ProMISE, Progress to date

Paul Mouncey (Trial Manager)
Scope

What is ProMISe?
The Team
Milestones
Lessons learnt
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Background

• Rivers *et al* 2001, single centre trial in the US comparing six hours of early, goal-directed, protocolised resuscitation with usual resuscitation

• Reduction of in-hospital mortality from 46.5% to 30.5%

• Is this generalisable to a UK setting?
A multicentre randomised controlled trial of the clinical and cost-effectiveness of early, goal-directed, protocolised resuscitation for emerging septic shock

Funder: NIHR HTA programme (07/37/47)
Sponsor: ICNARC
NIHR Portfolio number: 9820
Sample size/recruitment rate

• Rivers et al. ARR 16% (46.5 to 30.5%) in-hospital mortality

• Aim to achieve 80% power to detect ARR 8% in 90-day mortality from 40% to 32% (P<0.05)

• Require 630 patients per arm (1260 total) including refusals/lost to follow-up

• One patient per hospital per month
**Trial Protocol**

1. Screening
2. Consent
3. Randomising
   - Early, goal-directed, protocolised resuscitation
   - Usual resuscitation
4. 90 days post randomisation
5. 1 year post randomisation
Screening timeline

Presentation at ED/AMU

Up to SIX hours

Eligible

Note: average time to meet eligibility criteria is 1 hour 45 mins
Inclusion criteria

• Eligibility (met in **ANY** order):

<table>
<thead>
<tr>
<th>Infection</th>
<th>SIRS - <strong>two of</strong></th>
<th>Hypoperfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presumed or Known</td>
<td>Temperature ≥38 °C or ≤36 °C</td>
<td>Lactate 4 mmol l⁻¹ or higher</td>
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<tr>
<td></td>
<td>Heart rate ≥90 beats min⁻¹</td>
<td>or <strong>Hypotension</strong></td>
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<tr>
<td></td>
<td>WBC ≤4 × 10⁹ l⁻¹ or ≥12 × 10⁹ l⁻¹ or ≥10% immature neutrophils</td>
<td>SBP less than 90 mmHg, or MAP less than 65 mmHg after minimum one litre fluid challenge within 60 minutes</td>
</tr>
<tr>
<td></td>
<td>Respiratory rate or Hyperventilation ≥20 breaths min⁻¹ or PaCO₂ ≤4.3 kPa or acute mechanical ventilation</td>
<td></td>
</tr>
</tbody>
</table>
Consent/randomisation timeline

Inclusion criteria met

Up to two hours

Consent and randomise

Note: around 75\% of patients are randomised within three hours of presentation
Patients recruited

850

(67%)
Trial Protocol

- Screening
- Consenting
- Randomising

- Early, goal-directed, protocolised resuscitation
- Usual resuscitation

- 90 days post randomisation
- 1 year post randomisation
Follow up

<table>
<thead>
<tr>
<th>Primary Outcome</th>
<th></th>
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<tbody>
<tr>
<td>Mortality</td>
<td>90 days</td>
<td>99%</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Secondary Outcomes</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>one year</td>
<td>99%</td>
</tr>
<tr>
<td>Quality of life/</td>
<td>90 days</td>
<td>84%</td>
</tr>
<tr>
<td>Resource use</td>
<td>one year</td>
<td>80%</td>
</tr>
<tr>
<td>questionnaire</td>
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</tbody>
</table>
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What is ProMISe?

The Team

Milestones

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Trial Team

- Sites (n=50)
- Co-investigators
- PromiSe
- ICNARC CTU
- Trial Steering Committee
- Data Monitoring Committee
Regional site recruitment

- 9 sites @ 0.14
- 9 sites @ 0.27
- 9 sites @ 0.16
- 8 sites @ 0.23
- 10 sites @ 0.22
- 12 sites @ 0.19
Trial Team

Co-investigators
ProMISe
ICNARC CTU
Sites (n=50)
Trial Steering Committee
Data Monitoring Committee
Investigators

• Kathy Rowan (Chief Investigator)
• Derek Bell (Acute Medicine)
• Duncan Young (Critical Care Medicine)
• Julian Bion (Critical Care Medicine)
• Mervyn Singer (Critical Care Medicine)
• Tim Coats (Emergency Medicine)
• David Harrison (Statistical analysis)
• Richard Grieve (Economic evaluation)
Investigators

- Kathy Rowan (Chief Investigator)
- Derek Bell (Acute Medicine)
- Duncan Young (Critical Care Medicine)
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Cumulative patient recruitment

![Cumulative patient recruitment graph](image-url)
Half-way – November 2012
Interim analysis review – Dec 2012

Month

Patients


0 100 200 300 400 500 600 700 800 900
Two-thirds – April 2013
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Key features

• Enthusiastic and dedicated
• Flexible working going above and beyond
• Share with others
Top tips

• Regular ongoing training
• Keep research visible
• Provide positive feedback
• Research nurse ‘visible and embedded’
• Facilitate out of office hours recruitment
• Teamwork
Dedicated research nurse

- Months 1-12: 7 patients (0.14 patients per week)
- Months 13-20: 12 patients (0.42 patients per week)
Increased screening hours

• Months 1-10: 2 patients (0.06 patients per week)
• Months 11-24: 21 patients (0.34 patients per week)
Recruitment timeline
Collaborators’ Meeting

• Date: 30 May 2013
• Location: University College London
• Open to: Participating sites
Be involved in the final push...!

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The views and opinions expressed therein are those of authors and do not necessarily reflect those of the HTA programme, NIHR, NHS or the Department of Health