THE UNIVERSITY of ADELAIDE

Progressing towards core outcomes for maternal & perinatal trials & reviews

Emily Shepherd

seekLIGHT

Robinson Research Institute
Healthy children for life.

What is the issue?

How original should 'original research' be?

- Health care research is **'untidy'**
- Growing recognition that insufficient attention has been paid to **outcomes** for clinical trials
- Well known (including to systematic reviewers), **waste in research**:
  - **Heterogeneity** in outcome measurements
  - Important outcomes **not being assessed**
  - **Selective reporting** of outcomes

E.g. Inconsistent reporting of perinatal mortality

Bain E, Middleton P, Crowther CA. Cochrane Colloquium 2014.

- **68%** (50/74) reviews (2012-13) pre-specified ≥ 1 outcome relating to **perinatal morality**

- **Definitions varied substantially**, e.g.
  - *Perinatal mortality, defined as intrauterine deaths plus newborn deaths in the first week of life*
  - *Perinatal mortality (fetal death and neonatal death up to 28 days)*
  - *Perinatal mortality (variously defined by authors)*

- **32%** (16/50) reviews pre-specified the **components** of perinatal death as separate outcomes

- **48%** (24/50) reviews had **no data** from included trials

- **96%** (25/26) reviews were **unable to confirm/refute effects** (inconsistent reporting; limited reporting: few trials, participants, events)

The need for 'core outcome sets' (COS)

- 1992: **OMERACT** (Outcome Measures for Rheumatology Clinical Trials) collaboration recognised need for standardised outcomes

- 2010: **COMET** (Core Outcome Measures in Effectiveness Trials) Initiative launched (bringing together those interested in COS)
  - **Database**/repository of completed & ongoing COS
  - **Guidance** on developing & reporting COS

- **COS:** "***minimum*** *that should be measured & reported in all clinical trials of a specific condition… making it easier for the results to be* ***compared***, ***contrasted*** & ***combined*** *as appropriate.*"

What is best practice for COS development?

VI Meeting 10-11 November

No gold standard approach for COS development #COMETVI

We must involve **patients & the public** in core outcome set development to reduce research waste #COMETVI

COS developers should consider both **trialists' & systematic reviewers' perspectives** #COMETVI

Guidance documents for COS development

OMERACT
Outcome Measures in Rheumatology

The OMERACT Handbook

Maarten Boers, John Richard Kirwan, Peter Tugwell, Dorcas Beaton, Clifton O. Bingham III, Philip G. Conaghan, Maria-Antonietta D'Agostino, Maarten de Wit, Laure Gossec, Lyn March, Lee S. Simon Jasvinder A Singh, Vibeke Strand, George Wells

PERSPECTIVE

The Harmonizing Outcome Measures for Eczema (HOME) Roadmap: A Methodological Framework to Develop Core Sets of Outcome Measurements in Dermatology

Jochen Schmitt[1], Christian Apfelbacher[2], Phyllis I. Spuls[3], Kim S. Thomas[4], Eric L. Simpson[5], Masutaka Furue[6], Joanne Chalmers[4] and Hywel C. Williams[4]

Core outcome sets (COSs) are consensus-derived minimum sets of outcomes to be assessed in a specific situation. COSs are being increasingly developed to limit outcome-reporting bias, allow comparisons across trials, and strengthen clinical decision making. Despite the increasing interest in outcomes research, methods to develop COSs have not yet been standardized. The aim of this paper is to present the Harmonizing Outcomes

Williamson *et al. Trials* 2012, **13**:132
http://www.trialsjournal.com/content/13/1/132

TRIALS

COMET INITIATIVE

Home | About COMET | Search | Events | Resources | Links | Contact | COMET VI Meeting

Core Outcome Measures in Effectiveness Trials

- Database
- Blogs
- Publications
- Grant-funded projects
- Study protocols
- Downloadable slide set
- Core resource pack
- Plain Language Summary
- Adding trial meta-analysis
- Newsletter
- Public involvement

A walk through core outcome sets – useful references for core outcome set developers

The COMET (Core Outcome Measures in Effectiveness Trials) Initiative brings together researchers interested in the development, application and promotion of COS, derived using rigorous consensus methods, for effectiveness trials. COMET aims to collate and stimulate the development of relevant resources, both applied and methodological, to facilitate exchange of ideas and information, to work with patients, the public and their representatives to develop material to improve health service user engagement, and to foster methodological research in the area of COS. Data on relevant individual studies, both published and ongoing, are being included in a free, publically available internet-based resource. This is a unique resource, which is updated periodically, and which should serve to minimize duplication of effort in the development of COS. A systematic review to identify studies which sought to determine which outcomes/domains to measure in all clinical trials in a specific condition has been completed. This systematic review identified many health areas where a COS has been developed, but also highlights important gaps. It is a further step towards a comprehensive, up-to-date database of COS.

In an interesting commentary, Mike Clarke asks some important questions: Why do we need such initiatives? What's the problem? And are these and other initiatives the solution? This paper provides a good overview of the problems with outcomes in trials.

Accumulating work in this area has identified the need for general guidance on the development of core outcome sets, and this is ongoing. Williamson et al suggest key issues to consider in the development of a core outcome set including its scope, the stakeholder groups to involve, choice of consensus method and the achievement of a consensus. There is also a useful review of studies using the Delphi technique to determine which outcomes to measure in trials, that also provides guidance about using this technique to determine core outcome sets.

COMMENTARY Open Access

Developing core outcome sets for clinical trials: issues to consider

Paula R Williamson[1*], Douglas G Altman[2], Jane M Blazeby[3], Mike Clarke[4], Declan Devane[5], Elizabeth Gargon[1] and Peter Tugwell[6]

Abstract

The selection of appropriate outcomes or domains is crucial when designing clinical trials in order to compare directly the effects of different interventions in ways that minimize bias. If the findings are to influence policy and practice then the chosen outcomes need to be relevant and important to key stakeholders including patients and the public, health care professionals and others making decisions about health care. There is a growing recognition that insufficient attention has been paid to the outcomes measured in clinical trials. These issues could be addressed through the development and use of an agreed standardized collection of outcomes, known as a core outcome set, which should be measured and reported, as a minimum, in all trials for a specific clinical area. Accumulating work in this area has identified the need for general guidance on the development of core outcome sets. Key issues to consider in the development of a core outcome set include its scope, the stakeholder groups to involve, choice of consensus method and the achievement of a consensus.

Keywords: Core outcome set, Outcome reporting bias, Clinical trials, Systematic review, Methodology, Consensus

Steps in COS development

Step 1: Define scope & applicability
Population (condition); intervention; setting (e.g., trial, registry, clinical practice); geographical/regional scope; stakeholders

Step 2: Develop core set of outcomes
Identify existing knowledge; stakeholder involvement; consensus methods; achieve global consensus

Step 3: Identify core set of outcome measurements
Identification & recommendation of adequate measurement instrument(s) for each core outcome

Step 4: Disseminate
Prepare guidance material, review, & possibly revise core set of outcomes

Common methods in COS development

***Gorst al. Choosing important health outcomes for comparative effectiveness research: an updated review and user survey. PloS One 2016.* [> 200 COS studies]**

Identify existing knowledge
Systematic review of trials or reviews ➔
need for a COS &/or potential list of outcomes (~70%)

Stakeholder involvement
Clinical experts (~100%); patients & public representatives (59% & 🡅);
non-clinical research expert (~50%); authorities; industry; funders

Consensus method
E.g. Delphi technique (~30% & 🡅), expert panel meetings, focus groups

Achieve global consensus
E.g. Expert panels, conference workshops

Guidance for use of Delphi technique for COS

OPEN ACCESS Freely available online

PLOS MEDICINE

Guidelines and Guidance

Using the Delphi Technique to Determine Which Outcomes to Measure in Clinical Trials: Recommendations for the Future Based on a Systematic Review of Existing Studies

Ian P. Sinha[1]*, Rosalind L. Smyth[1¶], Paula R. Williamson[2¶]

1 University of Liverpool, Alder Hey Children's Hospital, Liverpool, United Kingdom, **2** Department of Biostatistics, Faculty of Medicine, University of Liverpool, Liverpool, United Kingdom

Keeley *et al. Trials* (2016) 17:230
DOI 10.1186/s13063-016-1356-7

Trials

METHODOLOGY Open Access

The use of qualitative methods to inform Delphi surveys in core outcome set development

T. Keeley[1*], P. Williamson[2], P. Callery[3], L. L. Jones[1], J. Mathers[1], J. Jones[1], B. Young[4] and M. Calvert[1]

Including patients in COS development

Young and Bagley *Research Involvement and Engagement* (2016) 2:25
DOI 10.1186/s40900-016-0039-6

Research Involvement and Engagement

COMMENTARY Open Access

Including patients in core outcome set development: issues to consider based on three workshops with around 100 international delegates

Bridget Young[1*] and Heather Bagley[2]

Reporting guidance for COS (COS-STAR)

PLOS | MEDICINE

GUIDELINES AND GUIDANCE

Core Outcome Set–STAndards for Reporting: The COS-STAR Statement

Jamie J. Kirkham[1], Sarah Gorst[1], Douglas G. Altman[2], Jane M. Blazeby[3], Mike Clarke[4], Declan Devane[5], Elizabeth Gargon[1], David Moher[6], Jochen Schmitt[7], Peter Tugwell[8], Sean Tunis[9], Paula R. Williamson[1]*

1 MRC North West Hub for Trials Methodology Research, Department of Biostatistics, University of Liverpool, Liverpool, United Kingdom, **2** Centre for Statistics in Medicine, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, United Kingdom, **3** MRC ConDuCT II Hub for Trials Methodology Research, School of Social and Community Medicine, University of Bristol, Bristol, United Kingdom, **4** Northern Ireland Hub for Trials Methodology Research, Centre for Public Health, Queen's University Belfast, Belfast, United Kingdom, **5** National University of Ireland Galway and HRB Trials Methodology Research Network, Ireland, **6** Ottawa Methods Centre, Ottawa Hospital Research Institute, Ottawa, Canada, **7** Center for Evidence-Based Healthcare, Medizinische Fakultät, Technische Universität Dresden, Dresden, Germany, **8** Institute of Population Health, University of Ottawa, Ottawa, Canada, **9** Center for Medical Technology Policy, Baltimore, Maryland, United States of America

* prw@liv.ac.uk

OPEN ACCESS

Citation: Kirkham JJ, Gorst S, Altman DG, Blazeby JM, Clarke M, Devane D, et al. (2016) Core Outcome Set–STAndards for Reporting: The COS-STAR Statement. PLoS Med 13(10): e1002148.

Abstract

Reporting guidance for COS (COS-STAR)

Table 1. Core Outcome Set-STandards for Reporting: The COS-STAR Statement.

SECTION/TOPIC	ITEM No.	CHECKLIST ITEM
TITLE/ABSTRACT		
Title	1a	Identify in the title that the paper reports the development of a COS
Abstract	1b	Provide a structured summary
INTRODUCTION		
Background and Objectives	2a	Describe the background and explain the rationale for developing the COS.
	2b	Describe the specific objectives with reference to developing a COS.
Scope	3a	Describe the health condition(s) and population(s) covered by the COS.
	3b	Describe the intervention(s) covered by the COS.
	3c	Describe the setting(s) in which the COS is to be applied.
METHODS		
Protocol/Registry Entry	4	Indicate where the COS development protocol can be accessed, if available, and/or the study registration details.
Participants	5	Describe the rationale for stakeholder groups involved in the COS development process, eligibility criteria for participants from each group, and a description of how the individuals involved were identified.
Information Sources	6a	Describe the information sources used to identify an initial list of outcomes.
	6b	Describe how outcomes were dropped/combined, with reasons (if applicable).
Consensus Process	7	Describe how the consensus process was undertaken.

Reporting guidance for COS (COS-STAR)

Outcome Scoring	8	Describe how outcomes were scored and how scores were summarised.
Consensus Definition	9a	Describe the consensus definition.
	9b	Describe the procedure for determining how outcomes were included or excluded from consideration during the consensus process.
Ethics and Consent	10	Provide a statement regarding the ethics and consent issues for the study.
RESULTS		
Protocol Deviations	11	Describe any changes from the protocol (if applicable), with reasons, and describe what impact these changes have on the results.
Participants	12	Present data on the number and relevant characteristics of the people involved at all stages of COS development.
Outcomes	13a	List all outcomes considered at the start of the consensus process.
	13b	Describe any new outcomes introduced and any outcomes dropped, with reasons, during the consensus process.
COS	14	List the outcomes in the final COS.
DISCUSSION		
Limitations	15	Discuss any limitations in the COS development process.
Conclusions	16	Provide an interpretation of the final COS in the context of other evidence, and implications for future research.
OTHER INFORMATION		
Funding	17	Describe sources of funding/role of funders.
Conflicts of Interest	18	Describe any conflicts of interest within the study team and how these were managed.

Guidance for outcome selection (COSMIN)

Prinsen *et al. Trials* (2016) 17:449
DOI 10.1186/s13063-016-1555-2

Trials

RESEARCH Open Access

How to select outcome measurement instruments for outcomes included in a "Core Outcome Set" – a practical guideline

Cecilia A. C. Prinsen[1*], Sunita Vohra[2,3,4], Michael R. Rose[5], Maarten Boers[1,6], Peter Tugwell[7], Mike Clarke[8], Paula R. Williamson[9] and Caroline B. Terwee[1]

1: Conceptual considerations
2. Finding existing OMIs
3. Quality assessment of OMIs
4. Generic recommendations on selection of OMIs for a COS

Guidance for COS implementation

Researchers are more likely to use each others toothbrush than each other's outcome set #COMETVI

- **Publication** consensus statement supplemented
- **Presentatio** etings)
- **Disseminati** funders, trial registries, journals, cons
- **Guidance m** amples of presentation)
- **Monitoring** plementation)
- **Review** & **up**

Are we progressing towards COS for maternal & perinatal trials & reviews?

Early support for standard outcomes

WOMBAT

- NHMRC enabling grant 2005-10: Australian researchers & practitioners, supporting high-quality **maternal & perinatal randomised trials**
- Support for **standard outcomes** to assist trialists
- Sets of standard outcomes on website, including for **GDM**
  - Developed in 2009 through extraction & group harmonisation of outcomes (from selected clinical trials & reviews)

Australian and New Zealand Journal of Obstetrics and Gynaecology 2016 DOI: 10.1111/ajo.12433

Short Communication

Progressing towards standard outcomes in gestational diabetes Cochrane reviews and randomised trials

Emily BAIN,[1] Philippa MIDDLETON[1] and Caroline A. CROWTHER[1,2]

[1]*Australian Research Centre for Health of Women and Babies, Robinson Research Institute, Discipline of Obstetrics and Gynaecology, School of Medicine, The University of Adelaide, Adelaide, South Australia, Australia and* [2]*Liggins Institute, The University of Auckland, Auckland, New Zealand*

Outcomes in gestational diabetes Cochrane protocols and reviews before and after development of 'standard outcomes' by WOMBAT (WOMen and Babies health and well-being: Action through Trials) were surveyed. An increase in 'common' outcomes (those prespecified by ≥50% of the protocols and reviews) over time was observed (2001–2009: 27 vs 2010–2014: 46). There were discrepancies in outcomes prespecified in reviews and reported by randomised trials. Efforts are needed to develop a core outcome set, to reduce research waste and improve health outcomes.

Key words: clinical trial, gestational diabetes, outcome assessment, research design, systematic review.

17 GDM Cochrane protocols/reviews

Year published	Scope	Included trials	Trials published
2001	Management	1	1993
2006	Management	4	1989-2004
2007	Management	5	1984-2005
2008	Prevention	3	1983-2006
2009	Management	8	1989-2005
2009	Management	NA (Protocol)	NA
2010	Management	0	NA
2011	Detection/management	5	1985-2004
2011	Follow up/type 2 prevention	NA (Protocol)	NA
2012	Prevention	5	2009-2012
2012	Prevention	NA (Protocol)	NA
2012	Management	4	1989-2011
2013	Prevention	NA (Protocol)	NA
2013	Management	9	1990-2011
2013	Prevention/management	0	NA
2014	Detection/management	4	1992-2003
2014	Follow up/type 2 prevention	1	2009
Total		**49**	**1983-2012**

Mother	Baby	Health services
GDM	Perinatal mortality	Hospital or health professional visits (mother)
Mode of birth (caesarean section)	Large-for-gestational age	Length of postnatal stay (mother)
Induction of labour	Macrosomia	Admission to neonatal ward
Pre-eclampsia	Birthweight	Length of postnatal stay (baby)
Perineal trauma	Small-for-gestational age*	Cost of maternal care
Weight gain during pregnancy*	Ponderal index*	Cost of offspring care*
Postpartum haemorrhage	Gestational age at birth	
Postpartum infection	Preterm birth	
Sense of wellbeing and quality of life	Shoulder dystocia	
View of the intervention	Bone fracture	
Use of insulin or other hypoglycaemic agent	Nerve palsy	
Longer-term	Respiratory distress syndrome	
BMI*	Apgar scores (less than seven at five minutes)*	
GDM in subsequent pregnancy*	Hyperbilirubinaemia requiring treatment	
Development of type 2 diabetes*	Neonatal hypoglycaemia requiring treatment	
Development of type 1 diabetes*	**Longer-term**	
Impaired glucose tolerance*	BMI, fat mass/fat-free mass, skin fold thickness*	
	Blood pressure*	
	Impaired glucose tolerance*	
	Development of type 1 diabetes*	
	Development of type 2 diabetes*	
	Dyslipidaemia or metabolic syndrome*	
	Neurodisability*	

Increase in 'common' outcomes

*Additional common outcomes in reviews published 2010-2014

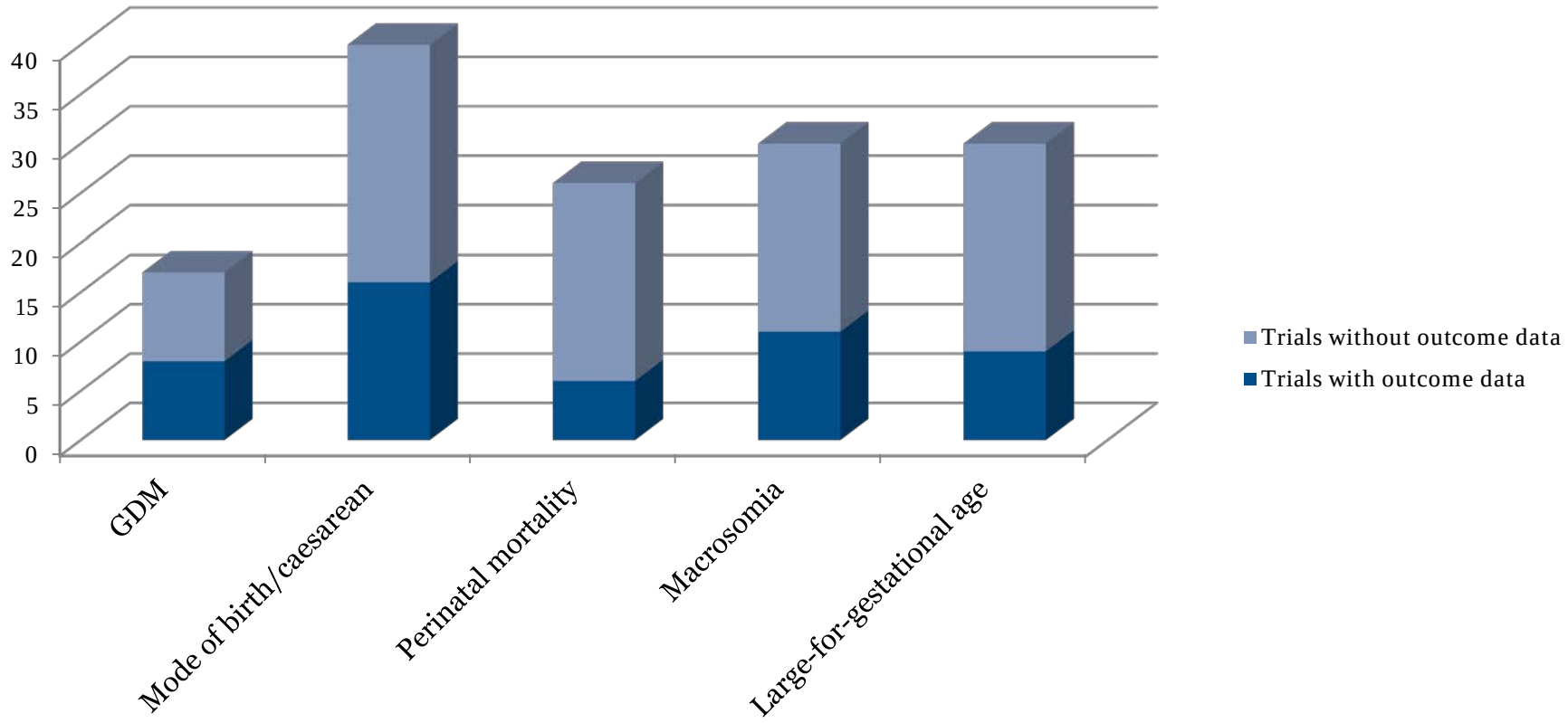
~ Consistent primary outcomes in GDM reviews

Outcome	Primary outcome in relevant reviews	Secondary outcome in relevant reviews
GDM	100%	
Type 2 diabetes	100%	
Caesarean birth	79%	21%
Perinatal mortality	71%	29%
Macrosomia	71%	29%
Large-for-gestational age	64%	36%

12 different primary maternal outcomes;
9 unique (e.g. health related QoL)

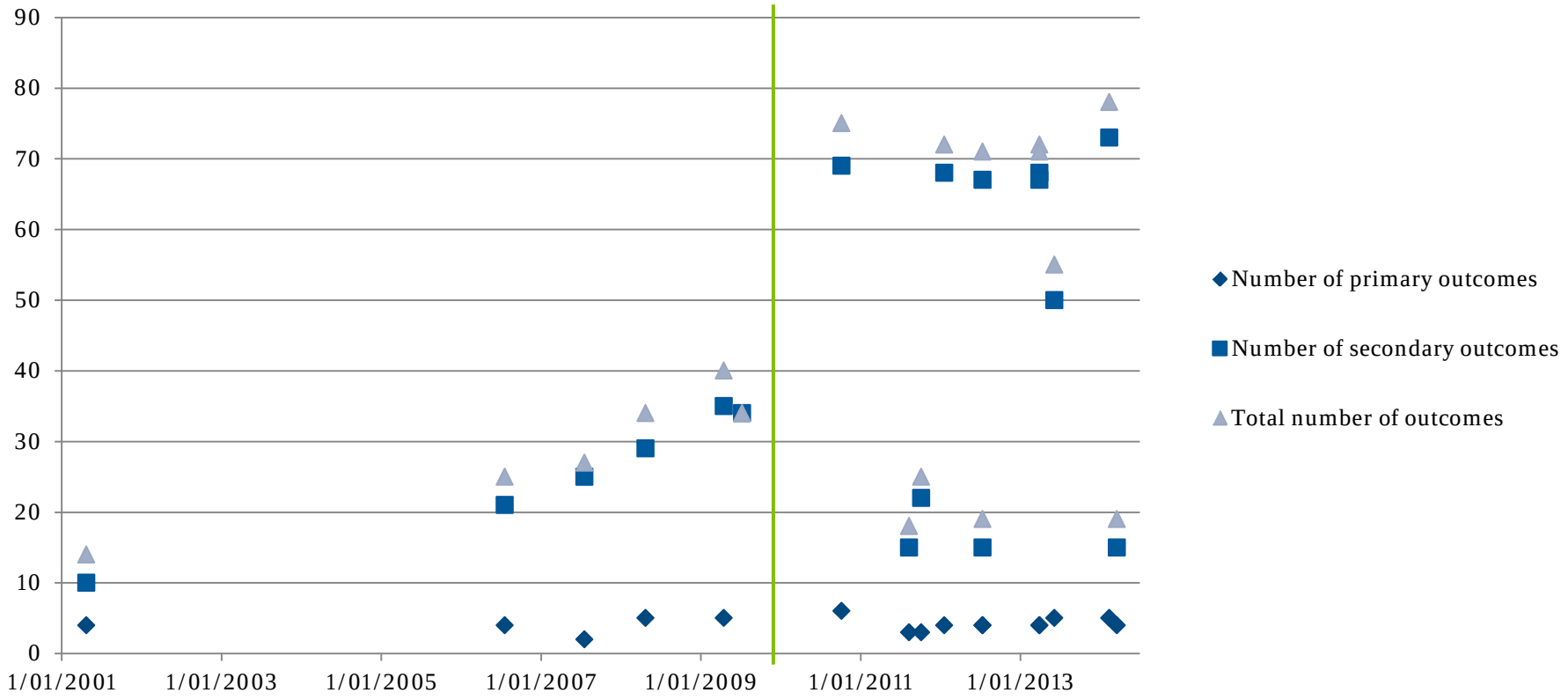
9 different primary infant outcomes;
6 unique (e.g. NICU admission)

Limited primary outcome data from GDM trials



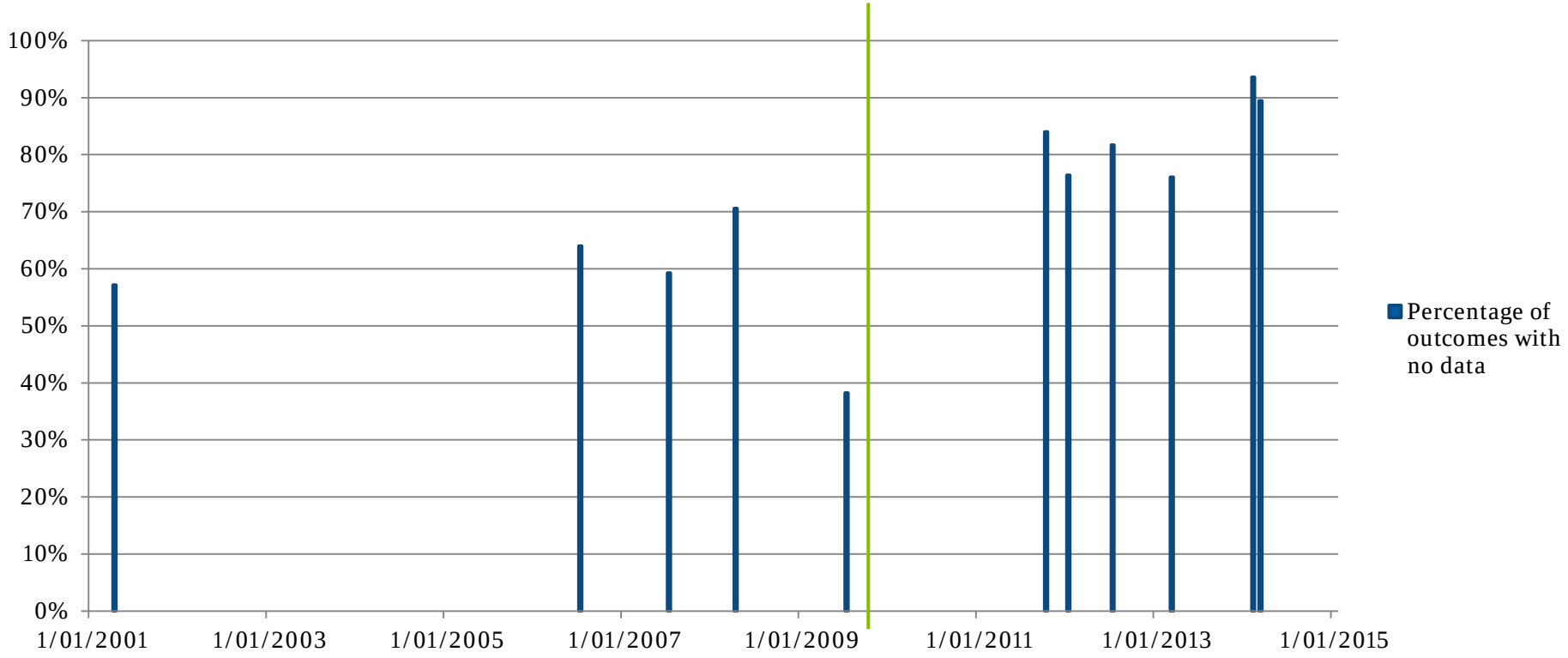
Number of trials reporting data on common primary outcomes

↑ in pre-specified outcomes in GDM reviews



Number of pre-specified review outcomes in GDM reviews

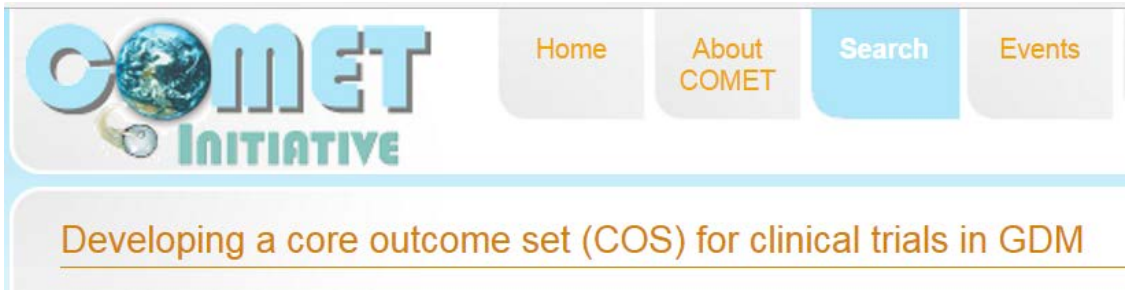
No outcome data from GDM trials



% pre-specified outcomes in GDM Cochrane reviews with no reported data

Progressing towards a GDM COS

- Some **progress**; **inconsistencies** persist… selective reporting of outcomes or outcomes not measured?
- **To date…**
  - WOMBAT 'standard outcomes' (Australia)
  - '*High priority needs for gestational diabetes mellitus*' (USA; outcome prioritisation; 9 individuals) (Bennett et al. J Women's Health 2012)
  - Need **international** GDM COS



Maternal & perinatal COS, where are we now?

Review of existing & planned COS developments

Survey of reviews using COS

46 pregnancy & childbirth COS studies

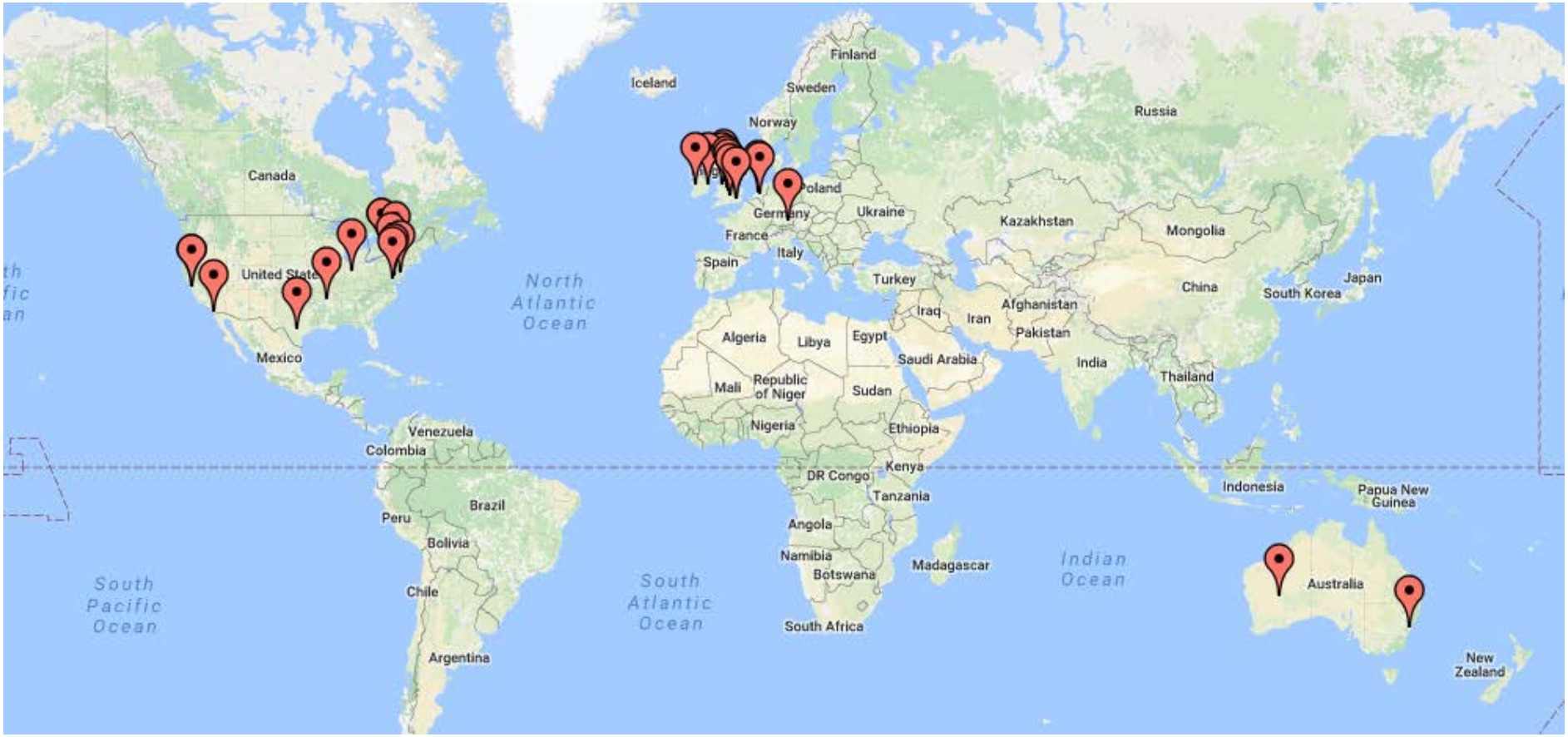
Topic area
Induced abortion
Miscarriage (prevention; surgical management; medical management) (3)
Bereavement care following intrauterine death, stillbirth, neonatal death
Reduced fetal movements
Hyperemesis gravidarum
Intrauterine growth restriction
Twin-to-twin transfusion syndrome
Hypertensive disorders; pre-eclampsia; late-onset pre-eclampsia (3)
Preconception care for pre-gestational diabetes
Gestational diabetes (2)
Salutogenic intrapartum care (2)
Intrapartum fetal assessment
Oxytocin for delay in labour
Induction of labour
Pain management in labour
Breech presentation (moxibuston)*

Topic area
Caesarean birth maternal infectious outcomes
Postpartum haemorrhage
Very preterm; preterm prevention; preterm in LMIC (5)
Breastfeeding
Pregnant women requiring ventilation
Immune thrombocytopenia
Iron deficiency anaemia
Cardiovascular disease after reproductive disorders
Cardiac disease
Epilepsy
Venous thromboembolism
Preconception & early pregnancy care (obesity)*
Multiple pregnancy
Pregnancy & childbirth
Maternity care
Maternal morbidity (definitions)
Endometriosis (2)
Infertility (2)

15 neonatal care COS studies

Topic area
Neonatology (routinely collected data)
Necrotising enterocolitis (definition)
Gastroschisis
Neonatal abstinence syndrome
Chronic lung disease
Infant nutrition (2)
Apneoa of prematurity
Newborn drug development
Cardiovascular instability in preterm infants
Neonatal analgesia and anaesthesia (2)
Postoperative cardiac dysfunction
Neonatal seizures
Human milk & infection in preterm infants

who's leading COS studies?



PIs on COMET registered studies

methods used in COS studies?

COS Study Methods	N = 30
Mixed methods Most commonly: Survey/systematic review ➔ Delphi technique (+/-interviews/focus group meetings) ➔ Consensus meeting	22
Systematic/literature review only	5
Unstructured group discussion only	1
Delphi technique only	2

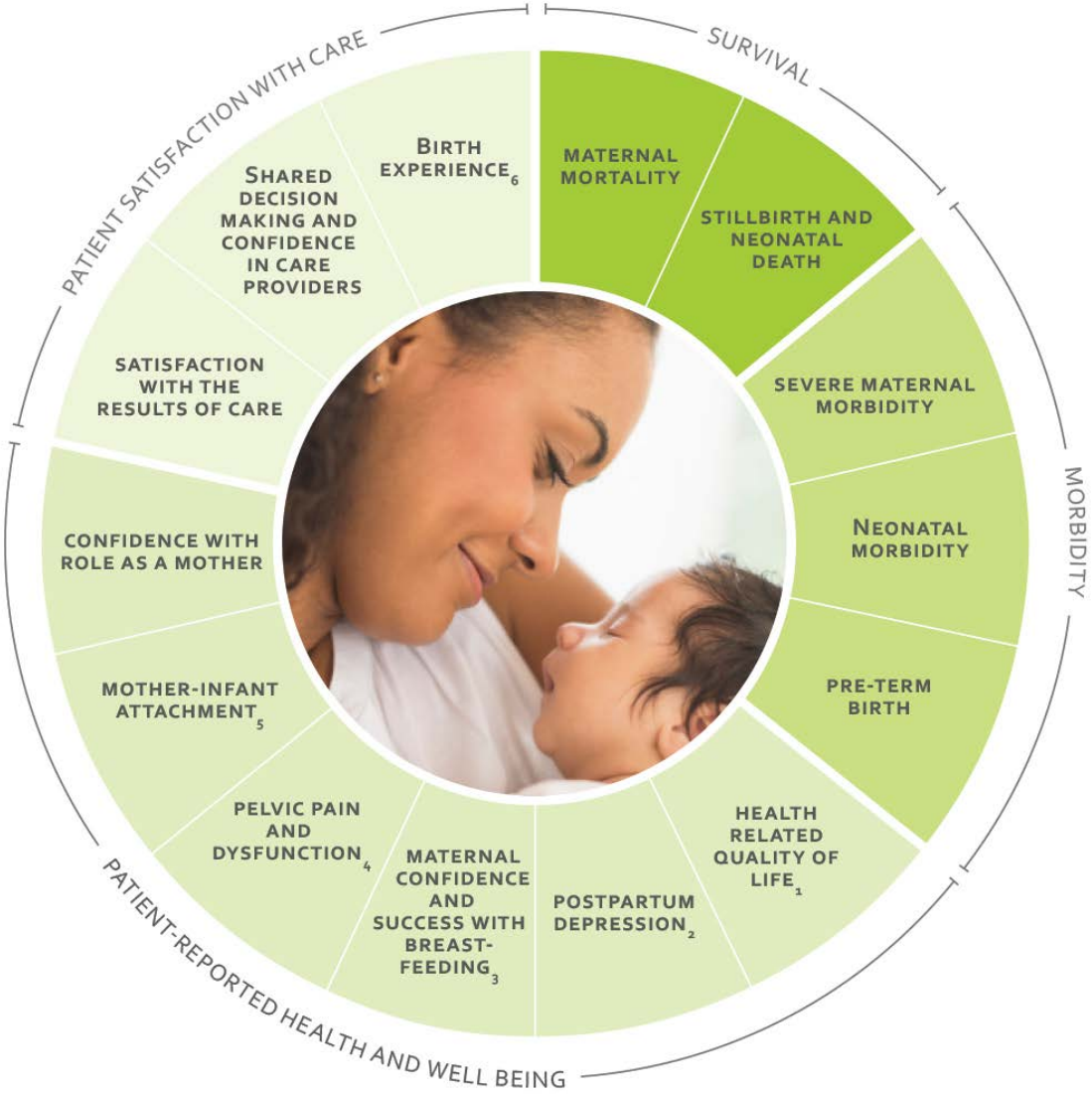
~1/3 studies published; others 'ongoing'

- **Predominately preliminary work**, e.g:
  - Hirsch et al. Variation in outcome reporting in **endometriosis** trials: a systematic review. Am J Obstet Gynaecol 2016.
  - Dapuzzo et al. Incomplete & inconsistent reporting of maternal & fetal outcomes in **infertility** treatment trials. Fertil Steril 2011.
  - Meher et al. Choice of primary outcomes in randomised trials & systematic reviews evaluating interventions for **preterm birth prevention**: a systematic review. BJOG 2014.
  - Begley et al. Outcome measures in studies on the use of **oxytocin for the treatment of delay in labour**: A systematic review. Midwifery 2014.
  - Gladstone et al. Survival, morbidity, growth & developmental delay for babies born **preterm** in low & middle income countries - a systematic review of outcomes measured. PloS One 2015.

~1/3 studies published; others 'ongoing'

- **Few completed maternal or perinatal COS**, e.g:
  - Devan et al. Evaluating **maternity care**: a core set of outcome measures. Birth 2007.
  - Jones et al. **Pain management** for women in **labour**: an overview of systematic reviews. Cochrane Database Sys Rev 2012.
  - Myatt et al. Strategy for standardization of **preeclampsia** research study design. Hypertension 2014.
  - Fong et al. Development of maternal and neonatal composite outcomes for trials evaluating management of **late onset pre-eclampsia**. Hypertens Pregnancy 2014.
  - Van't Hooft et al. A core outcome set for evaluation of interventions to **prevent preterm birth**. Obstet Gynecol 2016.
  - ICHOM. **Pregnancy and Childbirth**.

ICHOM: Pregnancy & Childbirth



ICHOM International Consortium for Health Outcomes Measurement

PREGNANCY & CHILDBIRTH DATA COLLECTION REFERENCE GUIDE

Version 1.1
Revised: November 17th, 2016

Cochrane reviews using COS

- **8% (73/890) make reference to 'generic protocol'**
  - E.g. Down's syndrome screening; preventing pre-eclampsia; treating pre-eclampsia; induction of labour; pain management for women in labour; perineal pain
- **2% (15/890) make reference to 'core outcomes'**
  - Pain management for women in labour (overview) (collaboration with PCG consumer group; stakeholder meeting (funders, researchers, editors, consumers); further consultation)
  - Prevention of postpartum haemorrhage; tocolysis for preterm labour (8); diabetes in pregnancy (2); retained placenta (2) (editors & authors); newborn ventilation (no COS – under development)

Cochrane Pregnancy and Childbirth

Cochrane Neonatal

Challenge of follow-up outcomes in COS

Cochrane Library

Cochrane Database of Systematic Reviews

Antenatal and intrapartum interventions for preventing cerebral palsy: an overview of Cochrane systematic reviews (Protocol)

Shepherd E, Middleton P, Makrides M, McIntyre SJ, Badawi N, Crowther CA

Cochrane Library

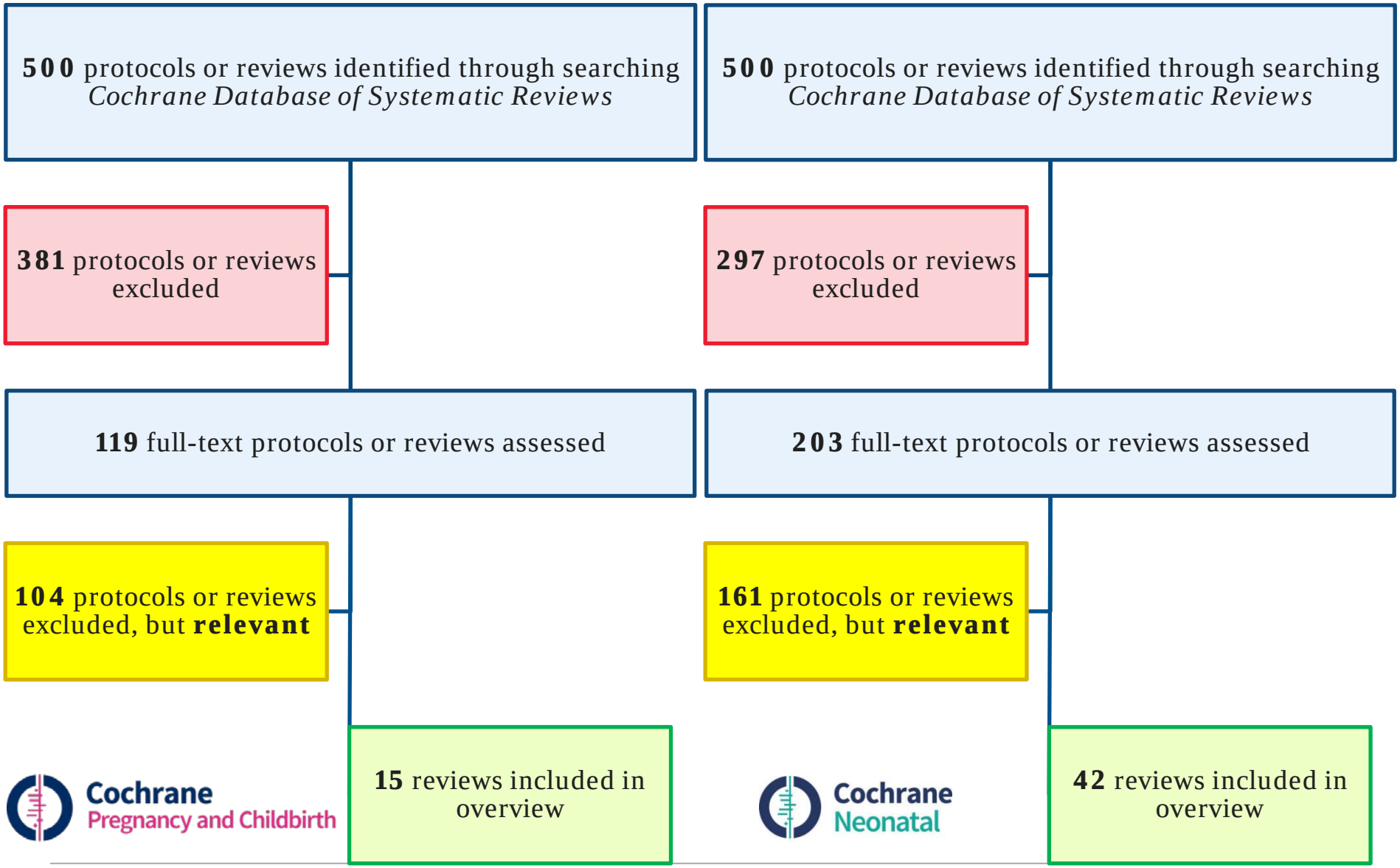
Cochrane Database of Systematic Reviews

Neonatal interventions for preventing cerebral palsy: an overview of Cochrane systematic reviews (Protocol)

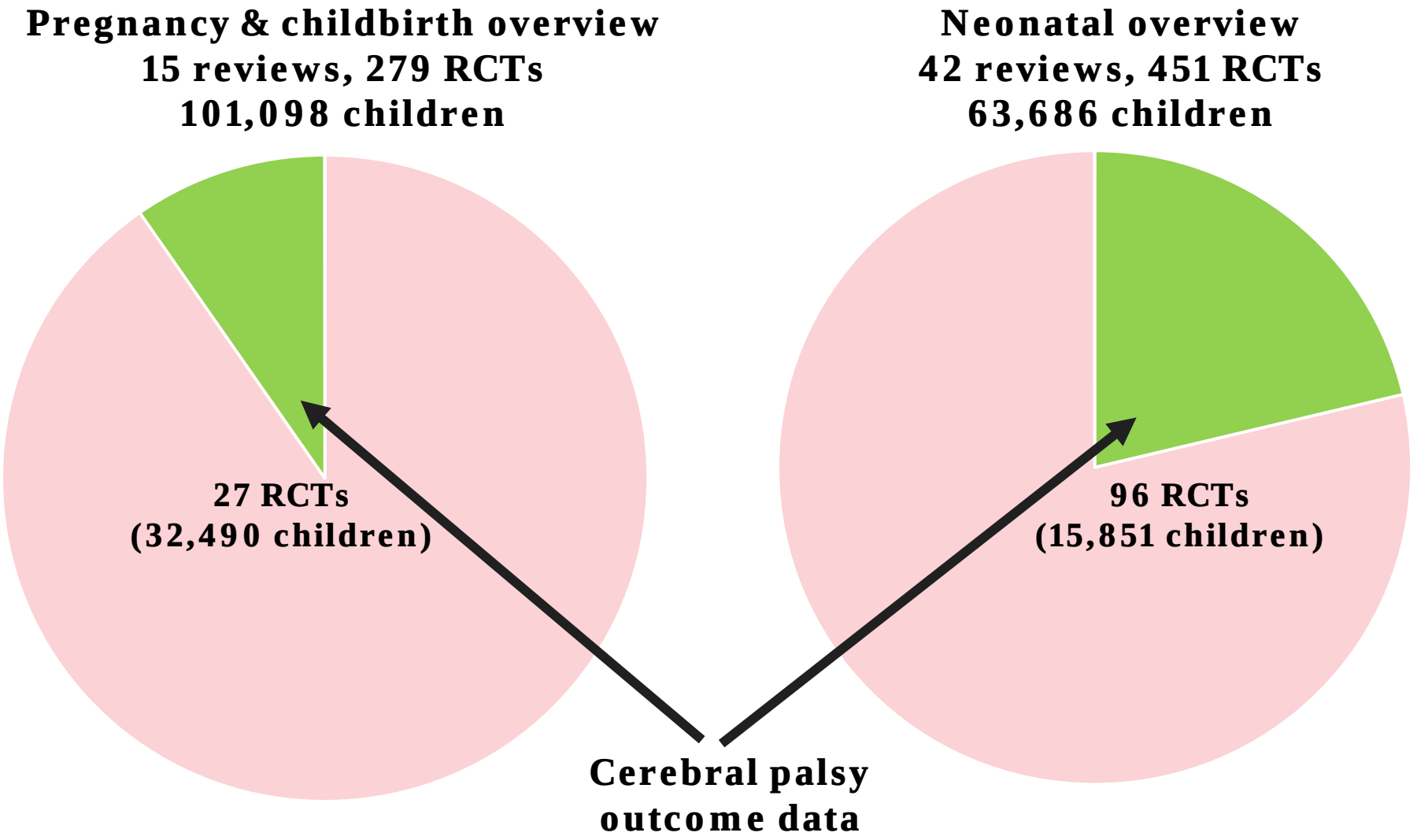
Shepherd E, Middleton P, Makrides M, McIntyre S, Badawi N, Crowther CA

Cerebral Palsy ALLIANCE RESEARCH FOUNDATION

Reporting of cerebral palsy in trials



Reporting of cerebral palsy in trials



Exploring data linkage for cerebral palsy

ACTOMgSO$_4$

CP Register

Piecing together the facts on cerebral palsy

The WISH Project

Routinely collected data & neonatal COS

Imperial College London

MRC Medical Research Council

Chelsea and Westminster Hospital NHS
NHS Foundation Trust

Core Outcomes In Neonatology

A Core Outcome Set based on routinely collected data

Core Outcomes In Neonatology

James Webbe[1], Ginny Brunton[2], Shohaib Ali[3], Neena Modi[1] and Chris Gale[1]

1 Neonatal Medicine, Imperial College London, Chelsea and Westminster Hospital Campus, SW10 9NH

2 Evidence for Policy and Practice Information and Coordinating (EPPI-) Centre, UCL Institute of Education, University College London, WC1H 0NR, United Kingdom

3. Faculty of Medicine, Imperial College London, London, SW10 9NH, United Kingdom

BACKGROUND

Each year 700,000 babies are born in the United Kingdom, and of these over 86,000 (almost 1 in 8) will require admission to a neonatal unit for medical care (1). The neonatal period is increasingly recognised as crucial to long-term health: 42% of all deaths in childhood occur in the neonatal period (2); neonatal conditions are a leading cause of morbidity in childhood and are implicated in the pathogenesis of adult non-communicable diseases (3). Despite this there is a paucity of evidence for even routine neonatal clinical practice such as feeding (4); this leads to wide variation in clinical care and is associated with wide variation in outcomes

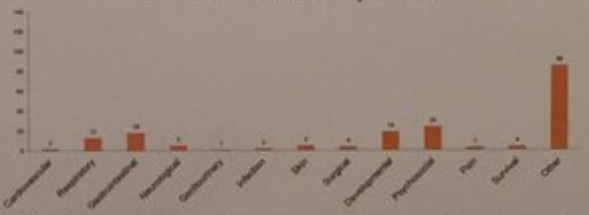
At present there is no Core Outcome Set for neonatal medicine, but neonatal medicine has the relatively unique advantage that a large amount of clinical data is collected as part of routine care by neonatal nurses and doctors every day (in the UK this data forms the National Neonatal Research Database (NNRD); similar repositories exist in other countries). Existing data sources could be used to collect data on Core Outcomes without additional workload burden.

A systematic review of Cochrane reviews in neonatology performed in 2013 (4) found the following:

- In 47% of reviews (122/262) specific recommendations were not issued and the review was inconclusive
- This proportion has been increasing (38% of reviews from 1996-2000: 58% of reviews from 2006-2010)
- Common reasons for inconclusive reviews were the small number of patients, insufficient data, insufficient methodological quality and heterogeneity of studies

IDENTIFYING POTENTIAL OUTCOMES

To identify outcomes measured in clinical trials involving preterm babies we searched CENTRAL, CINAHL, EMBASE and MEDLINE over the preceding 5 years. We systematically extracted and categorised outcomes reported in included trials. 95 trials were identified containing 461 outcomes. There was great diversity in outcomes (e.g. survival measured at 17 discrete time-points).



To identify which outcomes are important to patients, parents and clinicians qualitative research in neonatal medicine was identified from MEDLINE, CINAHL, EMBASE, Psycinfo and ASSIA over the preceding 20 years. We systematically extracted and

Progressing towards COS: what now?

How original should 'original research' be?
Too much originality won't help patients #COMETVI

- **Trial and systematic review development**
  - Search for COS; use it; consider adaptation of relevant COS
    - ↑ requirement of trial registries (e.g. ISRCTN), journals (e.g. CROWN), collaborations (e.g. Cochrane) and funders (e.g. NIHR)

- **COS development**
  - Register
  - Follow evolving best practice methodology (OMERACT, COMET, etc.)
    - Consider all stages of development: **scope** of COS; **what** to measure; **how** to measure; **implementation** & audit
  - Think **globally**

Thank you!

Multiple outcomes lead to a **measurement fruit salad**...

but this can be **stratified** #COMETVI