Health economic study evidence tables
Below are evidence tables for economic studies included in the guideline following a review of the literature. Studies are organised by section of the guideline. See methods section for search strategies and inclusion/exclusion criteria.

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### 1. Antiplatelets: aspirin (1 study)

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<th>Study details</th>
<th>Population &amp; interventions</th>
<th>Health outcomes</th>
<th>Costs</th>
<th>Cost effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Economic analysis:</td>
<td>CEA</td>
<td>Health outcomes incorporated:</td>
<td>Cost components incorporated:</td>
<td>Base case ICER (Intvn 2 vs Intvn 1):</td>
</tr>
<tr>
<td>Study design:</td>
<td>Mortality model used to estimate deaths prevented/postponed with aspirin treatment in UA over 1 year; median survival applied to extrapolate to life years gained.</td>
<td>Life years-gained (LYG)</td>
<td>Cost of aspirin</td>
<td>£58 per LYG</td>
</tr>
<tr>
<td>Perspective:</td>
<td>UK NHS</td>
<td>Primary outcome measure:</td>
<td>Total costs (mean):</td>
<td>Analysis of uncertainty:</td>
</tr>
<tr>
<td>Time horizon:</td>
<td>Lifetime</td>
<td>LYG</td>
<td>Mean per patient per group not reported</td>
<td>ICERs in different age ranges = £42-85 per LYG</td>
</tr>
<tr>
<td>Discounting:</td>
<td>Costs &amp; outcomes = 3.5%</td>
<td>Incremental (Intvn 2 – Intvn 1):</td>
<td>£207,937 (total)</td>
<td>ICERs were recalculated using minimum and maximum estimates for cost of aspirin, efficacy of aspirin and life years gained. ICERs ranged between £34 and £114 per LYG.</td>
</tr>
</tbody>
</table>

#### Data sources

- **Health outcomes:**
  - Baseline events – uses IMPACT model; a mortality model based CHD patient numbers, uptake of treatment, median survival in patients with and without CHD developed using data from sources describing England and Wales 2000.

- **Quality-of-life weights:**
  - n/a

- **Cost sources:**
  - Drug unit costs: BNF 40. 2000

#### Comments

- **Source of funding:**
  - North West Regional Research and Development Training Fellowship
### Limitations:
- Reporting of methods a bit unclear regarding cost calculations; unclear if aspirin use is specifically acute use or continued for rest of year
- Only incorporates cost of aspirin – other relevant events would have cost implications (such as MIs avoided); incorporation of treatment-related costs for full time horizon advocated by NICE and not done here
- Quality of life not incorporated – unlikely to change conclusions as ICERs are so low

**Other:**
Model assesses many other treatments also which are not reported here as not clinical questions for guideline

### Overall quality*: Potentially serious limitations | Overall applicability**: Directly applicable

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**Abbreviations:** BNF = British National Formulary; CEA = cost-utility analysis; CHD = coronary heart disease; ICER = incremental cost-effectiveness ratio; MI = myocardial infarction; LYG = life year gained; RCT = randomised controlled trial; UA = unstable angina

*Very serious limitations/Potentially serious limitations/Minor limitations; ** Directly applicable/Partially applicable/Not applicable

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#### 2. Antiplatelets: clopidogrel (3 studies)


<table>
<thead>
<tr>
<th>Study details</th>
<th>Population &amp; interventions</th>
<th>Health outcomes</th>
<th>Costs</th>
<th>Cost effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Economic analysis:</strong></td>
<td>CEA</td>
<td>Separate models run for various populations and interventions each based on a published trial. Only those relevant to clinical question are presented here.</td>
<td>Health outcomes incorporated: MI, stroke, death, bleeds</td>
<td>Cost components incorporated: Aspirin, clopidogrel, management of MI (fatal and non-fatal), stroke (fatal and non-fatal), other death (non-cardiovascular and cardiovascular) and bleeds</td>
</tr>
<tr>
<td><strong>Study design:</strong></td>
<td>Decision analytic model (Markov)</td>
<td>Common to all comparisons below was a population aged 60 on entering model and treatment duration of 1 year.</td>
<td>Primary outcome measure: Life years Mean per group not reported.</td>
<td></td>
</tr>
<tr>
<td><strong>Perspective:</strong></td>
<td>UK NHS</td>
<td>1. CURE Hypothetical cohort of patients admitted to hospital with UA or NSTEMI†</td>
<td>Incremental (Intvn b – Intvn a): 1. 0.1153 2. 0.0293 3. 0.1068</td>
<td></td>
</tr>
<tr>
<td><strong>Time horizon:</strong></td>
<td>Lifetime</td>
<td>Intervention a: Standard therapy (including 75–325mg/day aspirin)†</td>
<td>Total costs: Means not reported.</td>
<td></td>
</tr>
<tr>
<td><strong>Discounting:</strong></td>
<td>Costs &amp; outcomes = 3.5%</td>
<td>Intervention b: Standard therapy plus clopidogrel 75mg/day (300mg loading dose)†</td>
<td>Incremental (Intvn b – Intvn a): 1. £700 2. -£268 3. -£192</td>
<td></td>
</tr>
</tbody>
</table>

**Analysis of uncertainty:**
Probabilistic sensitivity analysis
At a £20,000 threshold clopidogrel was cost effective in 72–100% of simulations:

Drivers of uncertainty
Key drivers of uncertainty are reported as initial risk (i.e. in non-clopidogrel)
| 2. PCI-CURE | Population: Hypothetical cohort of patients admitted to hospital with UA or NSTEMI and undergoing PCI† | Intervention a: Standard therapy (including 75–325mg/day aspirin)† | Intervention b: Standard therapy plus clopidogrel 75mg/day (300mg loading dose)† |
| 3. CREDO | Population: Hypothetical cohort of patients undergoing PCI† | Intervention a: Standard therapy plus clopidogrel 75mg/day (300mg loading dose) for 28 days‡ | Intervention b: Standard therapy plus clopidogrel 75mg/day (300mg loading dose) for 1 year‡ |

Note: evaluation based on COMMIT study excluded as 93% STEMI

**Data sources**

**Health outcomes:**
- CURE RCT, PCI-CURE RCT (subgroup of CURE), CREDO RCT
- Literature and WHO life tables (age-related increases in risk of events)

**Cost sources:**
- BNF (aspirin, clopidogrel)
- Literature (MI, stroke, bleed management)
- NHS reference costs (non-cardiovascular death)

**Comments**

**Source of funding:** None

**Limitations:**
- Reporting quite unclear
- Event rates based on international trial data – TA80 reports that UK revascularisation and events rates are considerably different in UK to other

**Currency & cost year:** 2006 UK pounds

arm), relative risk reduction and clopidogrel price. It is not clear how these were identified.
countries and uses UK specific rather than trial baseline rates
- Use of cost per life year gained inhibits interpretation of results in NICE guideline context
- Uniform distributions used for costs and risk increase with age may not be the most appropriate
Other: None

Overall quality*: Potentially serious limitations
Overall applicability**: Partially applicable

Abbreviations: BNF = British National Formulary; CEA = cost-effectiveness analysis; COMMIT = ClOpidogrel and Metoprolo in Myocardial Infarction Trial; CREDO = Clopidogrel for the Reduction of Events During Observation (study); CURE = ClOpidogrel in Unstable angina to prevent Recurrent Events (study); ICER = incremental cost-effectiveness ratio; MI = myocardial infarction; NSTEMI = non-ST-segment-elevation myocardial infarction; PCI = percutaneous coronary intervention; RCT = randomised controlled trial; STEMI = ST-segment-elevation myocardial infarction; UA = unstable angina; WHO = World Health Organisation

†Assumed based on trial, not explicitly stated; *Very serious limitations/Potentially serious limitations/Minor limitations; ** Directly applicable/Partially applicable/Not applicable


<table>
<thead>
<tr>
<th>Study details</th>
<th>Population &amp; interventions</th>
<th>Health outcomes</th>
<th>Costs</th>
<th>Cost effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Economic analysis:</td>
<td>CUA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study design:</td>
<td>Decision analytic model (1-year decision tree with appended Markov model)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perspective:</td>
<td>UK NHS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time horizon:</td>
<td>Lifetime (until patients 100 years of age)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discounting:</td>
<td>Costs = 6%</td>
<td></td>
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</tr>
</tbody>
</table>

Population: Hypothetical cohort of patients diagnosed with non-ST-segment-elevation ACS (aged 66 years)

Intervention 1: Standard therapy (including 75-325mg/day aspirin) for life

Intervention 2: Standard therapy plus clopidogrel 75mg/day (300mg loading dose) for 1 year followed by standard therapy

Health outcomes incorporated:
- Vascular and non-vascular death, non-fatal MI, stroke and major bleeding; quality of life
- Primary outcome measure:†
  - Mean QALYs
    - Intvn 1: 7.9028
    - Intvn 2: 7.9604
- Other outcome measures (mean):†
  - Life years
    - Intvn 1: 7.3098
    - Intvn 2: 7.3645
  - Incremental (Intvn 2 – Intvn 1): 0.0547

Cost components incorporated:
- Clopidogrel, revascularisation, treatment of major bleeding events, non-fatal MI, stroke and remaining event free
- Total costs (mean):†
  - Intvn 1: £11,353
  - Intvn 2: £11,756
  - Incremental (Intvn 2 – Intvn 1): £403

Currency & cost year: 2002 UK pounds

Primary ICER (Intvn 2 vs Intvn 1): £7365 per QALY gained

Other:
- £6991 per life year gained
- £10,599 per event avoided (restricted time horizon to 1-year treatment period only)

Analysis of uncertainty:
- Probabilistic sensitivity analysis
  - At a £20,000 threshold clopidogrel was cost effective in ~77% of simulations.
- Various one- and two-way sensitivity analyses
  - Using CURE baseline bleed rates (higher) instead of the UK rates increased costs resulting in a cost of £7415 per QALY gained. Using CURE
### Health outcomes =

<table>
<thead>
<tr>
<th></th>
<th>alone for remaining lifetime</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1.5%</strong></td>
<td></td>
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</table>

### In 1-year treatment period:

<table>
<thead>
<tr>
<th></th>
<th>Intvn 1: 0.0911</th>
<th>Intvn 2: 0.0647</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MIs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Strokes</strong></td>
<td>Intvn 1: 0.0190</td>
<td>Intvn 2: 0.0138</td>
</tr>
<tr>
<td><strong>Vascular deaths</strong></td>
<td>Intvn 1: 0.0742</td>
<td>Intvn 2: 0.0690</td>
</tr>
</tbody>
</table>

Baseline revascularisation rates (higher) instead of UK rates reduced the cost per QALY gained to £6929. RRs are reported as the key drivers of cost effectiveness; if the upper 95% CI for vascular death is used, standard therapy dominates standard therapy + clopidogrel; varying other RRs had limited effect.

### Data sources

#### Health outcomes:
- CURE RCT (clopidogrel effectiveness)
- Interim life tables for England and Wales 1999-2001 (non-vascular death rate)

#### Quality-of-life weights:
- Literature – elicitation methods not stated

#### Cost sources:
- BNF (clopidogrel)
- NHS reference costs (revascularisation, major bleed treatment)
- NHAR data reported in literature (ACS patient remaining event free, ACS patient experiencing an MI)
- Estimates derived from expert opinion in literature (stroke)

### Comments

#### Source of funding:
Part funded by Sanofi-Synthelabo and Bristol-Myers Squibb

#### Limitations:
- Lack of recent and long-term event rate data

#### Other:
The paper states that the analysis ‘informed the decision made by NICE’ regarding clopidogrel (TA80) but does not appear to be the assessment group model and is part funded by the drug sponsors. Therefore, may be sponsor’s model. However, the results are not the same in TA80.

### Overall quality*: Minor limitations  | Overall applicability**: Directly applicable
Abbreviations: ACS = acute coronary syndromes; BNF = British National Formulary; CUA = cost-utility analysis; CURE = Clopidogrel in Unstable angina to prevent Recurrent Events (study); ICER = incremental cost-effectiveness ratio; MI = myocardial infarction; NHAR = Nottingham Heart Attack Register; PCI = percutaneous coronary intervention; PRAIS-UK = Prospective Registry of Acute Ischaemic Syndrome in the UK; QALY = quality-adjusted life year; RCT = randomised controlled trial; RR = relative risk;
†Calculated based on reported total figures; *Very serious limitations/Potentially serious limitations/Minor limitations; ** Directly applicable/Partially applicable/Not applicable


<table>
<thead>
<tr>
<th>Study details</th>
<th>Population &amp; interventions</th>
<th>Health outcomes</th>
<th>Costs</th>
<th>Cost effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Economic analysis:</td>
<td><strong>CEA</strong></td>
<td><strong>Primary outcome measure:</strong> Mean occurrences of cardiovascular death, MI and stroke &lt;br&gt;Intervention 1: 0.114 &lt;br&gt;Intervention 2: 0.093 RR = 0.8, P &lt; 0.001</td>
<td><strong>Cost components incorporated:</strong> Hospitalisation, revascularisation procedures, drugs taken in hospital and at home, coronary angiography, other diagnostic testing (inpatient only), therapeutic procedures. &lt;br&gt;Note: Ambulatory care and outpatient diagnostic testing were not recorded. Non-cardiovascular events were excluded.</td>
<td><strong>Primary ICER (1 year) (Intervention 2 vs Intervention 1):</strong> £10,366 per event (cardiovascular death, MI, stroke) avoided (95% CI: £4411–42,981)</td>
</tr>
<tr>
<td>Study design:</td>
<td>Within RCT analysis (patient level resource use and clinical outcomes from CURE, relevant unit costs applied)</td>
<td><strong>Other outcome measures (mean):</strong> Refractory ischemia &lt;br&gt;Intervention 1: 0.020 &lt;br&gt;Intervention 2: 0.014 P &lt; 0.01 &lt;br&gt;Heart failure &lt;br&gt;Intervention 1: 0.044 &lt;br&gt;Intervention 2: 0.037 P = 0.03</td>
<td><strong>Total costs (mean):</strong> &lt;br&gt;Intervention 1: £3104 &lt;br&gt;Intervention 2: £3312 Incremental cost (Intervention 2 - Intervention 1): £264 (95% CI: £119–£297)</td>
<td><strong>Currency &amp; cost year:</strong> 2001 UK pounds</td>
</tr>
</tbody>
</table>
| Perspective: | UK NHS+ | **Major bleeds:** <br>Intervention 1: 0.027 <br>Intervention 2: 0.037 P = 0.001 | **Life-threatening bleeds:** <br>Intervention 1: 0.018 <br>Intervention 2: 0.022 NS (p = 0.13) | **Analysis of uncertainty:** 

**Subgroup analyses:** Reported that benefits in CURE are consistent among low, intermediate and high-risk patients (stratified by TIMI score). Cost differences and ICERs were assessed and no significant heterogeneity was found. |
See CURE trial for more details.

Intvn 1: 0.024
Intvn 2: 0.051 NS (p = 0.13)

Bootstrap analysis (bias corrected and accelerated method) used to calculate CIs for costs and ICER.

Data sources

Health outcomes:
- CURE RCT

Cost sources:
- CURE RCT (resource use)
- Unit cost sources unclear

Comments

Source of funding:
Sanofi-Synthelabo and Bristol-Myers Squibb

Limitations:
- Resource use and event rates based on mix of countries with only 5.9% UK
  - Health care processes and therefore resource use may vary between countries
  - TA80 reports that UK revascularisation and events rates are different in UK to other countries
- Unit cost sources unclear (states that are available on journal website but could not be identified)
- Unclear if uncertainty around outcome is incorporated into CI for ICER
- Use of cost per event avoided and non-lifetime analysis inhibit interpretation of results in NICE guideline context

Overall quality*: Potentially serious limitations

Overall applicability**: Partially applicable

Abbreviations: ACS = acute coronary syndromes; BNF = British National Formulary; CEA = cost-effectiveness analysis; CI = confidence interval; CURE = Clopidogrel in Unstable angina to prevent Recurrent Events (study); ECG = electrocardiogram; ICER = incremental cost-effectiveness ratio; MI = myocardial infarction; N/a = not applicable; NS = non-significant; RCT = randomised controlled trial; RR = relative risk; TIMI = thrombolysis in myocardial infarction (study)
+ study included direct medical costs including drugs taken at home and therefore potentially non-prescription drugs paid for by patients themselves
*Very serious limitations/Potentially serious limitations/Minor limitations; ** Directly applicable/Partially applicable/Not applicable

3. Antiplatelets: glycoprotein IIb/IIIa inhibitors (2 studies)


<table>
<thead>
<tr>
<th>Study details</th>
<th>Population &amp; interventions</th>
<th>Health outcomes</th>
<th>Costs</th>
<th>Cost effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Economic analysis: CEA</td>
<td>Population: Patients presenting in the UK with non-ST-elevation ACS. Mean age: 65±12</td>
<td>Primary outcome measure: Events (death, new MI, refractory)</td>
<td>Cost components incorporated: Initial and subsequent hospitalisation, drugs,</td>
<td>Base case ICER (Intvn 2 vs Intvn 1): £13,388 per event averted</td>
</tr>
</tbody>
</table>

Subgroup 1 (Intvn 2 vs Intvn 1):
**Study design:**
Simple decision analysis based on a single RCT (but adjusted for UK baseline event rates)

**Perspective:**
UK NHS

**Time horizon:**
Events: 7 days
Costs: 180 days

**Discounting:**
N/a

<table>
<thead>
<tr>
<th>Risk subgroups:</th>
<th>Incremental cost (Intvn 2 – Intvn 1): 0.029</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intervention 1 (n = 797):</strong> Heparin plus placebo</td>
<td></td>
</tr>
<tr>
<td><strong>Intervention 2 (n = 773):</strong> Heparin plus tirofiban for mean duration of 72 hrs.</td>
<td></td>
</tr>
</tbody>
</table>

See PRISM-PLUS trial for more details.

**Risk subgroups:**
- **Subgroup 1** - Age 60 years or above with the presence of an abnormal ECG
- **Subgroup 2** - ST depression or bundle branch block on the admission ECG
- **Subgroup 3** - ST depression or bundle branch block on the admission ECG or acute MI diagnosed on admission based on initial cardiac enzymes

**Data sources**

**Health outcomes:**
- Baseline event rates: PRAIS-UK registry
- Effectiveness: PRISM-PLUS study (7 days)

**Cost sources:**
- CHKS database (Regression analysis)

**Analysis of uncertainty:**
A single one-way sensitivity analysis was conducted. A cost of £1500 was include for each major bleed.
Intvn 1: 0.8%
Intvn 2: 1.6%

The ICER increased to £13,773.

<table>
<thead>
<tr>
<th>Incremental cost (Intvn 2 – Intvn 1): £383</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total costs (mean):</strong></td>
</tr>
<tr>
<td>Intvn 1: £2436</td>
</tr>
<tr>
<td>Intvn 2: £2819</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Incremental cost (Intvn 2 – Intvn 1): £383</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Currency &amp; cost year:</strong> 1999 UK pounds</td>
</tr>
</tbody>
</table>

£10,856 per event averted
Subgroup 2 (Intvn 2 vs Intvn 1): £10,571 per event averted
Subgroup 3 (Intvn 2 vs Intvn 1): £5953 per event averted

**Source of funding:**
Merck, Sharp, Dohme Ltd

**Limitations:**
- Use of cost per event averted inhibits interpretation of results in NICE guideline context

### Study details

<table>
<thead>
<tr>
<th>Economic analysis:</th>
<th>Population &amp; interventions</th>
<th>Health outcomes</th>
<th>Costs</th>
<th>Cost effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>CEA</td>
<td>Western European patients with ACS and without significant ST-segment-elevation.</td>
<td><strong>Primary outcome measure:</strong> Life years</td>
<td><strong>Cost components incorporated:</strong> Initial hospitalisation including hotel costs, overheads, revascularisation procedures, diagnostic tests and CV drugs.</td>
<td><strong>Primary ICER (Intvn 2 vs Intvn 1):</strong> £8436 per life year gained</td>
</tr>
<tr>
<td><strong>Study design:</strong></td>
<td>Mean age = 65 Male = 69%</td>
<td><strong>Incremental (Intvn 2 – Intvn 1):</strong> 0.022</td>
<td>Subsequent hospitalisations including hotel costs, overheads, revascularisation, diagnostic coronary arteriograms. Stroke and bleeding management.</td>
<td><strong>Other:</strong> 30 day analysis: £22,760 per event avoided (death or MI).</td>
</tr>
<tr>
<td>Within RCT analysis (6-month patient level resource use and clinical outcomes from a subgroup of the PURSUIT RCT, relevant unit costs applied, statistically projected life expectancy using Cox Proportional Hazards regression)</td>
<td><strong>Intervention 1 (n = 1847):</strong> Standard therapy plus placebo</td>
<td><strong>Other outcome measures (mean): Combined death and non-fatal MI at 30 days</strong> Intvn 1: 0.147 Intvn 2: 0.137</td>
<td><strong>Total costs (mean):</strong> Intvn 1: £6070 Intvn 2: £6256</td>
<td><strong>Analysis of uncertainty:</strong> A cost effectiveness range was calculated using the 95% CI of resource consumption: £7800–£10,400.</td>
</tr>
<tr>
<td></td>
<td>Patients undergoing PCI on day 3 could receive an additional 24hrs at investigators discretion.</td>
<td><strong>Prescription of aspirin (80–</strong></td>
<td><strong>Incremental (Intvn 2 – Intvn 1):</strong> £186</td>
<td>Discounting outcomes by 0% and 6% resulted in a cost per life year gained of £6400 and £10,917 respectively.</td>
</tr>
<tr>
<td>Perspective:</td>
<td>Prescription of aspirin (80–</td>
<td><strong>Currency &amp; cost year:</strong> 1996 UK pounds</td>
<td>Excluding differences in hospital length of stay resulted in a small reduction in the ICER.</td>
<td>Excluding differences in hospital length of stay resulted in a small reduction in the ICER.</td>
</tr>
<tr>
<td>UK NHS</td>
<td></td>
<td><strong>Total costs (mean):</strong> Intvn 1: £6070 Intvn 2: £6256</td>
<td>Restricting resource use to countries with low rates of coronary arteriography (and related PCI rates) resulted in a decrease in the ICER to</td>
<td>Restricting resource use to countries with low rates of coronary arteriography (and related PCI rates) resulted in a decrease in the ICER to</td>
</tr>
<tr>
<td>Time horizon:</td>
<td></td>
<td><strong>Incremental (Intvn 2 – Intvn 1):</strong> £186</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lifetime</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Discounting:
Costs: N/a
Outcomes: 3%
See PURSUIT trial for more details.

| 325mg/day) and heparin was encouraged. | £2164 per life year gained, while using data from countries with high rates increased it to £12,952. |

Data sources
Health outcomes:
- Western European subgroup of PURSUIT RCT (treatment effect)
- Duke University Medical Centre survival data for MI/UA patients (survival modelling post 6 months)

Cost sources:
- Western European subgroup of PURSUIT RCT (resource use)
- Unit cost sources unclear although appears to be possibly detailed in another publication cited

Comments
Source of funding:
Merck, Sharp, Dohme Ltd

Limitations:
- Resource use and event rates based on mix of 28 countries
  - Health care processes and therefore resource use may vary between countries
  - TA47 reports that UK revascularisation and events rates are different in UK to other countries
- Unit cost sources unclear
- Use of cost per life year gained inhibits interpretation of results in NICE guideline context
- Only resource use up to 6 months is included; ongoing disease-related costs are not incorporated.

Overall quality*: Potentially serious limitations
Overall applicability**: Partially applicable

4. Antithrombin therapy: heparins (1 study)

<table>
<thead>
<tr>
<th>Study details</th>
<th>Population &amp; interventions</th>
<th>Health outcomes</th>
<th>Costs</th>
<th>Cost effectiveness</th>
</tr>
</thead>
</table>

Abbreviations: ACS = acute coronary syndromes; BNF = British National Formulary; CEA = cost-effectiveness analysis; CI = confidence interval; CURE = Clopidogrel in Unstable angina to prevent Recurrent Events (study); CV = cardiovascular; ICER = incremental cost-effectiveness ratio; MI = myocardial infarction; N/a = not applicable; PCI = percutaneous coronary intervention; PURSUIT = Platelet IIa/IIIb in Unstable Angina: Receptor Suppression Using Integrilin Therapy (study); RCT = randomised controlled trial; UA = unstable angina
†Converted from Euros as reported using exchange rate stated in paper; *Very serious limitations/Potentially serious limitations/Minor limitations; ** Directly applicable/Partially applicable/Not applicable
<table>
<thead>
<tr>
<th>Economic analysis:</th>
<th>CUA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study design:</td>
<td>Decision analytic model (primarily based on single RCT data)</td>
</tr>
<tr>
<td>Perspective:</td>
<td>UK NHS</td>
</tr>
<tr>
<td>Time horizon:</td>
<td>1 year</td>
</tr>
<tr>
<td>Discounting:</td>
<td>N/a</td>
</tr>
</tbody>
</table>

**Population:** Hypothetical cohort of patients with UA or NSTEMI (mean weight 79kg)

**Intervention 1:** UFH 5000U loading dose + iv infusion 1000U/hr for 2.6 days

**Intervention 2:** Enoxaparin 1ml/kg twice a day for 2.6 days

**Health outcomes incorporated:**
- Death, MI, recurrent angina, quality of life
- QALYs (mean)
- Mean per patient per group not reported

**Primary outcome measure:**
- Incremental (Intvn 2 – Intvn 1): 0.013

**Cost components incorporated:**
- Enoxaparin, UFH, drug administration (consumables, iv pump, monitoring, nursing time), hospital length of stay at 30 days, revascularisation at 1 year
- Total costs (mean): Mean per patient per group not reported
- Incremental (Intvn 2 – Intvn 1): -£317 (saving)

**Currency & cost year:**
- 1998 UK pounds

**Base case ICER (Intvn 2 vs Intvn 1):**
- Intvn 2 is dominant (cost savings and QALY gains).

**Analysis of uncertainty:**
- Using treatment costs of cardiac events at 1 year instead of a cost based on differences in length of stay reduced the cost saving by ~45%.
- Comprehensive one-way sensitivity analyses were performed. Results are reported as being very sensitive to rates of revascularisation, and duration and cost of length of stay.
- In all but one sensitivity analysis Intvn 2 remained dominant. When length of stay was used from a UK sub-group of ESSENCE there was a net cost (due to increased length of stay in the enoxaparin group) with an incremental cost effectiveness of £3305 per QALY gained.

**Data sources**

**Health outcomes:**
- Effectiveness: ESSENCE RCT in base case (TIMI IIB RCT data used in sensitivity analysis)

**Quality-of-life weights:**
- Modified Rosser-Kind matrix (magnitude estimation). Values from UK mix of general population, patients and healthcare professionals.

**Cost sources:**
- Drug and drug administration costs: 1998 Canadian resource use study (nursing time and monitoring requirements), manufacturer list prices (iv pump, consumables), BNF 1998 (enoxaparin, UFH), hospital trust data (aPTT test cost, annual nursing hours, products used), Royal College of Nursing data (nurse salary)
- Hospital stay costs: PSSRU unit costs 95/96 (inflated) and 98/99
- Event costs (PCI, CABG, acute MI, angina): HRG national statistics 95/96 (inflated)
Comments

Source of funding:
South East Region Research and Development (Development and Evaluation Service)

Limitations:
- ESSENCE trial published 1997 – stent-use noted to be low in trial
- Costs and effect not extrapolated to lifetime (as mortality effected this might be considered most appropriate)
- Quality of life valuation not choice based method

Other:
- Impact of haemorrhage assumed to be captured by cost per day for the length of stay and through quality of life measures

Overall quality*: Potentially serious limitations
Overall applicability**: Directly applicable

Abbreviations: aPTT = activated partial thromboplastin time; BNF = British National Formulary; CABG = coronary artery bypass graft; CUA = cost-utility analysis; ESSENCE = Efficacy and Safety of Subcutaneous Enoxaparin in Non-Q-Wave Coronary Events; HRG = healthcare resource group; ICER = incremental cost-effectiveness ratio; MI = myocardial infarction; NSTEMI = non-ST-segment-elevation myocardial infarction; PCI = percutaneous coronary intervention; PSSRU = Personal Social Services Research Unit; QALY = quality-adjusted life year; RCT = randomised controlled trial; TIMI = Thrombolysis in Myocardial Infarction; UA = unstable angina; UFH = unfractionated heparin

*Very serious limitations/Potentially serious limitations/Minor limitations; ** Directly applicable/Partially applicable/Not applicable

5. Antithrombin therapy: fondaparinux (no studies)

6. Antithrombin therapy: bivalirudin (2 studies)

<table>
<thead>
<tr>
<th>Study details</th>
<th>Population &amp; interventions</th>
<th>Health outcomes</th>
<th>Costs</th>
<th>Cost effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Economic analysis: CCA</td>
<td>Population (n = 7851): UA/NSTEMI patients undergoing early invasive strategy (angiography within 72hrs)</td>
<td>In-hospital outcome measures (mean):</td>
<td>Cost components incorporated:</td>
<td>Primary ICER (Intvn 2 vs Intvn 1): ICER not presented</td>
</tr>
<tr>
<td>Study design: Within RCT analysis (30-day costs and outcomes from US subgroup analysis of ACUITY study, relevant unit costs)</td>
<td>US subgroup of ACUITY study Mean age = 62 Male = 68%</td>
<td>Death Intvn 1: 0.8% Intvn 2: 0.3% Intvn 3: 0.7% Intvn 4: 0.8% Intvn 5: 0.9% (p = 0.35)</td>
<td>Resource use during procedure and follow-up</td>
<td>Analysis of uncertainty: None reported</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MI Intvn 1: 4.7% Intvn 2: 4.9% Intvn 3: 5.1%</td>
<td>Total 30-day costs (mean): Intvn 1: £9535 Intvn 2: £9347 Intvn 3: £9859 Intvn 4: £9482 Intvn 5: £9270 P = 0.005</td>
<td></td>
</tr>
</tbody>
</table>

Ref ID: 4161
Intervention 1: Heparin + upstream GPI
Intervention 2: Heparin + cath lab GPI
Intervention 3: Bivalirudin + upstream GPI
Intervention 4: Bivalirudin + cath lab GPI
Intervention 5: Bivalirudin monotherapy

- Heparin = UFH or LMWH (standard weight adjusted doses)
- Upstream GPI = eptifibatide or tirofiban (at approved doses)
- Cath lab GPI = eptifibatide or abciximab at time of PCI (at approved doses)
- Bivalirudin was administered upstream; iv bolus 0.1mg/kg and infusion 0.25mg/kg/hr and before PCI additional iv bolus 0.5mg/kg and infusion increased to 1.75mg/kg/hr.

Intervention 4: 4.8%
Intervention 5: 5.0% (p = 0.99)

Unplanned revascularisation
Intervention 1: 0.9%
Intervention 2: 0.8%
Intervention 3: 1.1%
Intervention 4: 1.6%
Intervention 5: 0.9% (p = 0.22)

Major bleeding
Intervention 1: 5.1%
Intervention 2: 4.3%
Intervention 3: 6.1%
Intervention 4: 3.7%
Intervention 5: 2.7% (p<0.001)

Minor bleeding
Intervention 1: 28.2%
Intervention 2: 20.9%
Intervention 3: 27.5%
Intervention 4: 22.8%
Intervention 5: 14.1% (p<0.001)

Death or MI and Death, MI or unplanned revasc also reported in paper.

30-day outcome measures (mean):
Not reported in full for this subgroup but noted as similar findings to inhospital. See clinical review for 30 day outcomes from full ACUITY study.

In-hospital costs (mean):
Intervention 1: £9053
Intervention 2: £8810
Intervention 3: £9373
Intervention 4: £8888
Intervention 5: £8694
P<0.001

Discharge to 30 days costs:
Intervention 1: £482
Intervention 2: £538
Intervention 3: £486
Intervention 4: £593
Intervention 5: £576
P = 0.658

Currency & cost year:
2005 US dollars (presented here as 2005 UK pounds)
- Effectiveness: ACUITY US subgroup

**Cost sources:**
- Resource use from ACUITY US subgroup
- Unit costs: hospital billing data, mean hospital acquisition costs, wholesale drug costs, hospitals Medicare cost report and Medicare Fee schedule (2005).

**Comments**

**Source of funding:** Medicines Co.

**Limitations:**
US perspective for resource use and unit costs; overall impact on outcomes (e.g. QALYs or life years) not assessed – inhibits interpretation

**Other:**
~10% of bivalirudin monotherapy patients received provisional GPI

**Overall quality**: Potentially serious limitations
**Overall applicability**: Partially applicable

Abbreviations: ACS = acute coronary syndromes; ACUITY = Acute Catheterisation and Urgent Intervention Triage Strategy (study); CCA = cost-consequence analysis; GPI = glycoprotein IIb/IIIa inhibitor; ICER = incremental cost-effectiveness ratio; LMWH = low molecular weight heparin; MI = myocardial infarction; NSTEMI = Non-ST elevation myocardial infarction; PCI = percutaneous coronary intervention; QALYs = quality-adjusted life years; RCT = randomised controlled trial; UA = instable angina; UFH = unfractionated heparin;

† Converted using 2005 Purchasing Power Parities (Organisation for Economic Co-operation and Development (OECD), 2008 3285 /id); *Very serious limitations/Potentially serious limitations/Minor limitations; ** Directly applicable/Partially applicable/Not applicable

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<table>
<thead>
<tr>
<th>Study details</th>
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<th>Health outcomes</th>
<th>Costs</th>
<th>Cost effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Economic analysis:</strong></td>
<td>CCA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Study design:</strong></td>
<td>Within RCT analysis (30-day costs and 30-day, 6-month and 1-year outcomes from REPLACE-2 subgroup analysis)</td>
<td>Population (n = 1351): Patients undergoing PCI with ACS defined as MI within 7 days or UA within 48hrs of enrolment (acute MI was excluded)</td>
<td>Primary outcome measure: 30-day death/MI/urgent revascularisation/major bleeding (mean) Intvn 1: 0.110 Intvn 2: 0.099 Incremental (Intvn 2 – Intvn 1): -0.011 (ns, p = 0.50)</td>
<td>Total costs (mean): Intvn 1: £8042.17 Intvn 2: £7796.62 Incremental (Intvn 2 – Intvn 1): -£245.55 (p&lt;0.001)</td>
</tr>
</tbody>
</table>
| | | Mean age = 61 Male = 74% MI/UA = 37%/63% | Other outcome measures (mean): 30-day Death Intvn 1: 0.004 | Currency & cost year: 2002 US dollars (presented here as 2002 UK pounds†) | At 30 days bivalirudin is potentially dominant given the lower costs and the overall numerically lower complications. However, there is uncertainty due to numerically higher rates of MI and urgent revascularisation. Further uncertainty arises from the
<table>
<thead>
<tr>
<th><strong>Perspective:</strong></th>
<th>US – reported as societal but appears to be hospital costs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Time horizon:</strong></td>
<td>30 days to 1 year</td>
</tr>
<tr>
<td><strong>Discounting:</strong></td>
<td>Not required</td>
</tr>
</tbody>
</table>

**Intervention 1:**
Heparin (6S U/kg bolus) + planned GPI (eptifibatide or abciximab)

**Intervention 2:**
Bivalirudin (iv 0.75mg/kg bolus and 1.75mg/kg/hr infusion for length of PCI) + provisional GPI

<table>
<thead>
<tr>
<th>Event</th>
<th>Intervention 1</th>
<th>Intervention 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI</td>
<td>0.004 (ns, p = 0.99)</td>
<td>0.069</td>
</tr>
<tr>
<td>Urgent revascularisation</td>
<td>Intvn 1: 0.016</td>
<td>Intvn 2: 0.023 (ns, p = 0.40)</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>Intvn 1: 0.045</td>
<td>Intvn 2: 0.027 (ns, p = 0.07)</td>
</tr>
<tr>
<td>Minor bleeding</td>
<td>Intvn 1: 0.268</td>
<td>Intvn 2: 0.129 (p&lt;0.001)</td>
</tr>
</tbody>
</table>

**6 months**

- **Death**
  - Intvn 1: 0.013
  - Intvn 2: 0.009 (ns, p = 0.46)

- **MI**
  - Intvn 1: 0.076
  - Intvn 2: 0.081 (ns, p = 0.76)

- **Revascularisation**
  - Intvn 1: 0.084
  - Intvn 2: 0.117 (p = 0.04)

**1-year**

- **Death**
  - Intvn 1: 0.018
  - Intvn 2: 0.015 (p = 0.70)

**Data sources**

**Health outcomes:**
- Effectiveness: REPLACE-2 ACS subgroup

**Cost sources:**
- Procedural costs: REPLACE-2 resource use for all patients and 2002 unit costs (source not reported)

Significantly higher 6-months revascularisation with bivalirudin as this may impact costs and outcomes.

**Analysis of uncertainty:**
None reported
- Other hospital costs: billed resource use from selected patients in REPLACE-2 for initial hospitalisation and subsequent cardiovascular hospitalisations, and from patients who experienced a major in-hospital complication, and the hospital’s Medicare cost report; costs were imputed for patients whose bills were not obtained based on a regression model

**Comments**

**Source of funding:** Medicines Co.

**Limitations:**
US perspective; Overall impact on outcomes (e.g. QALYs or life years) not assessed – inhibits interpretation

**Other:**
Other outcomes reported but not presented here were:
- 30-day endpoints: death/MI/urgent revascularisation; death/MI; urgent PCI; urgent CABG
- 6-month endpoints: death/MI

In REPLACE-2 ACS subgroup 8.2% of bivalirudin patients received provisional GPI

**Overall quality***: Potentially serious limitations **Overall applicability***: Partially applicable

Abbreviations: ACS = acute coronary syndromes; CABG = coronary artery bypass graft; CCA = cost-consequence analysis; GPI = glycoprotein IIb/IIIa inhibitor; ICER = incremental cost-effectiveness ratio; MI = myocardial infarction; NS = not significant; PCI = percutaneous coronary intervention; QALYs = quality-adjusted life years; RCT = randomised controlled trial; REPLACE-2 = second Randomized Evaluation of PCI Linking Angiomax to Reduced Clinical Events (study); UA = instable angina; UFH = unfractionated heparin

‡ Converted using 2002 Purchasing Power Parities (Organisation for Economic Co-operation and Development (OECD), 2008 3285 / id); * Very serious limitations/Potentially serious limitations/Minor limitations; ** Directly applicable/Partially applicable/Not applicable

7. Management strategies: Early invasive versus conservative management (1 study)


<table>
<thead>
<tr>
<th>Study details</th>
<th>Population &amp; interventions</th>
<th>Health outcomes</th>
<th>Costs</th>
<th>Cost effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Economic analysis: CUA</td>
<td>Population: UA/NSTEMI</td>
<td>Health outcomes incorporated: Death, MI, quality of life</td>
<td>Cost components incorporated: Angiogram, PCI, CABG, days on wards (for all causes), visits to family doctor/ community nurse/ outpatients, MI, key cardiac</td>
<td>Base case ICER (Intvn 2 vs Intvn 1): Patient level analysis for RITA-3 patients: Results only presented graphically. Early interventional strategy cost-effective for more patients as risk increased but with a considerable spread of ICERs within each risk group.</td>
</tr>
<tr>
<td>Study design: Decision analytic model (short-term decision tree for index)</td>
<td>RITA 3: N = 1810, Median age = 63, Male = 61%</td>
<td>Primary outcome measure: QALYs (mean)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
hospitalisation plus a long-term Markov model representing post-index period) based primarily on effectiveness, QOL and resource use data from single RCT (RITA-3).

**Perspective:**
UK NHS

**Time horizon:**
Lifetime

**Discounting:**
Costs & outcomes = 3.5%

<table>
<thead>
<tr>
<th><strong>UK setting</strong></th>
<th><strong>Mean per patient per group not reported</strong></th>
<th><strong>Mean per patient per group not reported</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Results analysed by risk group (1, 2, 3, 4a, 4b – quartiles of risk in RITA-3 with highest risk split into two)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Intervention 1:</strong> Conservative strategy (ischemia or symptom-driven angiography)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Intervention 2:</strong> Early angiography (routine angiography &lt;72hrs followed by revascularisation if clinically indicated)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mean per patient per group not reported</strong></td>
<td><strong>Incremental (Intvn 2 – Intvn 1):</strong></td>
<td><strong>Pooled effectiveness data:</strong></td>
</tr>
<tr>
<td></td>
<td>Base case:</td>
<td>Risk group 1 = 0.091</td>
</tr>
<tr>
<td></td>
<td>Risk group 2 = 0.213</td>
<td>Risk group 2 = 0.185</td>
</tr>
<tr>
<td></td>
<td>Risk group 3 = 0.283</td>
<td>Risk group 3 = 0.240</td>
</tr>
<tr>
<td></td>
<td>Risk group 4a = 0.547</td>
<td>Risk group 4a = 0.452</td>
</tr>
<tr>
<td></td>
<td>Risk group 4b = 0.512</td>
<td>Risk group 4b = 0.418</td>
</tr>
<tr>
<td><strong>Pooled effectiveness data:</strong></td>
<td><strong>Allowing treatment effect to vary with baseline risk:</strong></td>
<td>Risk group 1 = -0.019</td>
</tr>
<tr>
<td>Risk group 1 = 0.082</td>
<td>Risk group 2 = 0.095</td>
<td>Risk group 2 = 0.095</td>
</tr>
<tr>
<td>Risk group 2 = 0.188</td>
<td>Risk group 3 = 0.188</td>
<td>Risk group 3 = 0.240</td>
</tr>
<tr>
<td>Risk group 4a = 0.551</td>
<td>Risk group 4a = 0.547</td>
<td>Risk group 4a = 0.452</td>
</tr>
<tr>
<td>Risk group 4b = 0.418</td>
<td>Risk group 4b = 0.512</td>
<td>Risk group 4b = 0.418</td>
</tr>
<tr>
<td><strong>Alternative durations of effect of treatment</strong></td>
<td><strong>Not reported</strong></td>
<td><strong>Not reported</strong></td>
</tr>
<tr>
<td><strong>Not reported</strong></td>
<td><strong>Not reported</strong></td>
<td><strong>Not reported</strong></td>
</tr>
</tbody>
</table>

**Medications (aspirin, beta blockers, statins, LA nitrates, CCBs, ACEs, clopidogrel**

Cost analyses accounted for covariates.

**NB:** resource use collected in trial for 1 year; cost are extrapolated past this.

**Total costs (mean):**
Mean per patient per group not reported

<table>
<thead>
<tr>
<th><strong>Incremental (Intvn 2 – Intvn 1):</strong></th>
<th><strong>Pooled effectiveness data:</strong></th>
<th><strong>Allowing treatment effect to vary with baseline risk:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Base case:</td>
<td>Risk group 1 = £4885</td>
<td>Risk group 1 = £53,760 (1%/12%)</td>
</tr>
<tr>
<td>Risk group 2 = £4898</td>
<td>Risk group 2 = £22,949 (33%/75%)</td>
<td></td>
</tr>
<tr>
<td>Risk group 3 = £6045</td>
<td>Risk group 3 = £21,325 (41%/81%)</td>
<td></td>
</tr>
<tr>
<td>Risk group 4a = £6538</td>
<td>Risk group 4a = £11,957 (95%/98%)</td>
<td></td>
</tr>
<tr>
<td>Risk group 4b = £6530</td>
<td>Risk group 4b = £12,750 (92%/98%)</td>
<td></td>
</tr>
<tr>
<td><strong>Pooled effectiveness data:</strong></td>
<td>Risk group 1 = £4819</td>
<td>Risk group 1 = £50,131 (7%/26%)</td>
</tr>
<tr>
<td>Risk group 2 = £4852</td>
<td>Risk group 2 = £29,711 (17%/51%)</td>
<td></td>
</tr>
<tr>
<td>Risk group 3 = £5788</td>
<td>Risk group 3 = £11,898 (94%/98%)</td>
<td></td>
</tr>
<tr>
<td>Risk group 4a = £6163</td>
<td>Risk group 4a = £10,476 (98%/99%)</td>
<td></td>
</tr>
<tr>
<td>Risk group 4b = £4746</td>
<td>Risk group 4b = £14,673 (83%/96%)</td>
<td></td>
</tr>
</tbody>
</table>

**Alternative scenarios**

**Pooled effectiveness data:**
Risk group 1 = £58,490 (0.2%/6%) |
Risk group 2 = £26,265 (19%/63%) |
Risk group 3 = £24,143 (25%/71%) |
Risk group 4a = £13,646 (87%/96%) |
Risk group 4b = £14,673 (83%/96%) |

**Allowing treatment effect to vary with baseline risk:**
Risk group 1 = Dominated (0.1%/3%) |
Risk group 2 = £50,131 (7%/26%) |
Risk group 3 = £29,711 (17%/51%) |
Risk group 4a = £11,898 (94%/98%) |
Risk group 4b = £10,476 (98%/99%) |

**Alternative durations of effect of treatment**
(base case = 5 years (trial follow-up)): |

<table>
<thead>
<tr>
<th><strong>10 yrs</strong></th>
<th><strong>15 yrs</strong></th>
<th><strong>Lifetime</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Constant RITA-3 treatment effect</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>£34,901</td>
<td>£27,949</td>
</tr>
<tr>
<td>2</td>
<td>£15,410</td>
<td>£11,652</td>
</tr>
<tr>
<td>3</td>
<td>£15,754</td>
<td>£13,159</td>
</tr>
<tr>
<td>4a</td>
<td>£9631</td>
<td>£8446</td>
</tr>
<tr>
<td>4b</td>
<td>£9707</td>
<td>£8904</td>
</tr>
</tbody>
</table>

**Illustrative patient for each risk group**
(probability CE at £20,000/£30,000 threshold): |

<table>
<thead>
<tr>
<th><strong>Risk group 1</strong></th>
<th><strong>Risk group 2</strong></th>
<th><strong>Risk group 3</strong></th>
<th><strong>Risk group 4a</strong></th>
<th><strong>Risk group 4b</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>£13,920</td>
<td>£27,949</td>
<td>£11,652</td>
<td>£13,159</td>
<td>£8,446</td>
</tr>
</tbody>
</table>

**Alternative scenarios**

**Pooled effectiveness data:**
Risk group 1 = £58,490 (0.2%/6%) |
Risk group 2 = £26,265 (19%/63%) |
Risk group 3 = £24,143 (25%/71%) |
Risk group 4a = £13,646 (87%/96%) |
Risk group 4b = £14,673 (83%/96%) |

**Allowing treatment effect to vary with baseline risk:**
Risk group 1 = Dominated (0.1%/3%) |
Risk group 2 = £50,131 (7%/26%) |
Risk group 3 = £29,711 (17%/51%) |
Risk group 4a = £11,898 (94%/98%) |
Risk group 4b = £10,476 (98%/99%) |

**Alternative durations of effect of treatment**
(base case = 5 years (trial follow-up)): |
| Risk group 2 | £4774 |
| Risk group 3 | £5574 |
| Risk group 4a | £6552 |
| Risk group 4b | £7214 |
| Alternative durations of effect of treatment |
| Not reported |
| Currency & cost year: |
| UK pounds, £2003/4 |

| Interaction between treatment effect and risk at randomisation |
|---------------------|---------------------|---------------------|
| 1                   | £187,947            | £121,044            | £45,130            |
| 2                   | £28,163             | £21,553             | £14,354            |
| 3                   | £19,681             | £16,218             | £12,781            |
| 4a                  | £9450               | £8334               | £7600              |
| 4b                  | £7934               | £7348               | £6906              |

Other
Results were robust to other sensitivity analyses

Data sources

Health outcomes:
- Base case: RITA-3 trial(Fox, 2002 3433 /id; Fox, 2005 3420 /id) – various statistical analyses were undertaken using RITA-3 data accounting for covariates; lifetables were used for non-cv death rate.
- Pooled effectiveness data for alternative scenario: meta analysis using Mehta et al(Mehta, 2005 3421 /id) meta analysis and updating with ICTUS trial(de, 2005 1022 /id) data, long-term results from RITA-3(Fox, 2005 3420 /id) and FRISC II(Lagerqvist, 2006 3440 /id).

Quality-of-life weights:
- EQ-5D data from RITA-3 collected at randomisation, 4 months and 1 year.

Cost sources:
- Resources use data from RITA-3 with unit costs applied from national sources or collected from hospital in RITA 3 or RITA 2 published previously(Epstein, 2008 3402 /id)

Comments

Source of funding:
RITA-3 funded by British Heart Foundation (who received a donation from Aventis Pharma); additional governmental support also obtained. Analysis and preparation of manuscript undertaken independently.

Limitations:
- RITA-3 enrolled 1997-2001 and so may not reflect current practice (increased angiography and revascularisation, increased clopidogrel and GPI use)
- The pooled estimate of effectiveness included studies from the pre-stent era

Other:

Overall quality*: Minor limitations
Overall applicability**: Directly applicable

Abbreviations: ACEs = angiotensin-converting enzyme inhibitors; CAGB = coronary artery bypass graft; CCBs = calcium channel blockers; CUA = cost-utility analysis; ICER = incremental cost-effectiveness ratio; LA = long-acting; MI = myocardial infarction; NSTEMI = non-ST-segment-elevation myocardial infarction; PCI = percutaneous coronary intervention; QALY = quality-adjusted life year; RCT = randomised controlled trial; RITA-3= Randomized Intervention Trial of unstable Angina 3; UA = unstable angina
*Very serious limitations/Potentially serious limitations/Minor limitations; ** Directly applicable/Partially applicable/Not applicable
8. Management strategies: PCI vs CABG (2 studies)


<table>
<thead>
<tr>
<th>Study details</th>
<th>Population &amp; interventions</th>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>Economic analysis:</strong></td>
<td><strong>Population:</strong> Patients with multivessel disease and unstable angina deemed equally treatable with either PCI or CABG.</td>
<td>Health outcomes incorporated: Major adverse cardiac and cerebrovascular events (MACCE): death (all causes), cerebrovascular accident (stroke, TIA, reversible ischemic neurological deficits), non-fatal MI (spontaneous &amp; peri-procedural), repeat revascularisation (PCI &amp; CABG)</td>
<td>Cost components incorporated: Direct medical costs including initial procedure, initial hospitalisation, follow-up event diagnostic test, rehospitalisation, medication</td>
<td>Base case ICER (Intvn 2 vs Intvn 1): £20,701 per year MACCE-free survival 95% CI: £8,403–£76,769</td>
</tr>
<tr>
<td><strong>Study design:</strong> Within RCT analysis (patient level resource use and clinical outcomes from ARTS, relevant unit costs applied)</td>
<td><strong>Primary outcome measure:</strong> MACCE-free survival at 1 year (% patients) Intvn 1: 74.3% Intvn 2: 85.3% Incremental (Intvn 2 – Intvn 1) 11.0% (P&lt;0.0001)</td>
<td><strong>Breakdown of MACCE (% patients):</strong> Death Intvn 1: 2.7% Intvn 2: 2.2% (NS)</td>
<td><strong>Total costs (mean):</strong> Intvn 1: £7,002 Intvn 2: £9,278 Incremental (Intvn 2 – Intvn 1): £2,276 (NS)</td>
<td></td>
</tr>
<tr>
<td><strong>Perspective:</strong> Health service, country unclear&lt;sup&gt;a&lt;/sup&gt;</td>
<td><strong>Intervention 1:</strong> PCI (with bare metal stent)</td>
<td><strong>Breakdown of MACCE (% patients):</strong> CVA Intvn 1: 0.4% Intvn 2: 3.1% (NS)</td>
<td>Currency &amp; cost year:</td>
<td>Analysis of uncertainty: None</td>
</tr>
<tr>
<td><strong>Time horizon:</strong> 1 year</td>
<td><strong>Intervention 2:</strong> CABG</td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Discounting:</strong> N/a</td>
<td></td>
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</tbody>
</table>

<sup>a</sup> Resource use from ARTS trial but countries not stated. Netherlands unit costs used, results expressed in US dollars.

<sup>b</sup> Year not reported so cost year assumed to be same as publication year

<sup>c</sup> Converted using 2002 Purchasing Power Parities [Organisation for Economic Co-operation and Development (OECD), 2008 3285 /id}
| MI | Intvn 1: 5.8%  
|    | Intvn 2: 5.8% (NS)  
| CABG | Intvn 1: 6.2%  
|     | Intvn 2: 0.9% (P<0.01)  
| Repeat PCI | Intvn 1: 10.6%  
|        | Intvn 2: 2.7% (P<0.01)  

### Data sources

**Health outcomes:**
- ARTS trial unstable angina subgroup

**Cost sources:**
- Resource use from ARTs RCT unstable angina subgroup
- Netherlands unit costs – sources unspecified

### Comments

**Source of funding:**
None reported

**Limitations:**
- Chosen outcome measure difficult to interpret in NICE guideline context
- Short time horizon (1 year)
- Costing methodology unclear
- Based on single trial so treatment effects may not reflect whole body of evidence in area
- Bare metal stent used – use of drug eluting stents in contemporary practice may reduce revascularisation in PCI arm

**Other:**
Paper also presents results for stable patients which are not reported here

### Overall quality

*Very serious limitations/Potentially serious limitations/Minor limitations; ** Directly applicable/Partially applicable/Not applicable

Abbreviations: ARTS = Arterial Revascularisation Therapies Study; CABG = coronary artery bypass graft; CUA = cost-utility analysis; ICER = incremental cost-effectiveness ratio; MI = myocardial infarction; NSTEMI = non-ST-segment-elevation myocardial infarction; PCI = percutaneous coronary intervention; QALY = quality-adjusted life year; RCT = randomised controlled trial; UA = unstable angina;
<table>
<thead>
<tr>
<th>Study details</th>
<th>Population &amp; interventions</th>
<th>Health outcomes incorporated:</th>
<th>Costs</th>
<th>Cost effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Economic analysis:</td>
<td>CCA</td>
<td>Health outcomes incorporated:</td>
<td>Cost components incorporated:</td>
<td>Base case ICER (Intvn 2 vs Intvn 1):</td>
</tr>
<tr>
<td>Study design:</td>
<td>Within RCT analysis (Patient level resource use and clinical outcomes from SOS trial, relevant unit costs applied)</td>
<td>Death (all cause), Q-wave MI, bleeding, cerebrovascular accident (CVA), repeat revascularisation (PCI &amp; CABG), health status.</td>
<td>Resource use during procedure and follow-up.</td>
<td>ICER not calculated</td>
</tr>
<tr>
<td>Perspective:</td>
<td>UK NHS</td>
<td></td>
<td></td>
<td>Analysis of uncertainty:</td>
</tr>
<tr>
<td>Time horizon:</td>
<td>1 year</td>
<td></td>
<td></td>
<td>None</td>
</tr>
<tr>
<td>Discounting:</td>
<td>N/a</td>
<td></td>
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<tr>
<td>Population:</td>
<td>Patients with multivessel disease and ACS eligible for both PCI and CABG. Note: this is a subgroup of the SOS trial.</td>
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<tr>
<td>N = 242 (PCI 116; CABG 126)</td>
<td>Median age = 62 years Male = 73%</td>
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<tr>
<td>Intervention 1:</td>
<td>PCI (with bare metal stent)</td>
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<tr>
<td>Intervention 2:</td>
<td>CABG</td>
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<tr>
<td>1-year outcomes:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>Intvn 1: 2.6%</td>
<td>Intvn 2: 1.6% Incremental (Intvn 2 –Intvn 1): -1.0% (P = 0.63)</td>
<td></td>
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</tr>
<tr>
<td>Q-wave MI</td>
<td>Intvn 1: 3.5%</td>
<td>Intvn 2: 4.0% Incremental (Intvn 2 –Intvn 1): 0.5% (P = 1.00)</td>
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</tr>
<tr>
<td>Death or Q-wave MI</td>
<td>Intvn 1: 5.2%</td>
<td>Intvn 2: 5.6% Incremental (Intvn 2 –Intvn 1): 0.4% (P = 89)</td>
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</tr>
<tr>
<td>Bleeding</td>
<td>Intvn 1: 2.6%</td>
<td>Intvn 2: 4.0% Incremental (Intvn 2 –Intvn 1): 1.4% (P = 0.56)</td>
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<tr>
<td>CVA</td>
<td></td>
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<tr>
<td>Total one-year costs (mean):</td>
<td>Intvn 1: £8,014</td>
<td>Intvn 2: £10,080 Incremental (Intvn 2 –Intvn 1): £2,066 (95% CI: -£690 to £3487)</td>
<td></td>
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<tr>
<td>Index hospitalisation costs:</td>
<td>Intvn 1: £5,015</td>
<td>Intvn 2: £8,248</td>
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<tr>
<td>One-year follow-up costs:</td>
<td>Intvn 1: £2,998</td>
<td>Intvn 2: £1,832</td>
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<tr>
<td>Currency &amp; cost year:</td>
<td>2000 UK pounds</td>
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<tr>
<td>Intvn 1: 0%</td>
<td>Intvn 2: 1.6%</td>
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<tr>
<td><strong>Incremental (Intvn 2 – Intvn 1): 1.6% (P = 0.50)</strong></td>
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</tbody>
</table>

**Repeat revascularisation**  
Intvn 1: 15.5%  
Intvn 2: 7.1%  
**Incremental (Intvn 2 – Intvn 1): -8.4% (P = 0.04)**

**Data sources**  
**Health outcomes:**  
- SOS trial ACS subgroup  

**Cost sources:**  
- Resource use from SOS RCT ACS subgroup  
- UK unit costs – sources unspecified

**Comments**  
**Source of funding:**  
None reported  

**Limitations:**  
- QALYs not used  
- Short time horizon (1 year)  
- Based on single trial so treatment effects may not reflect whole body of evidence in area  
- Bare metal stent used – use of drug eluting stents in contemporary practice may reduce revascularisation in PCI arm  

**Other:**  
Paper also present results for non-ACS patients which are not reported here

**Overall quality**: Partially applicable  
**Overall applicability**: Potentially serious limitations

**Abbreviations:**  
ACS = acute coronary syndrome; CCA = cost-consequence analysis; CI = confidence interval; ICER = incremental cost-effectiveness ratio; MI = myocardial infarction; PCI = percutaneous coronary intervention; CABG = coronary artery bypass graft; QALY = quality-adjusted life year; RCT = randomised controlled trial; SOS = Stent or Surgery (Study)

*Very serious limitations/Potentially serious limitations/Minor limitations; ** Directly applicable/Partially applicable/Not applicable

9. Management strategies: IABP (no studies)  
10. Management strategies: testing for ischemia (no studies)  
11. Management strategies: testing for LV function (no studies)
12. Management strategies: specialist care (no studies)
13. Management strategies: rehabilitation and discharge planning (no studies)