POSTPARTUM HAEMORRHAGE

CORE OUTCOME SETS PROJECT

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BACKGROUND

• Choice of outcomes used to reflect benefit / harm in RCTs is variable

  ➔ 16 RCTs for treatment of PPH used 14 different primary outcomes (1997-2015)
  ➔ Difficult to compare effects across studies

• Variations in definitions of same outcome

  ➔ Blood loss most common outcome in 121 RCTS for prevention of PPH
  ➔ mean/median, >300, >400, >/= 500, >750 mls, >800, >/= 1000, >1500 mls
  ➔ measured at 30 mins, 1 hr, 2 hrs, 4 hrs, 8 hrs, 24 hrs, 48 hrs
  ➔ Difficult to synthesise data for systematic reviews/guidelines

• Surrogate outcome used instead of important measures

  ➔ Maternal mortality reported in only 50% of PPH treatment RCTs
  ➔ Data may not be meaningful / relevant to users
SOLUTION: CORE OUTCOME SETS (COS)

• A minimum set of critically important outcomes

• Must be measured and reported in all clinical trials of a condition

• Agreed by relevant stakeholders through an iterative process: patients, clinicians, researchers, policy makers

• Not the only outcomes reported in the study

• Not necessarily the primary outcome of the study
POSTPARTUM HAEMORRHAGE CORE OUTCOME SETS PROJECT

Aim
To develop Core Outcome Sets for evaluation of interventions for
1) Prevention of PPH
2) Treatment of PPH

Steering committee (University of Liverpool)
Shireen Meher (PI), Anna Cuthbert, Zarko Alfirevic, Jamie Kirkham, Paula Williamson

Affiliations
• Funded by British Medical Association
• Endorsed by COMET Initiative, CROWN and World Health Organisation

International stakeholders
• Obstetricians, midwives, anaesthetists, haematologists, neonatologists, health strategists, methodologist and parent representatives
• Scientific Advisory Group (n=16, 10 countries)
• Delphi participants (n=221, 44 countries)
1. IDENTIFICATION OF OUTCOMES

1. SYSTEMATIC REVIEW OF OUTCOMES REPORTED IN PPH RCTS
   PCG Register, Medline, EMBASE, CENTRAL, SCOPUS, Web of Knowledge 1997-2015

2. CONSULTATION WITH STAKEHOLDERS

PREVENTION OF PPH = 121 RCTs
TREATMENT OF PPH = 16 RCTs

Outcomes grouped into domains
Similar outcomes combined
Outcome definitions recorded

N=51 OUTCOMES
N=49 OUTCOMES
2. DELPHI SURVEY: TO BUILD CONSENSUS

**Round 1**
- Prevention N= 213
- Treatment N= 221

**Round 2**
- Response rates
  - Prevention = 76%
  - Treatment = 78%

**Delphi Survey of Stakeholder Groups**

**Inclusion Criteria for COS**
In each stakeholder group, 70% score outcome as critically important (7-9) AND <15% score as not important (1-3)

**Survey of How to Report Potential Included Outcome** N= 19
3. Stakeholder Face to Face Meeting

Delphi results presented and discussed

Final Core Outcome Sets agreed
- Participants scored each outcome between 1-9
- Included if > 70% participants scored outcome as 7-9

Expert Committee Recommendations:
- How to report outcomes
  - Survey results and Expert presentations
  - Voting: Consensus if >70% preferred one option
FACE TO FACE MEETING (N=24, 9 countries)

• Chair: Prof Jim Neilson

• Obstetricians
  – Edgardo Abalos – Argentina
  – Bukola Fawole – Nigeria
  – Andrew Weeks – UK
  – Zarko Alfirevic - UK
  – Nasreen Aflaifel – UK

• Midwives
  – Declan Devane – Ireland
  – Caroline Homer – Australia
  – Kathryn Gutteridge – UK

• Methodologists/Statisticians
  – Jamie Kirkham – UK
  – Haleema Shakur – UK
  – Steven Lane – UK

• Neonatologists
  – Julie Nycyk – UK

• Anaesthetists
  – Anne-Sophie Ducloy-Bouthers – France
  – Shuba Mallalah – UK

• Haematologists
  – Peter Collins – UK
  – Beverley Hunt - UK

Health strategists
  – JP Souza- World Health Organization
  – Jennifer Blum – Gynuity, USA
  – Jeffrey Smith – Johns Hopkins JPEIGO, USA

• Parent representatives
  – Gill Gyte – UK
  – Alina Bishop – Mexico
  – Michelle Beacock – UK
  – Carolyn Markham – UK
## RESULTS: COS FOR PPH PREVENTION TRIALS

<table>
<thead>
<tr>
<th>Domain</th>
<th>Outcome</th>
<th>% scoring 7-9 at meeting</th>
<th>% scoring 7-9 Delphi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood loss assessment</td>
<td>1. Blood loss after birth</td>
<td>95%</td>
<td>All &gt;70%</td>
</tr>
<tr>
<td>Morbidity / Mortality</td>
<td>2. Shock</td>
<td>74%</td>
<td>All &gt;70%</td>
</tr>
<tr>
<td></td>
<td>3. Maternal death</td>
<td>100%</td>
<td>All &gt;70%</td>
</tr>
<tr>
<td>Use of additional interventions</td>
<td>4. Blood transfusion (RBC)</td>
<td>84%</td>
<td>67-100%</td>
</tr>
<tr>
<td></td>
<td>5. Use of additional uterotonics</td>
<td>90%</td>
<td>67-95%</td>
</tr>
<tr>
<td>Use of resources</td>
<td>6. Transfer to higher level of care</td>
<td>79%</td>
<td></td>
</tr>
<tr>
<td>Patient reported outcomes</td>
<td>7. a) Women’s sense of wellbeing</td>
<td>a) 79%</td>
<td>31-95%</td>
</tr>
<tr>
<td></td>
<td>7. b) Women’s acceptability of and satisfaction with intervention</td>
<td>b) 79%</td>
<td>11-81%</td>
</tr>
<tr>
<td>Neonatal outcomes</td>
<td>8. Breastfeeding</td>
<td>79%</td>
<td>9-56%</td>
</tr>
<tr>
<td>Adverse effects</td>
<td>9. Adverse effects of the intervention for mother and baby</td>
<td>79%</td>
<td>All &gt;70%</td>
</tr>
</tbody>
</table>
## Results: COS for PPH Treatment Trials

<table>
<thead>
<tr>
<th>Domain</th>
<th>Outcome</th>
<th>Meeting</th>
<th>Delphi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood loss assessment</td>
<td>1. Blood loss</td>
<td>90%</td>
<td>All &gt;70%</td>
</tr>
<tr>
<td>Morbidity / Mortality</td>
<td>2. Shock</td>
<td>95%</td>
<td>All &gt;70%</td>
</tr>
<tr>
<td></td>
<td>3. Coagulopathy</td>
<td>74%</td>
<td>All &gt;70%</td>
</tr>
<tr>
<td></td>
<td>4. Hysterectomy</td>
<td>90%</td>
<td>All &gt;70%</td>
</tr>
<tr>
<td></td>
<td>5. Any organ dysfunction</td>
<td>95%</td>
<td>All &gt;70%</td>
</tr>
<tr>
<td></td>
<td>6. Maternal death</td>
<td>100%</td>
<td>All &gt;70%</td>
</tr>
<tr>
<td>Use of additional interventions</td>
<td>7. Blood transfusion a) RBC</td>
<td>a) 95%</td>
<td>All &gt;70%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>b) blood products</td>
<td>b) 74%</td>
</tr>
<tr>
<td></td>
<td>8. Use of any additional haemostatic</td>
<td>90%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>intervention</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use of resources</td>
<td>9. Transfer to higher level of care</td>
<td>82%</td>
<td></td>
</tr>
<tr>
<td>Patient reported outcomes</td>
<td>10. a) Women’s sense of wellbeing</td>
<td>a) 84%</td>
<td>38-75%</td>
</tr>
<tr>
<td></td>
<td>b) Women’s acceptability of and</td>
<td>b) 82%</td>
<td>22-81%</td>
</tr>
<tr>
<td></td>
<td>satisfaction with intervention</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neonatal outcomes</td>
<td>11. Breastfeeding</td>
<td>82%</td>
<td>0-50%</td>
</tr>
<tr>
<td>Adverse effects</td>
<td>12. Adverse effects of the intervention</td>
<td>94%</td>
<td>All &gt;70%</td>
</tr>
</tbody>
</table>
## HOW TO REPORT OUTCOMES

<table>
<thead>
<tr>
<th>Outcome</th>
<th>COS</th>
<th>Expert committee Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood loss</td>
<td>Prevention</td>
<td>≥500 mls AND ≥1000 mls AND mean/median blood loss</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Time frame: from birth of baby to cessation of active bleeding</td>
</tr>
<tr>
<td>Treatment</td>
<td>Mean + SD / Median + IQ range</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Time frame: any additional blood loss after intervention up to cessation of active bleeding.</td>
</tr>
</tbody>
</table>

Blood loss may be measured or estimated
### HOW TO REPORT COS OUTCOMES

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Expert Committee Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shock</td>
<td>Based on <strong>clinical assessment</strong> as defined by trialists</td>
</tr>
<tr>
<td>Maternal death</td>
<td>Death from <strong>all causes</strong> and from PPH (<strong>cause specific</strong>)</td>
</tr>
<tr>
<td>Hysterectomy</td>
<td>Hysterectomy to stop PPH (<strong>cause specific</strong>)</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>Any blood transfusion <strong>AND mean / median</strong> RBC units</td>
</tr>
<tr>
<td>Transfer to higher level of care</td>
<td>Transfer to hospital, higher facility, or ITU</td>
</tr>
<tr>
<td>Use of additional uterotonic</td>
<td>Any additional uterotonic</td>
</tr>
<tr>
<td>Use of additional haemostatic</td>
<td>Any additional haemostatic intervention</td>
</tr>
<tr>
<td>intervention</td>
<td></td>
</tr>
<tr>
<td>Coagulopathy</td>
<td>As defined by <strong>WHO Near-miss Approach</strong></td>
</tr>
<tr>
<td>Organ dysfunction</td>
<td>As defined by the <strong>WHO Near-miss Approach</strong></td>
</tr>
<tr>
<td>Adverse effects</td>
<td>As defined by trialists (<strong>intervention specific</strong>)</td>
</tr>
</tbody>
</table>
## RESEARCH AGENDA

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Expert Committee Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient reported outcomes:</strong></td>
<td>Need to explore / develop tools to capture what issues are most important to women in the context of PPH</td>
</tr>
<tr>
<td>a) Women’s sense of wellbeing</td>
<td></td>
</tr>
<tr>
<td>b) Acceptability /satisfaction with intervention</td>
<td></td>
</tr>
<tr>
<td><strong>Breastfeeding</strong></td>
<td></td>
</tr>
</tbody>
</table>
NEXT STEPS

• Dissemination
  • Publication
  • Conferences
  • Websites: COMET, CROWN, WHO RHL

• Implementation
  • Engaged with international stakeholders from the outset
  • Pilot in new/ongoing PPH trials
  • Use in Cochrane reviews relevant to PPH
  • Through funding bodies and research networks
CONCLUSION

The PPH Core Outcome Sets, developed through an international multidisciplinary effort, will help us move towards standardisation of outcome reporting in the evaluation of interventions for PPH.
Acknowledgements

Scientific Advisory Group

Obstetricians
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Parent representatives
Gill Gyte – UK
Alina Bishop – Mexico

Neonatologists
Zulfiqar Bhutta – Pakistan

Thank you!
OUTCOMES DOMAINS

PREVENTION OF PPH
161 OUTCOMES

1. Assessment of blood loss = 86
2. Morbidity / mortality = 10
3. Patient reported outcomes = 3
4. Additional interventions = 1
5. Placental outcomes = 11
6. Use of resources = 5
7. Neonatal outcomes = 6
8. Adverse effects = 5

TREATMENT OF PPH
95 OUTCOMES

1. Assessment of blood loss = 37
2. Morbidity / mortality = 5
3. Patient reported outcomes = 0
4. Additional interventions = 27
5. Use of resources = 4
6. Neonatal outcome = 0
7. Adverse effects = 10
Coagulation dysfunction:
- Failure to form clots or
- blood transfusion ≥ 5 units or
- low platelets <50,000/ml
Prevention COS – Blood loss after birth

All blood loss after birth

Outcome: PREVENTION: Blood loss after birth

Obstetricians (n=61) - 89%
Neonatologists (n=9) - 89%
Haematologists (n=19) - 88%
Anaesthetists (n=11) - 91%

Midwives (n=21) - 95%
Patient Representatives (n=22) - 95%
Policy Makers (n=19) - 79%
SAG (n=16) - 81%
Prevention COS – Blood loss after birth

1. Not important
2. Not important
3. Not important
4. Important but not critical
5. Important but not critical
6. Important but not critical
7. Critical and should be included
8. Critical and should be included
9. Critical and should be included