Interpreting RCTs of AAA or Carotid Treatments
Why and How they can be misleading or misinterpreted

Thomas L. Forbes, MD

VEITH Symposium 2017

Disclosures

Our division receives research and educational support from Cook Medical, Gore Medical, Endologix, LeMaitre, LivaNova, Medtronic

No personal conflicts of interest

Randomized Controlled Trials

• Results relevant to those who meet inclusion criteria
• Inclusion depends on clinical equipoise
• Results valid to specific centers & practitioners
• Lower event rates in experimental & control group
• Issues of Study Interpretation

Randomized Controlled Trials

• Results relevant to those who meet inclusion criteria
• Inclusion depends on clinical equipoise
• Results valid to specific centers & practitioners
• Lower event rates in experimental & control group
• Issues of Study Interpretation

External Validity
Randomized Controlled Trials

- Results relevant to those who meet inclusion criteria
- Inclusion depends on clinical equipoise
- Results valid to specific centers & practitioners
- Lower event rates in experimental & control group
- Issues of Study Interpretation

---

<table>
<thead>
<tr>
<th></th>
<th>RCT’s for Open vs Endovascular Repair for RAAAs</th>
<th>Early Mortality</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Nottingham</td>
<td>OSR 53%</td>
<td>EVAR 53%</td>
</tr>
<tr>
<td></td>
<td>AJAX</td>
<td>OSR 25%</td>
<td>EVAR 21%</td>
</tr>
<tr>
<td></td>
<td>ECAR</td>
<td>OSR 24%</td>
<td>EVAR 18%</td>
</tr>
<tr>
<td></td>
<td>IMPROVE</td>
<td>OSR 37.4%</td>
<td>EVAR 35.4%</td>
</tr>
</tbody>
</table>

---

<table>
<thead>
<tr>
<th></th>
<th>Differences in Study Design</th>
<th>RCT’s for Open vs Endovascular Repair for RAAAs</th>
<th>Early Mortality</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AJAX</td>
<td>Nottingham</td>
<td>OSR 53%</td>
<td>EVAR 53%</td>
</tr>
<tr>
<td></td>
<td>ECAR</td>
<td>Nottingham</td>
<td>OSR 25%</td>
<td>EVAR 21%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nottingham</td>
<td>OSR 24%</td>
<td>EVAR 18%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nottingham</td>
<td>OSR 37.4%</td>
<td>EVAR 35.4%</td>
</tr>
</tbody>
</table>

But ...

Differences in Study Design & Randomization

What patients were included?
RCT’s for Open vs Endovascular Repair for RAAAs

Differences in Study Design

RAAA → Clinical Diagnosis → +/- CT → OSR

IMPROVE → AJAX

EVAR

RAAA → Clinical Diagnosis → +/- CT → OSR

IMPROVE ≠ AJAX

EVAR

What patients were included?

<table>
<thead>
<tr>
<th></th>
<th>Nottingham</th>
<th>AJAX</th>
<th>ECAR</th>
<th>IMPROVE</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAAA ID'ed</td>
<td>103</td>
<td>520</td>
<td>524</td>
<td>1275</td>
</tr>
<tr>
<td># Randomized</td>
<td>32</td>
<td>116</td>
<td>107</td>
<td>613</td>
</tr>
<tr>
<td>Randomized</td>
<td>31%</td>
<td>22%</td>
<td>20%</td>
<td>48%</td>
</tr>
</tbody>
</table>

36%

Randomized Controlled Trials

- Results relevant to those who meet inclusion criteria
- Inclusion depends on clinical equipoise
- Results valid to specific centers & practitioners
- Lower event rates in experimental & control group

- Issues of Study Interpretation

Interpretation of Negative Trials

- Statistically insignificant results
  - "just as good as"
  - "no better"
  - "could not show a difference"
Interpretation of Negative Trials

“just as good as”
“no better”
“could not show a difference”

RCT Statistically Insignificant Results

“just as good as”
“no better”
“could not show a difference”

Differences in Interpretation

SPIN = “use of specific reporting strategies, from whatever motive, to highlight that the experimental treatment is beneficial, despite a nonsignificant difference for the primary outcome, or to distract the reader from statistically nonsignificant results.”

Boutron I et al. JAMA 2010;303:2058-64

RCT’s for Open vs Endovascular Repair for RAAAs

<table>
<thead>
<tr>
<th></th>
<th>OSR 25%</th>
<th>EVAR 21%</th>
<th>P-value</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>AJAX</td>
<td>25%</td>
<td>21%</td>
<td>0.56</td>
<td><em>did not show significant difference...</em></td>
</tr>
<tr>
<td>ECAR</td>
<td>24%</td>
<td>18%</td>
<td>0.24</td>
<td><em>EVAR was found to be equal...</em></td>
</tr>
<tr>
<td>IMPROVE</td>
<td>37.4%</td>
<td>35.4%</td>
<td>0.62</td>
<td><em>not associated with significant reduction...</em></td>
</tr>
</tbody>
</table>

RCT’s for Open vs Endovascular Repair Nonruptured AAAs

<table>
<thead>
<tr>
<th></th>
<th>OSR 29%</th>
<th>EVAR 26%</th>
<th>P-value</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVAR – 1</td>
<td>29%</td>
<td>26%</td>
<td>N.S.</td>
<td><em>EVAR offers no advantage...</em></td>
</tr>
<tr>
<td>EVAR – 2</td>
<td>62%</td>
<td>66%</td>
<td>N.S.</td>
<td><em>EVAR did not improve survival...</em></td>
</tr>
<tr>
<td>DREAM</td>
<td>10.4%</td>
<td>10.3%</td>
<td>N.S.</td>
<td><em>survival advantage... is not sustained</em></td>
</tr>
<tr>
<td>OVER</td>
<td>37%</td>
<td>41%</td>
<td>N.S.</td>
<td><em>similar long term survival</em></td>
</tr>
<tr>
<td>ACE</td>
<td>3.1%</td>
<td>6.8%</td>
<td>N.S.</td>
<td><em>open repair of AAA is as safe as EVAR</em></td>
</tr>
</tbody>
</table>

Randomized Controlled Trials

- Results relevant to those who meet inclusion criteria
- Inclusion depends on clinical equipoise
- Results valid to specific centers & practitioners
- Lower event rates in experimental & control group
- Issues of Study Interpretation