What Size of Study is Required to Impact Guidelines

AF-Screen International Collaboration Meeting

Renate B. Schnabel

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Study Design Outcome Study
Screening for AF

Screening population

Sample size settings
Power 0.8
Alpha 0.05
AF Prevalence

- Systematic
- Defined subgroups
- Opportunistic

Wilke T, Europace 11
Background Stroke Risk

Feigin VL, Neuroepi 15
AF Detection Rate

- Duration
- Intensity
- Quality
Stroke Risk Reduction by Treatment

- Response to treatment

![Graph showing the adjusted cumulative incidence of fatal and non-fatal stroke over years after cohort entry. The graph compares IA-AF and Non-AF groups.]

**Adjusted cumulative incidence (%)**

<table>
<thead>
<tr>
<th>Years after cohort entry</th>
<th>IA-AF: 5555</th>
<th>4878</th>
<th>4007</th>
<th>3101</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-AF: 24705</td>
<td>23401</td>
<td>20442</td>
<td>1680</td>
<td></td>
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</tbody>
</table>
Incidence

Proportion undetected AF:

- 0.1% (Svennberg E, Circ 15)

Diagnostic test

AF-DETECT rate (sensitivity)

- 80% detection rate (Svennberg E, Circ 15)

Risk of stroke

without AF (background risk)

- 0.01 (Feigin VL, Neuroepi 15)

with an undetected AF

- 0.05 (Svennberg E, Circ 15, Schnabel R 16)

after detected (and treated) AF

- 0.01 (Martinez C, Thromb Haemost 14)

10%?? (Svennberg E, Circ 15)

3% new AF, 5.1% untreated AF

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

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

70-75% risk reduction – 1.41
(Martinez C, Thromb Haemost. 14)
Flow Chart
Weight of Different Factors

**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

Total sample size
N=37,546
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 CHA\textsubscript{2}DS\textsubscript{2}-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)
10%?? (Svennberg E, Circ 15)

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

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

Median CHA$_2$DS$_2$-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)

Total sample size
N=418,608
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