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

COMET INITIATIVE

CROWN CORE OUTCOMES IN WOMEN'S HEALTH

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

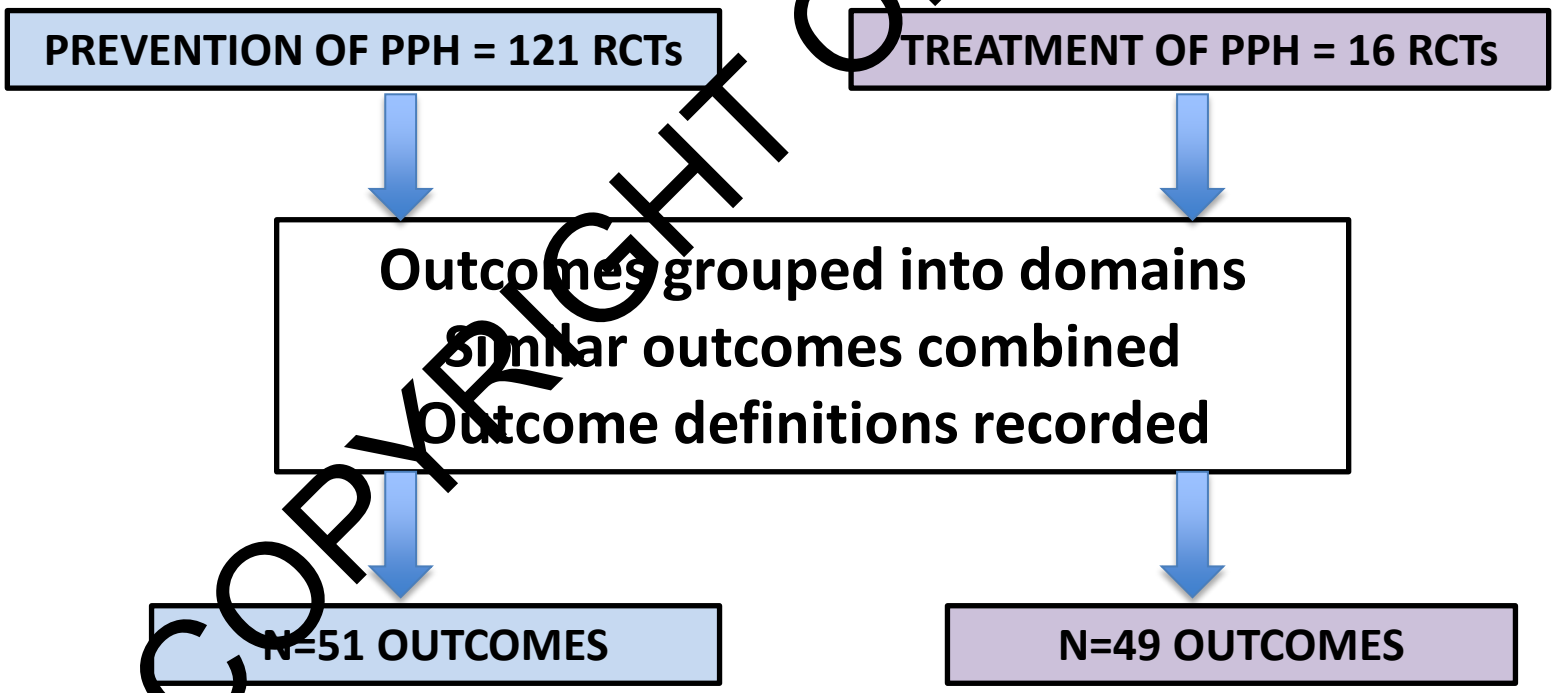
International stakeholders
- Obstetricians, midwives, anaesthetists, haematologists, neonatologists, health strategists, methodologist and parent representatives
- Scientific Advisory Group (n=16, 10 countries)
- Delphi participants (n=221, 44 countries)

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



2. DELPHI SURVEY: TO BUILD CONSENSUS

Participant scored each outcome between 1-9
1-3 – not important
4-6 – important but not critical
7-9 – critically important to include in COS

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 Mallaiah – 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

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

Results: COS for PPH Treatment Trials

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

HOW TO REPORT OUTCOMES

Outcome	COS	Expert committee Recommendation
Blood loss	**Prevention**	**≥500 mls** AND **≥1000 mls** AND **mean/median** blood loss Time frame: from birth of baby to cessation of active bleeding
	Treatment	**Mean + SD / Median + IQ range** Time frame: any additional blood loss after intervention up to cessation of active bleeding.
	Blood loss may be measured or estimated	

HOW TO REPORT COS OUTCOMES

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

RESEARCH AGENDA

Outcome	Expert Committee Recommendation
Patient reported outcomes: a) Women's sense of wellbeing b) Acceptability /satisfaction with intervention	Need to explore / develop tools to capture what issues are most important to women in the context of PPH
Breastfeeding	

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

Edgardo Abalos – Argentina
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Andrew Weeks – UK
Nasreen Aflaifel – UK

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Haematologists

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Parent representatives

Gill Gyte – UK
Alina Bishop – Mexico

Neonatologists

Zulfiqar Bhutta – Pakistan

FACE TO FACE MEETING, LIVERPOOL 2016

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

Evaluating the quality of care for severe pregnancy complications

The WHO near-miss approach for maternal health

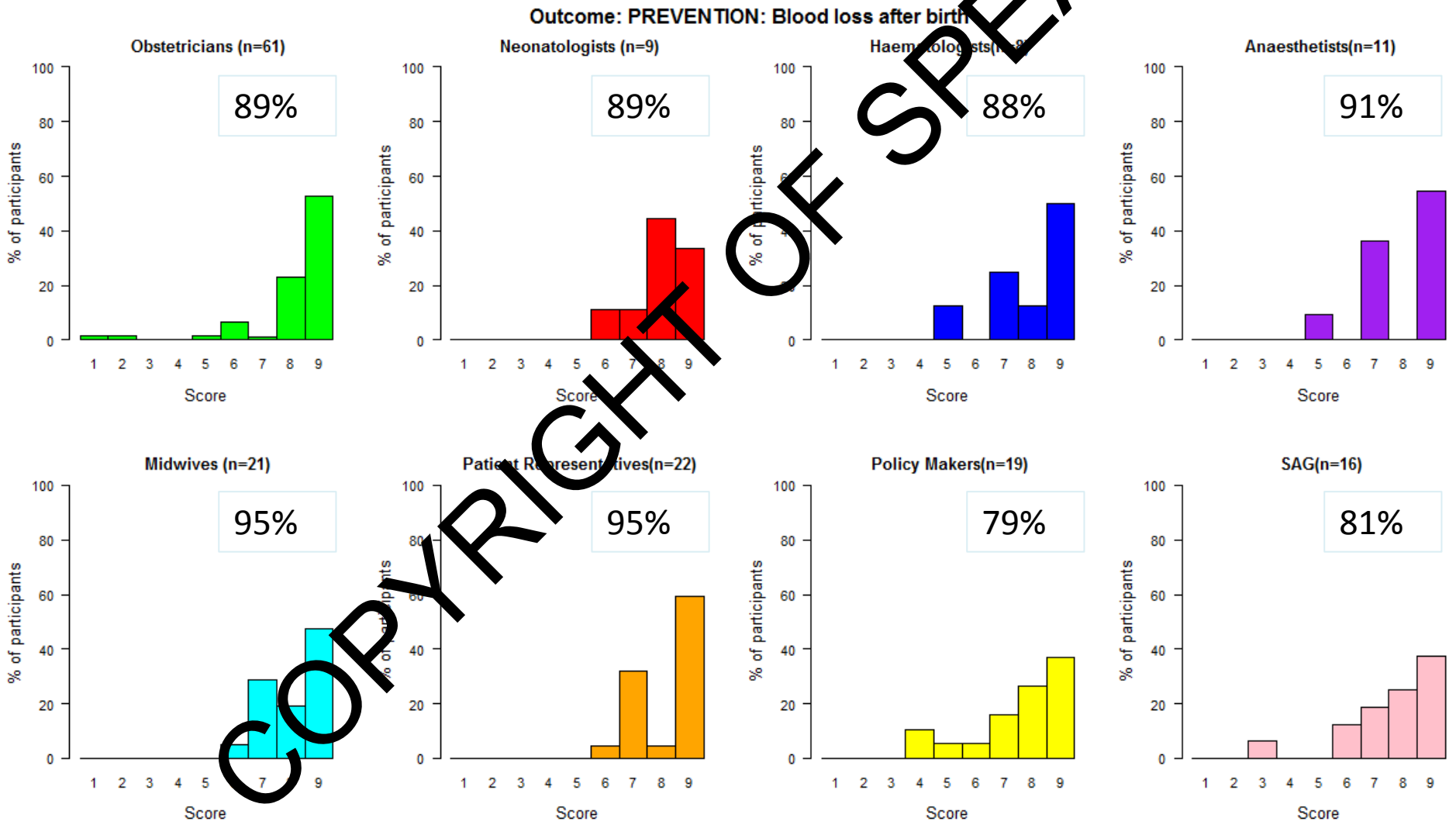
3. Organ dysfunction / life-threatening conditions

- ☐ C0 **Cardiovascular dysfunction**
  [shock, use of continuous vasoactive drugs, cardiac arrest, cardio-pulmonary resuscitation, severe hypoperfusion (lactate >5 mmol/L or >45mg/dL) or severe acidosis (pH<7.1)]
- ☐ C1 **Respiratory dysfunction**
  [acute cyanosis, gasping, severe tachypnea (respiratory rate>40 bpm), severe bradypnea (respiratory rate<6 bpm), severe hypoxemia (PAO2/FIO2<200 O2 saturation <90% for ≥60min) or intubation and ventilation not related to anaesthesia]
- ☐ C2 **Renal dysfunction**
  [oliguria non responsive to fluids or diuretics, dialysis for acute renal failure or severe acute azotemia (creatinine ≥300umol/ml or ≥3.5mg/dL)]
- ☐ C3 **Coagulation/hematologic dysfunction**
  [failure to form clots, massive transfusion of blood or red cells (≥ 5 units) or severe acute thrombocytopenia (<50,000 platelets/ml)]
- ☐ C4 **Hepatic dysfunction**
  [jaundice in the presence of pre-eclampsia, severe acute hyperbilirubinemia (bilirubin>100umol/L or >6.0mg/dL)]
- ☐ C5 **Neurologic dysfunction**
  [prolonged unconsciousness / coma (lasting >12 hours), stroke, status epilepticus / uncontrollable fits, total paralysis]
- ☐ C6 **Uterine dysfunction / Hysterectomy**
  [haemorrhage or infection leading to hysterectomy]

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



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