COST-EFFECTIVENESS OF BLOOD PRESSURE LOWERING WITH A FIXED COMBINATION OF PERINDOPRIL AND INDAPAMIDE IN TYPE 2 DIABETES MELLITUS: A TRIAL-BASED ANALYSIS USING THE ADVANCE STUDY

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The primary aim of ADVANCE was to determine the effects on macrovascular and microvascular disease in high-risk individuals with Type 2 diabetes of:

- Blood pressure lowering (with an ACE inhibitor–diuretic combination vs placebo);
- Intensive glucose lowering.

Recruitment commenced June 2001 and was completed in March 2003.
Study Participants

- 11,140 randomized participants from 20 countries (3,293 from China; 978 from Australia; 1,325 from the UK)

- Characteristics:
  - Average 66 years
  - 43% female
  - Duration of diabetes 8 years
  - Systolic BP 145mmHg
  - HbA$_{1c}$ 7.5%
Economic evaluation

Comparison: intensive versus conventional blood in Type 2 diabetic patients

Data: patient level data on costs and outcomes from ADVANCE study including clinical data and linked administrative data from Australia

Outcome measure: Life years gained

Time period: within trial effects extrapolated over lifetime (median follow-up 4.3 years for blood pressure trial)

Perspective: Australian health care system

Result: Incremental cost per life year gained in 2007$s ($1 = $US 0.90)
Costs and resource use

- **Therapy:**
  - **Study drug** (Perindopril–indapamide combination @ $29.83 per month)
  - **Other drugs** (other anti-hypertensive, anti-diabetic from linked administrative information)
  - **Standard practice** (to reflect the cost of implementing policies in a general health care setting we assumed 3 additional visits associated with prescribing these therapies)

- **Complications:**
  - **Hospital admissions:** length of stay, diagnosis (costing uses Australian DRG cost-weights)
  - **Non-inpatient services:** used linked Australian Administrative data from Medicare.
Pharmaceutical use by allocation

![Bar chart showing pharmaceutical use by allocation categories: Antihypertensives, Other cardiac, Lipid lowering (statins, etc), Diabetes drugs, Other drugs. The chart includes p-values for comparisons between active and placebo groups: P=0.04, P=0.54, P=0.42, P=0.80, and P=0.45.](chart.png)
### Within trial costs

Mean (SD) cost per patient (A$) for Australian participants (n = 978)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Perindopril (n = 5569)</th>
<th>Indapamide (n = 5571)</th>
<th>Placebo (n = 5571)</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention costs</td>
<td>1 368</td>
<td>0</td>
<td>1368</td>
<td></td>
</tr>
<tr>
<td>Other drug therapies</td>
<td>8 616 (6 212)</td>
<td>8 948 (5 678)</td>
<td>-332 (−1092 to 428)</td>
<td></td>
</tr>
<tr>
<td>Outpatient visit costs</td>
<td>5 317 (3 583)</td>
<td>5 389 (3 807)</td>
<td>-72 (−547 to 404)</td>
<td></td>
</tr>
<tr>
<td>Hospital costs</td>
<td>7 913 (11 826)</td>
<td>8 323 (12 957)</td>
<td>-410 (−2007 to 1187)</td>
<td></td>
</tr>
<tr>
<td>Total costs (undiscounted)</td>
<td>23 214 (16 155)</td>
<td>22 660 (17 002)</td>
<td>555 (−730 to 1580)</td>
<td></td>
</tr>
</tbody>
</table>


Within trial effects

Source: The Lancet, 2007
Estimating Outcomes

- Calculated the increase in life expectancy within trial as the area under a KM survivor function;
- Predicted life expectancy of survivors beyond the close of the study based on multistate life-table under the assumption of no continuing benefits from the within-trial treatment.
- Life tables were constructed from parametric survival models using ADVANCED study data which enable us to account for uncertainty.
## Outcomes: life expectancy

<table>
<thead>
<tr>
<th>Type of outcome</th>
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<th>Placebo (n = 5571)</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Within-trial</td>
<td>4.17 (4.15–4.18)</td>
<td>4.14 (4.12–4.16)</td>
<td>0.03 (0.00–0.05)</td>
</tr>
<tr>
<td>Total</td>
<td>15.0 (13.8–16.4)</td>
<td>14.9 (13.7–16.4)</td>
<td>0.09 (0.06–0.12)</td>
</tr>
<tr>
<td>Total (3% discount)</td>
<td>12.3 (11.5–12.6)</td>
<td>12.2 (11.4–12.5)</td>
<td>0.06 (0.04–0.07)</td>
</tr>
<tr>
<td>Total (5% discount)</td>
<td>10.9 (10.3–11.1)</td>
<td>10.8 (10.2–11.1)</td>
<td>0.05 (0.03–0.06)</td>
</tr>
</tbody>
</table>
Cost-effectiveness

- When a 5% rate is applied to costs and effects: A$10,040 per life-year gained.
- Analysis of uncertainty showed there is a 30% chance the treatment is cost-neutral or cost-reducing and a 95% chance the cost per life year is less than A$40 000
- Robust to assumptions regarding cost of therapy and implementation
Conclusions

- Our analysis shows use of perindopril–indapamide combination for people with diabetes is a highly cost-effective in an Australian health care setting;
- Useful to replicate this analysis in an Asian setting, by taking into account:
  - Different rates of complications;
  - Patterns and levels of resource use;
  - Local resource costs.
- Our analysis is due to be published in the Medical Journal of Australia
Acknowledgements

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- Thanks are due to Servier for providing funds for travel to this meeting;
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