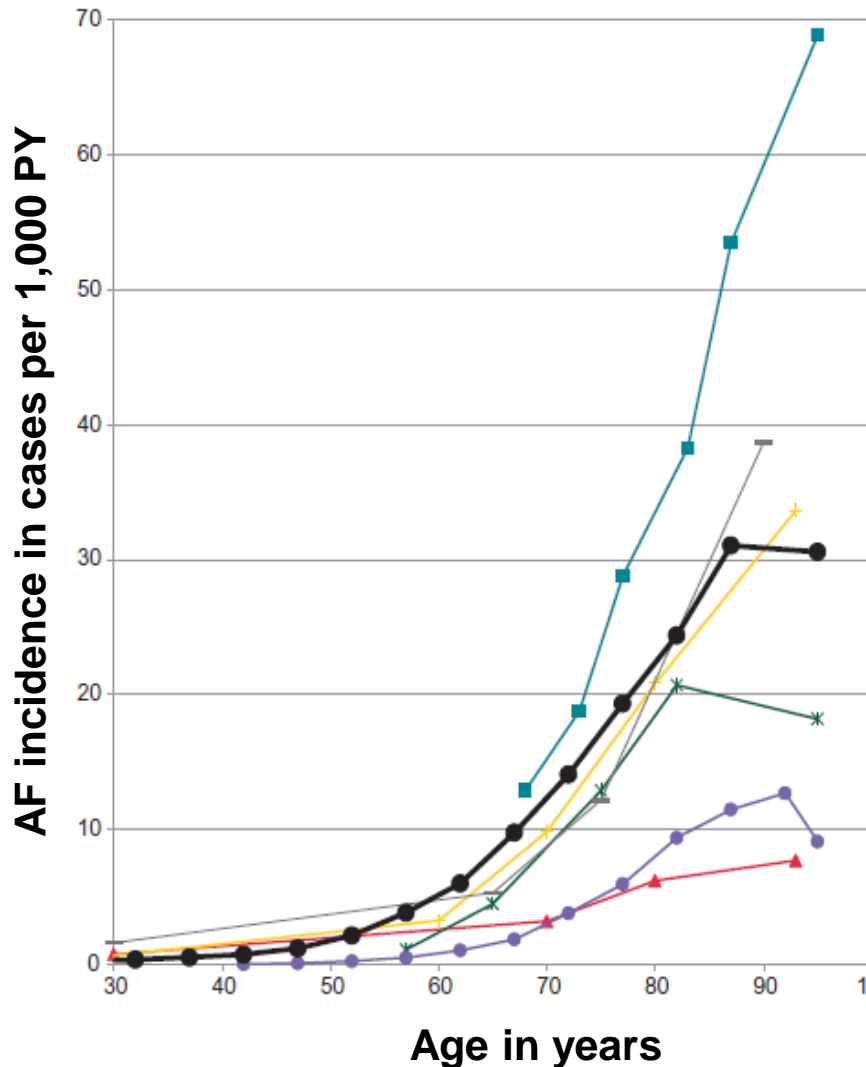


Sample size settings

Power 0.8

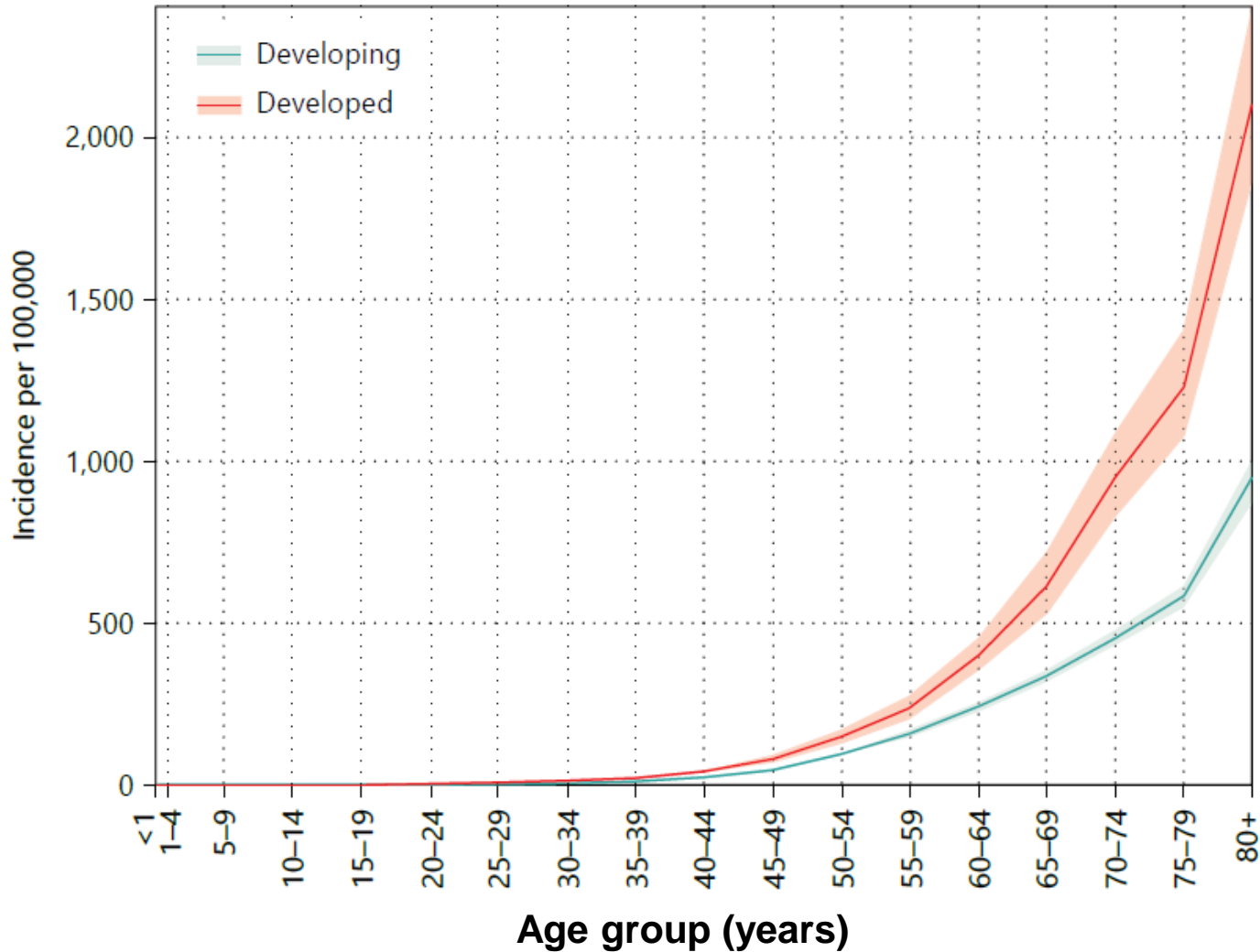
Alpha 0.05

AF Prevalence

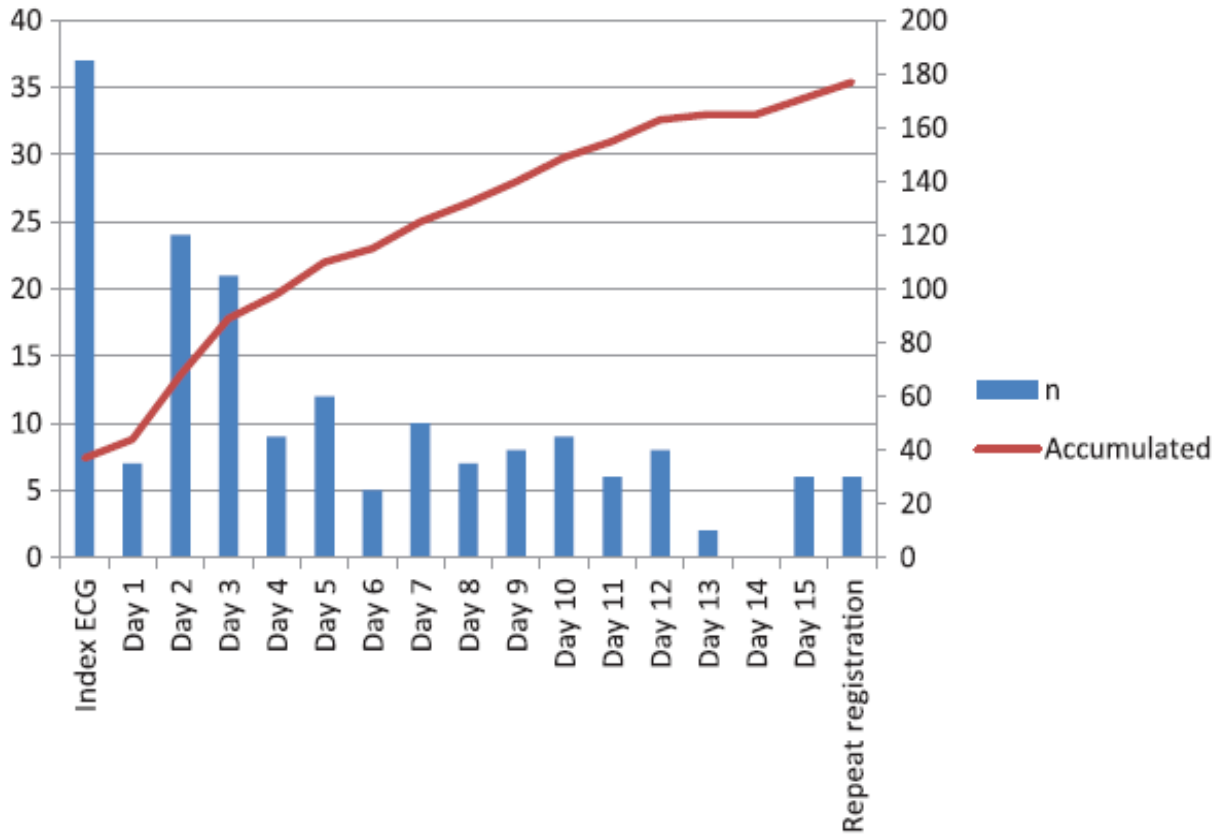


- Systematic
- Defined subgroups
- Opportunistic

Background Stroke Risk



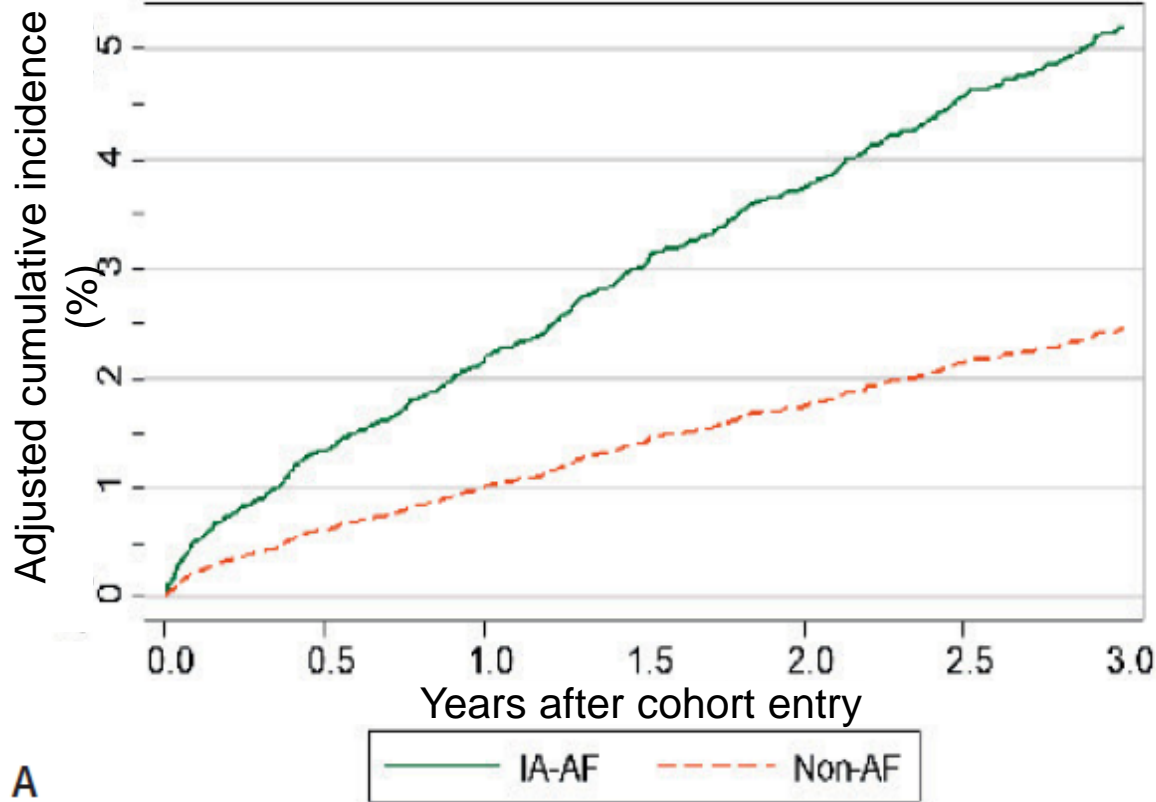
AF Detection Rate



- Duration
- Intensity
- Quality

Stroke Risk Reduction by Treatment

Fatal and non-fatal stroke



- Response to treatment

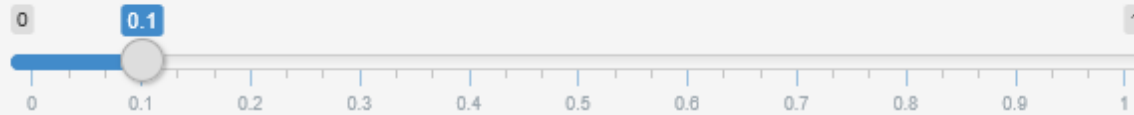
A

IA-AF:	5555	4878	4007	3101
Non-AF:	24705	23401	20442	1680

Sample Size Calculations Assumptions

Incidence

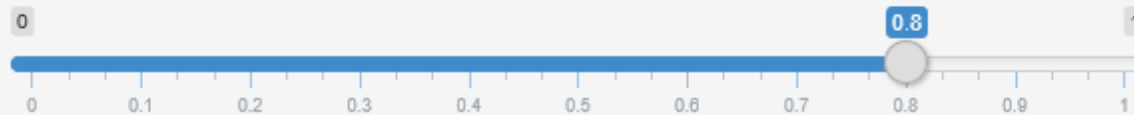
Proportion undetected AF:



10%?? (Svennberg E, Circ 15)

Diagnostic test

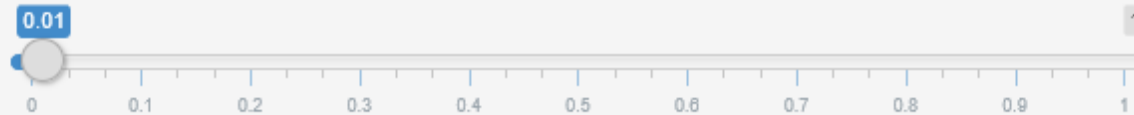
AF-DETECT rate (sensitivity)



3% new AF, 5.1% untreated AF - 80% detection rate (Svennberg E, Circ 15)

Risk of stroke

without AF (background risk)



1000 per 100000 total, so <math>< 0.01</math> (Feigin VL, Neuroepi 15)

with an undetected AF



Median CHA_2DS_2 -VASc score 3 - 4.7% annual stroke risk, (Svennberg E, Circ 15, Schnabel R 16)

after detected (and treated) AF



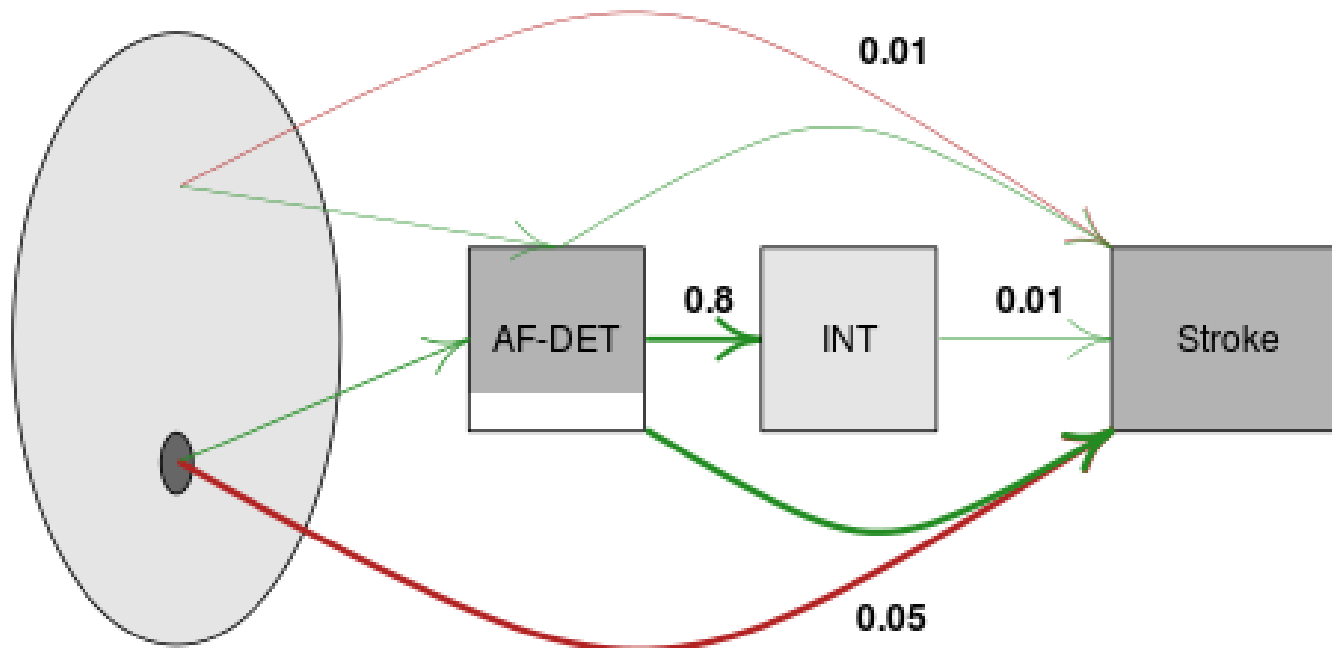
70-75% risk reduction – 1.41 (Martinez C, Thromb Haemost. 14)

Flow Chart

Weight of Different Factors

Population
 Undetected AF

Control
 Intervention



Total sample size
N=37,546

Treatment effect within AF population

Risk difference -0.032, relative risk 0.36

Treatment effect in screening population

Risk of stroke screened 0.011, unscreened 0.014

Risk difference -0.003, relative risk 0.771

Sample Size Calculations Assumptions

Incidence

Proportion undetected AF:



10%?? (Svennberg E, Circ 15)

Diagnostic test

AF-DETECT rate (sensitivity)



1.4% undiagnosed AF
(Lowres N, Thromb Haemost 13, 14)

Risk of stroke

without AF (background risk)



1,000 per 100,000 total, so <0.01
(Feigin VL, Neuroepi 15)

with an undetected AF



Median CHA₂DS₂-VASc score 3
- 4.7% annual stroke risk,
(Svennberg E, Circ 15, Schnabel 16)

after detected (and treated) AF



70-75% risk reduction – 1.41
(Martinez C, Thromb Haemost 14)

Sample Size Calculations Assumptions

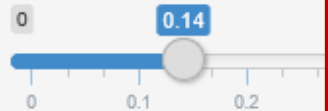
Incidence

Proportion undetected AF:



Diagnostic test

AF-DETECT rate (sensitivity)



**Total sample size
N=418,608**

Risk of stroke

without AF (background risk)



with an undetected AF



after detected (and treated) AF



10%?? (Svennberg E, Circ 15)

1.4% undiagnosed AF
(Lowres N, Thromb Haemost 13, 14)

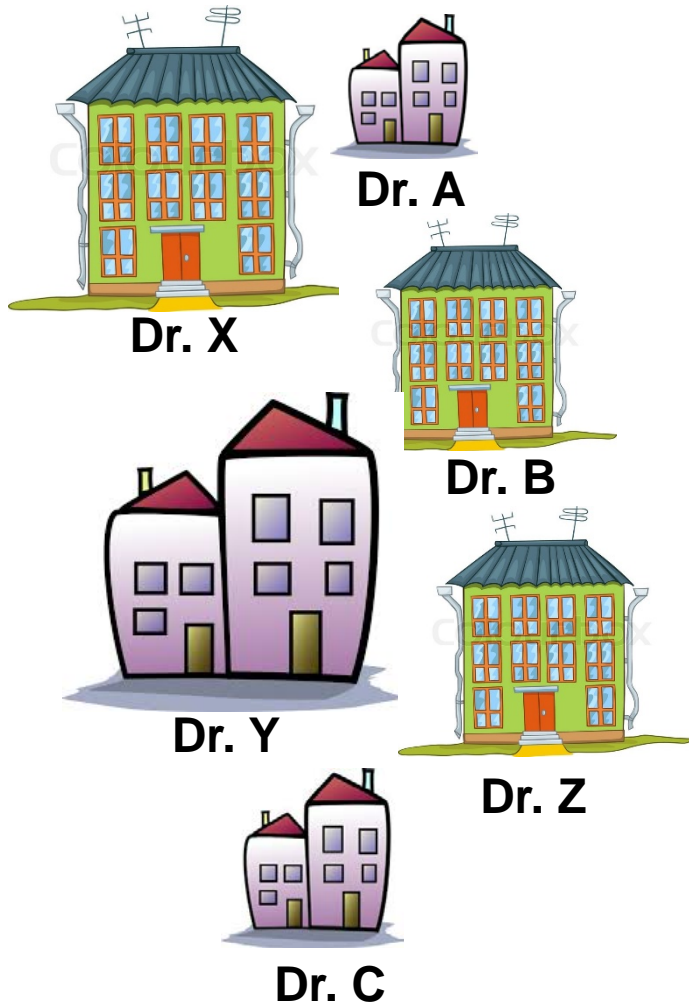
1000 per 100000 total, so <math>< 0.01</math>
(Feigin VL, Neuroepi 15)

Median CHA₂DS₂-VASc score 3
- 4.7% annual stroke risk,
(Svennberg E, Circ 15, Schnabel 16)

70-75% risk reduction – 1.41
(Martinez C, Thromb Haemost 14)

Sample Size Calculations

Cluster Randomization by Practice



- 1000 people aged >65 per practice
- 37 practices in intermittent screening
- 400 practices in single-time point screening
- Slightly higher numbers (cluster randomization, OAC not 100%)
- Countries with central stroke/mortality outcome data

Guideline-relevant Screening Study Size and Dimension

- Community screening vs. high risk individuals
- Sensitivity of screening approach
- OAC Uptake (50-93%)
- Across countries
 - Numbers
 - Generalizability
- Undertreated and undiagnosed/SCAF combined
- Heterogeneity of AF prevalence and stroke risk across different racial/ethnic groups
- Heterogeneity of healthcare systems

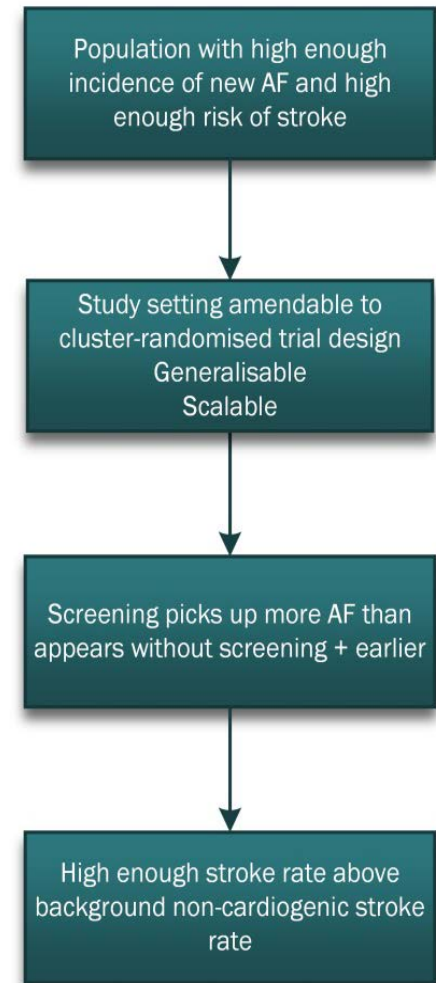


Figure: Consensus document