Treatment of hypertension in the very elderly (≥80 yrs)

The value of systematic review and exploration of heterogeneity
Outline

- Where would you go to get the answer?
- Does antihypertensive treatment decrease mortality?
- What can be learned from exploring the heterogeneity?
- Conclusions
- Clinical implications.
Treatment of elevated blood pressure in the very elderly
Less is better

Risk of serious adverse cardiovascular events increases with advancing age and with higher blood pressure. Falls and other serious adverse events associated with postural hypotension also increase with age and with antihypertensive drug therapy. It is therefore important to know whether drug treatment improves not only cardiovascular outcomes, but also measures of net health which combine benefit and harm: total mortality and all patients with any serious adverse event (see Therapeutics Letter 42). This Letter focuses on the best available evidence about drug treatment of elevated blood pressure in individuals over 79 years of age.

What is the evidence for drug treatment of elevated blood pressure in patients 60 to 79 years of age?
A Cochrane review published in 1998, quantified the morbidity and mortality benefit of anti-hypertensive drug therapy for hypertensive patients (systolic BP ≥160 mmHg) 60 years of age and older. It included 15 total stroke, RR 0.67 (95% CI 0.48, 0.93), but no decrease in mortality, RR 1.09 (95% CI 0.95, 1.25). The authors concluded that, because of the potential for an increase in mortality due to treatment, further trials were necessary.

What have we learned from the two HYVET studies?
Pharmacotherapy for hypertension in the elderly (Review)

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This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in The Cochrane Library 2010, Issue 1

http://www.thecochranelibrary.com
Comparison: 2 Antihypertensive drug therapy vs control in very elderly 80 years or older, Outcome: 2.1 Total mortality

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment</th>
<th>Control</th>
<th>Weight</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1.1 Very elderly 80 years or older</td>
<td></td>
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<tr>
<td>EWPHE 1989</td>
<td>58</td>
<td>70</td>
<td>12.2%</td>
<td>1.17 [0.99, 1.40]</td>
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<tr>
<td>HEP 1986</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>1.82 [Not estimable]</td>
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<tr>
<td>HYVET 2008</td>
<td>196</td>
<td>1933</td>
<td>335</td>
<td>0.82 [0.69, 0.99]</td>
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<tr>
<td>HYVET P 2003</td>
<td>57</td>
<td>857</td>
<td>22</td>
<td>1.29 [0.80, 2.08]</td>
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<tr>
<td>SHEP 1991</td>
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<td>331</td>
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<td>10</td>
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<td>STOP 1991</td>
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<td>122</td>
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<tr>
<td>Syst-Eur 1991</td>
<td>72</td>
<td>231</td>
<td>53</td>
<td>1.23 [0.91, 1.67]</td>
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</tbody>
</table>

Subtotal (95% CI)

| Total events | 3617 | 3084 | 100.0% | 0.98 [0.87, 1.10] |

Heterogeneity: Chi² = 12.92, df = 6 (P = 0.04); I² = 54%
Test for overall effect: Z = 0.35 (P = 0.72)
Exploration of the heterogeneity in total mortality from very elderly subgroup

Very elderly 80 and over are expected to be particularly vulnerable to harmful effects of antihypertensive drugs.
A - Total mortality and SBP reduction

- Relative Risk reduction
- SBP reductions

Intercept = -35.2
Slope = 2.9
p-value = 0.17
B - Total mortality and intensity of therapy

Relative Risk reduction vs Intensity of antihypertensive therapy

Intercept = -29.8
Slope = 9.2
p-value = 0.05
Conclusions:
For patients ≥80 years:

- Various antihypertensive therapies for primary prevention in relatively healthy patients with systolic BP >160 mmHg reduced stroke, but had no proven effect on mortality.
- Using low-dose thiazide as first-line therapy followed by a low-medium dose ACE inhibitor reduced mortality as well as serious adverse events in one large RCT.
- With this regimen a blood pressure of <150/80 mmHg can be expected in about 50% of patients.
Clinical implications for the very elderly

- Use the treatment regimen from the HYVET trial with a target BP of < 150/80 mmHg.
- Initial therapy the lowest dose of a thiazide or thiazide-like drug.
- If target not achieved add half the recommended starting dose of an ACE inhibitor.
- If target not achieved double the dose of the ACE inhibitor.
Clinical implications for the very elderly (cont)

- No additional antihypertensive therapy unless systolic BP > 220 mmHg on two successive office visits.

- Using this regimen about half the patients will **NOT** achieve the target BP of <150/80 mmHg.

- This approach would substantially reduce health care resources and costs.
A needed RCT

- Patients: All patients 70 year and over with resting BP consistently > 160 mmHg.
- Outcome: Total mortality and serious morbidity.
- Study design: Randomised open with blinded assessment of outcomes.
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