Is research waste avoidable?

Marie Österberg

SBU

SWEDISH AGENCY FOR HEALTH TECHNOLOGY ASSESSMENT AND ASSESSMENT OF SOCIAL SERVICES

PLOS MEDICINE

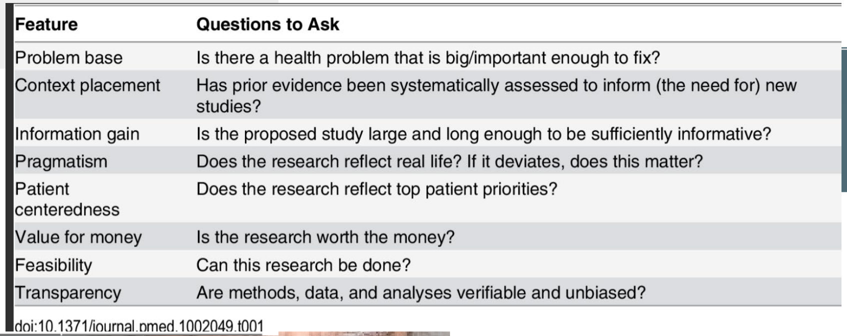
OPEN ACCESS

ESSAY

Why Most Clinical Research Is Not Useful

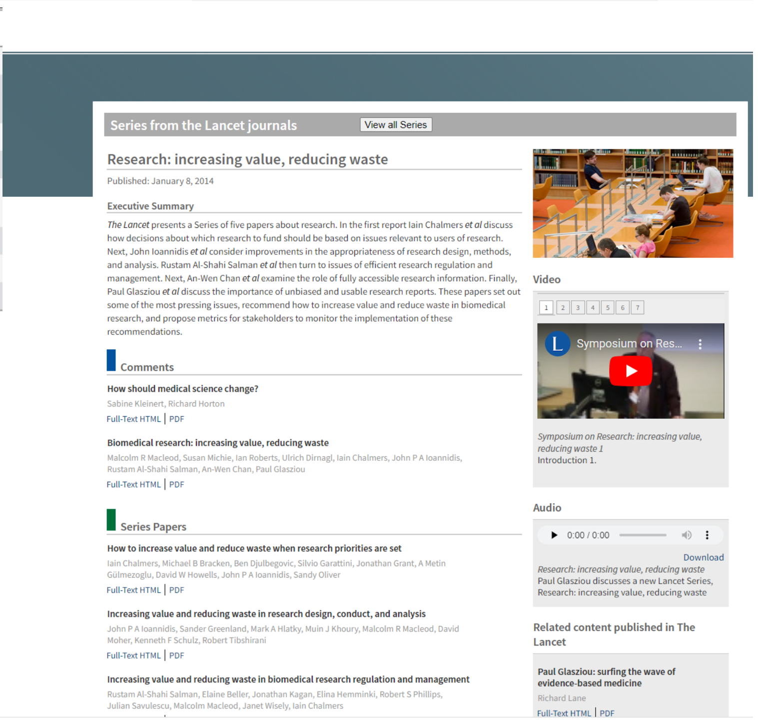
John P. A. Ioannidis

Published: June 21, 2016 • https://doi.org/10.1371/journal.pmed.1002049



Feature	Questions to Ask
Problem base	Is there a health problem that is big/important enough to fix?
Context placement	Has prior evidence been systematically assessed to inform (the need for) new studies?
Information gain	Is the proposed study large and long enough to be sufficiently informative?
Pragmatism	Does the research reflect real life? If it deviates, does this matter?
Patient centeredness	Does the research reflect top patient priorities?
Value for money	Is the research worth the money?
Feasibility	Can this research be done?
Transparency	Are methods, data, and analyses verifiable and unbiased?

doi:10.1371/journal.pmed.1002049.t001



Research: increasing value, reducing waste

Published: January 8, 2014

Executive Summary

The Lancet presents a Series of five papers about research. In the first report Iain Chalmers *et al* discuss how decisions about which research to fund should be based on issues relevant to users of research. Next, John Ioannidis *et al* consider improvements in the appropriateness of research design, methods, and analysis. Rustam Al-Shahi Salman *et al* then turn to issues of efficient research regulation and management. Next, An-Wen Chan *et al* examine the role of fully accessible research information. Finally, Paul Glasziou *et al* discuss the importance of unbiased and usable research reports. These papers set out some of the most pressing issues, recommend how to increase value and reduce waste in biomedical research, and propose metrics for stakeholders to monitor the implementation of these recommendations.

Comments

How should medical science change?
Sabine Kleinert, Richard Horton
Full-Text HTML | PDF

Biomedical research: increasing value, reducing waste
Malcolm R Macleod, Susan Michie, Ian Roberts, Ulrich Dirnagl, Iain Chalmers, John P A Ioannidis, Rustam Al-Shahi Salman, An-Wen Chan, Paul Glasziou
Full-Text HTML | PDF

Series Papers

How to increase value and reduce waste when research priorities are set
Iain Chalmers, Michael B Bracken, Ben Djulbegovic, Silvio Garattini, Jonathan Grant, A Metin Gülmezoglu, David W Howells, John P A Ioannidis, Sandy Oliver
Full-Text HTML | PDF

Increasing value and reducing waste in research design, conduct, and analysis
John P A Ioannidis, Sander Greenland, Mark A Hlatky, Muin J Khoury, Malcolm R Macleod, David Moher, Kenneth F Schulz, Robert Tibshirani
Full-Text HTML | PDF

Increasing value and reducing waste in biomedical research regulation and management
Rustam Al-Shahi Salman, Elaine Beller, Jonathan Kagan, Elina Hemminki, Robert S Phillips, Julian Savulescu, Malcolm Macleod, Janet Wisely, Iain Chalmers

Video

Symposium on Research: increasing value, reducing waste 1
Introduction 1.

Audio

Research: increasing value, reducing waste
Paul Glasziou discusses a new Lancet Series, Research: increasing value, reducing waste

Related content published in The Lancet

Paul Glasziou: surfing the wave of evidence-based medicine
Richard Lane
Full-Text HTML | PDF

85% of Health Research

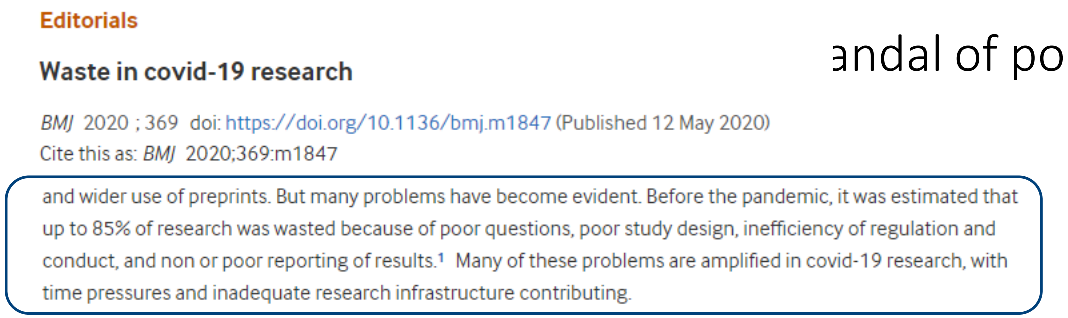
Funding is wasted avoidable

Sir Iain Chalmers and Paul Glasziou
'Avoidable waste in the production and reporting of research evidence', The Lancet, Volume 374, Issue 9683, Pages 86 - 89, 4 July 2009,

We need less research, better research and

ne for the right reasons

andal of poor medical research BMJ 1994

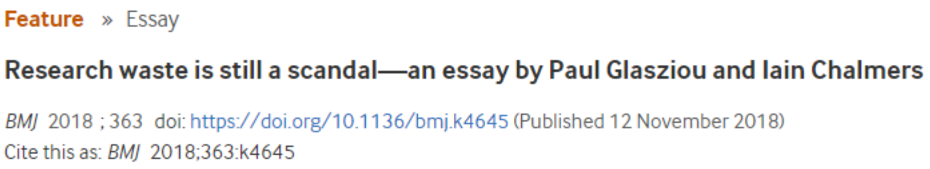


Editorials

Waste in covid-19 research

BMJ 2020 ; 369 doi: https://doi.org/10.1136/bmj.m1847 (Published 12 May 2020)
Cite this as: *BMJ* 2020;369:m1847

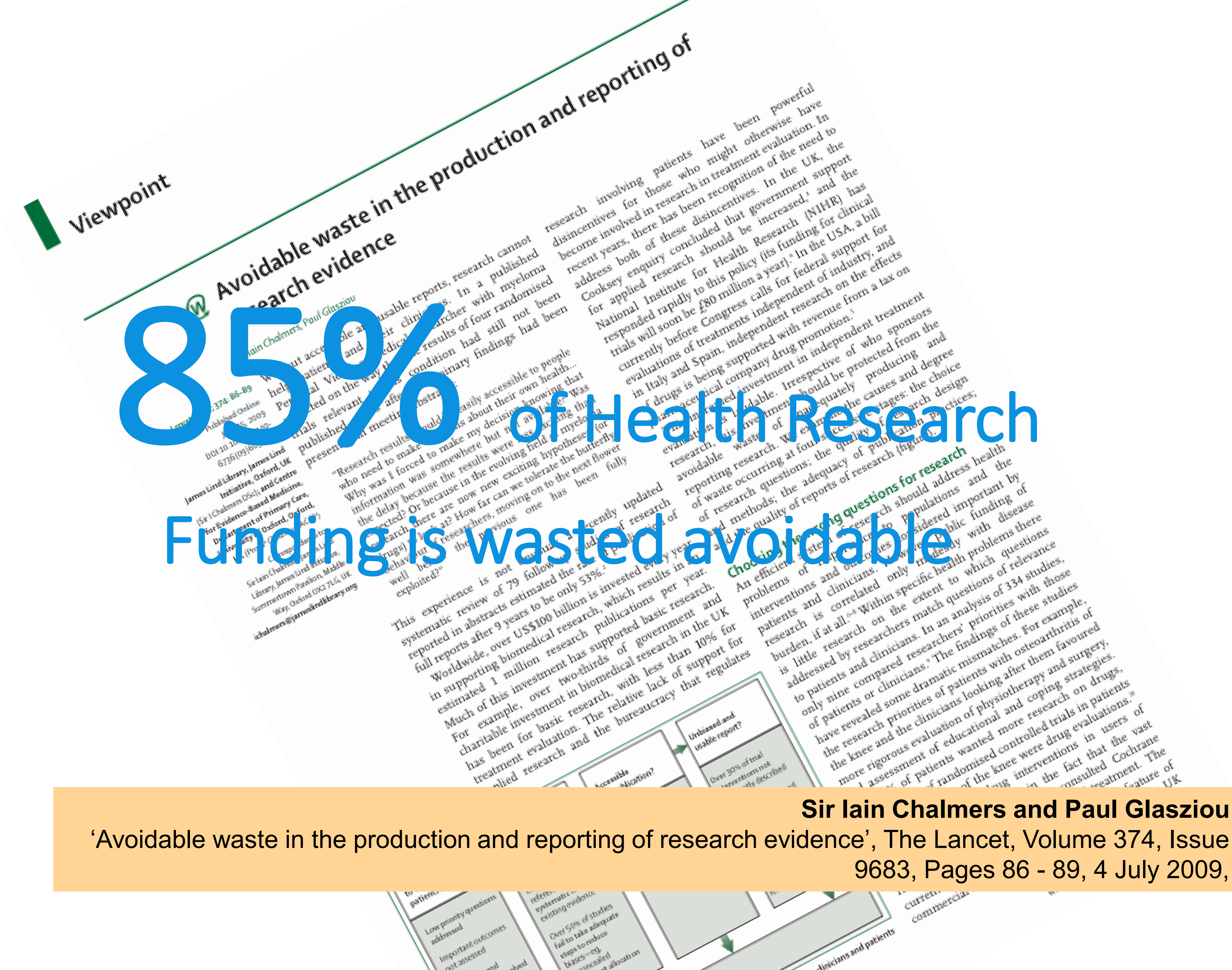
and wider use of preprints. But many problems have become evident. Before the pandemic, it was estimated that up to 85% of research was wasted because of poor questions, poor study design, inefficiency of regulation and conduct, and non or poor reporting of results.[1] Many of these problems are amplified in covid-19 research, with time pressures and inadequate research infrastructure contributing.



Feature » Essay

Research waste is still a scandal—an essay by Paul Glasziou and Iain Chalmers

BMJ 2018 ; 363 doi: https://doi.org/10.1136/bmj.k4645 (Published 12 November 2018)
Cite this as: *BMJ* 2018;363:k4645

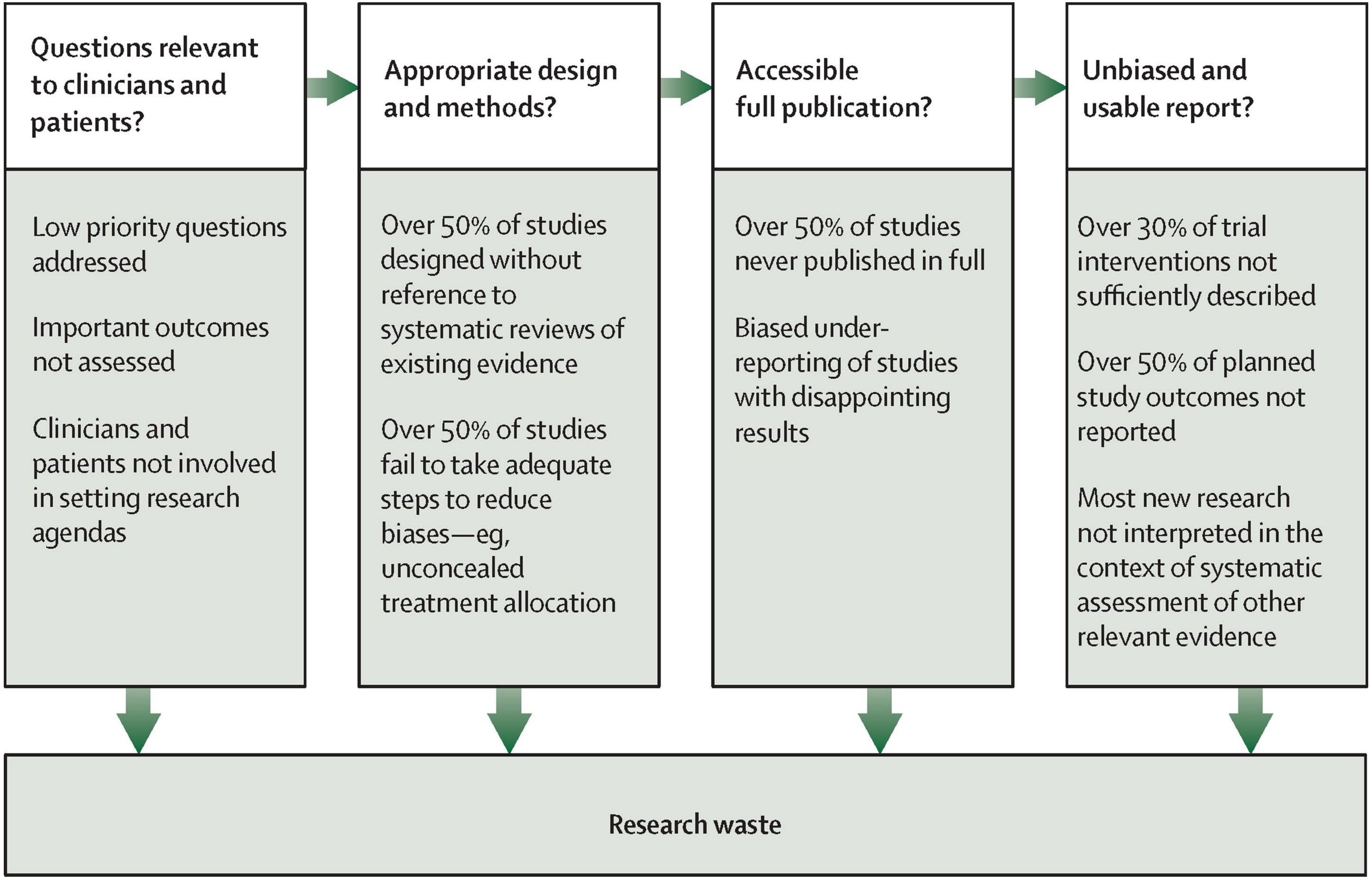

Viewpoint

Avoidable waste in the production and reporting of research evidence

Iain Chalmers, Paul Glasziou

85% of Health Research Funding is wasted avoidable

Sir Iain Chalmers and Paul Glasziou
‘Avoidable waste in the production and reporting of research evidence’, The Lancet, Volume 374, Issue 9683, Pages 86 - 89, 4 July 2009,



Questions relevant to clinicians and patients?

Low priority questions addressed

Important outcomes not assessed

Clinicians and patients not involved in setting research agendas

Appropriate design and methods?

Over 50% of studies designed without reference to systematic reviews of existing evidence

Over 50% of studies fail to take adequate steps to reduce biases—eg, unconcealed treatment allocation

Accessible full publication?

Over 50% of studies never published in full

Biased under-reporting of studies with disappointing results

Unbiased and usable report?

Over 30% of trial interventions not sufficiently described

Over 50% of planned study outcomes not reported

Most new research not interpreted in the context of systematic assessment of other relevant evidence

Research waste

Questions relevant to clinicians and patients

Poor engagement of end users of research in research questions and design

- Increase involvement of patients and clinicians in shaping research agendas and specific questions and outcomes

How can families be supported to problem-solve for themselves and take more control over their lives?

Best way for families to access real practical support

How can practitioners work best with men and fathers?

Social Care Research Wales – Family Support Services

(priority setting in association with the JLA) Top 10

Appropriate design and methods

Incentives in fellowships and career paths to do primary research even if of low relevance

- Emphasise initial training in critical appraisal and systematic reviews rather than the conduct of primary research

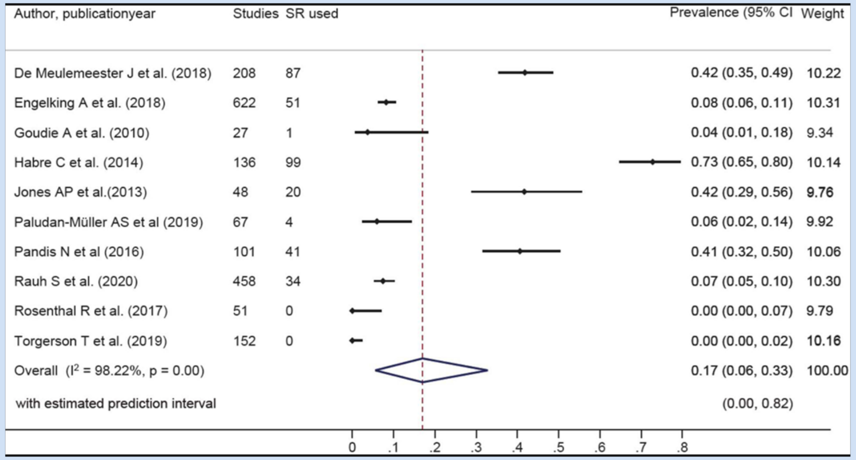
Incentives for primary research ignore the need to use and improve on existing research on the same question

- Research funding bodies should require—and support—grant proposals to build on systematic reviews of existing evidence

Published research fails to set the study in the context of all previous similar research

- Journal editors should require new studies to be set in the context of systematic assessments of related studies

Systematic reviews are rarely used to inform study design - a systematic review and meta-analysis.



Nørgaard B, Draborg E, Andreasen J, Juhl CB, Yost J, Brunnhuber K, Robinson KA, Lund H. Systematic reviews are rarely used to inform study design - a systematic review and meta-analysis. J Clin Epidemiol. 2022 May;145:1-13. doi: 10.1016/j.jclinepi.2022.01.007. Epub 2022 Jan 16. PMID: 35045317. https://pubmed.ncbi.nlm.nih.gov/35045317/

Appropriate design and methods

Poor training in research methods and research reporting

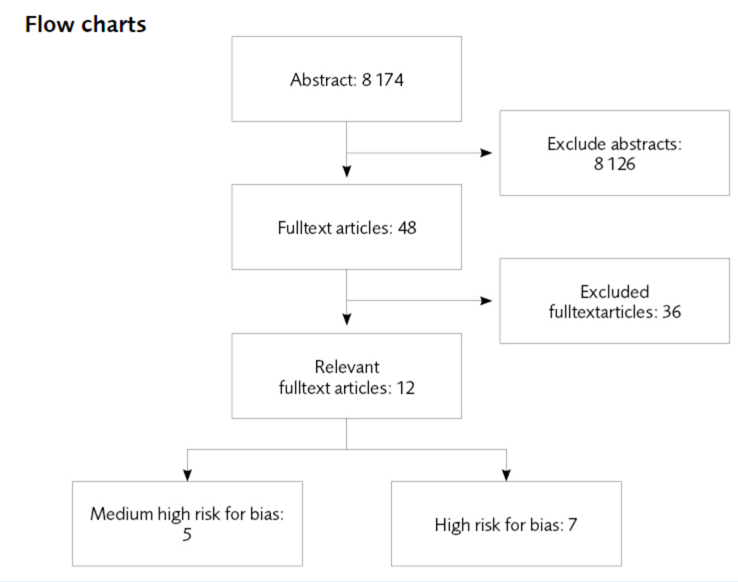
- Require training of all clinicians in methodological flaws and biases in research; improve training in research methods for those doing research apprenticeships

Lack of methodological input to research design and review of research

- Increase numbers of methodologists in health- and social care research, in the assessment of funding application and in ethical review

Many journal reviews focus on expert judgments about contribution to knowledge, rather than methods and usability

- Supplement peer review of studies with review by methodologists and end users



Flow charts

Abstract: 8 174

Exclude abstracts: 8 126

Fulltext articles: 48

Excluded fulltextarticles: 36

Relevant fulltext articles: 12

Medium high risk for bias: 5

High risk for bias: 7

Psychological and psychosocial interventions in forensic psychiatric care

Accessible full publication & Unbiased and usable report

Non-registration of trials

- Require—by incentives and regulation—registration and publication of protocols for all clinical trials at inception

Failure of sponsors and authors to submit full reports of completed research

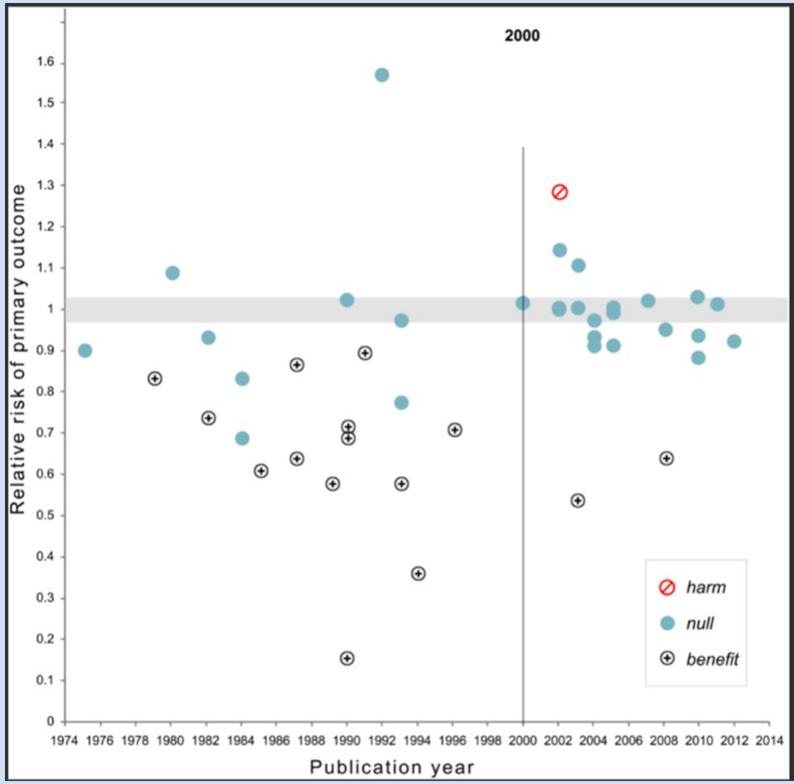
- Support timely open access to full results on completion

Poor awareness and use by authors and editors of reporting guidelines

- Increase author and journal awareness of and training in reporting guidelines, such as CONSORT and STARD statements

Space restrictions in journals prevent publication of details of interventions and tests

- Support free access repositories—separate from any publications—so that clinicians and researchers have details of the treatments, test, or instruments studied



Relative risk of showing benefit or harm of treatment by year of publication for large NHLBI trials on pharmaceutical and dietary supplement interventions

What is James Lind Alliance?

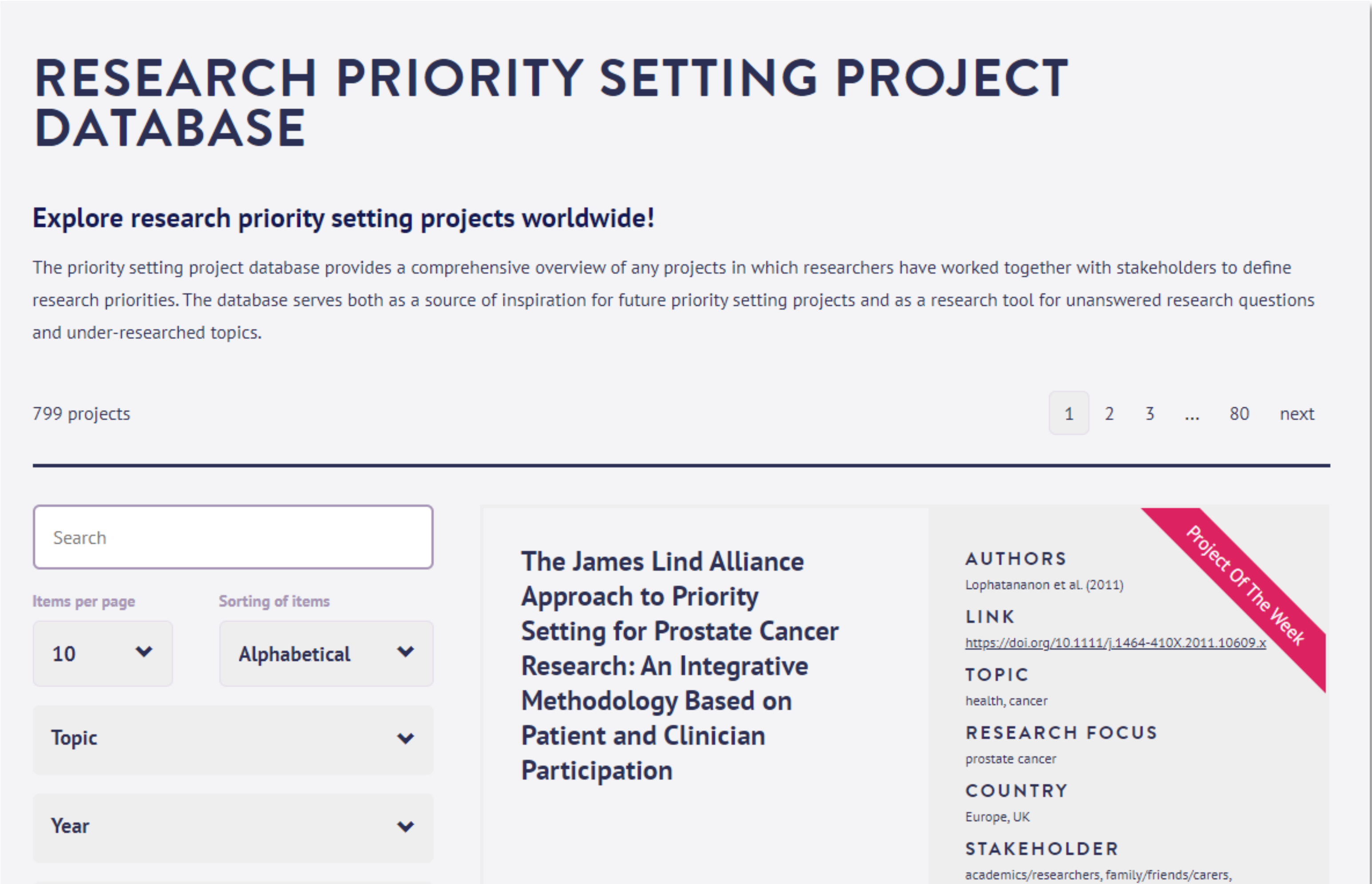
By prioritizing research questions with the JLA method, you can get an additional perspective on which questions are most important to answer

Involvement of consumers in research prioritisation process of evidence gaps

- JLA is an independent organisation in England that was established in 2004
- Funded by the National Institute for Health Research (NIHR) and operated by the NIHR Evaluation, Trials and Studies Coordinating Centre (NETSCC)
- Patients, consumers, carers and profession identify and prioritise the most important evidence gaps in their area
- The top list of the research priorities are published
- ”Prioritising setting partnerships”

Published prioritising projects in Research priority setting database

https://ois.lbg.ac.at/en/project-database



RESEARCH PRIORITY SETTING PROJECT DATABASE

Explore research priority setting projects worldwide!

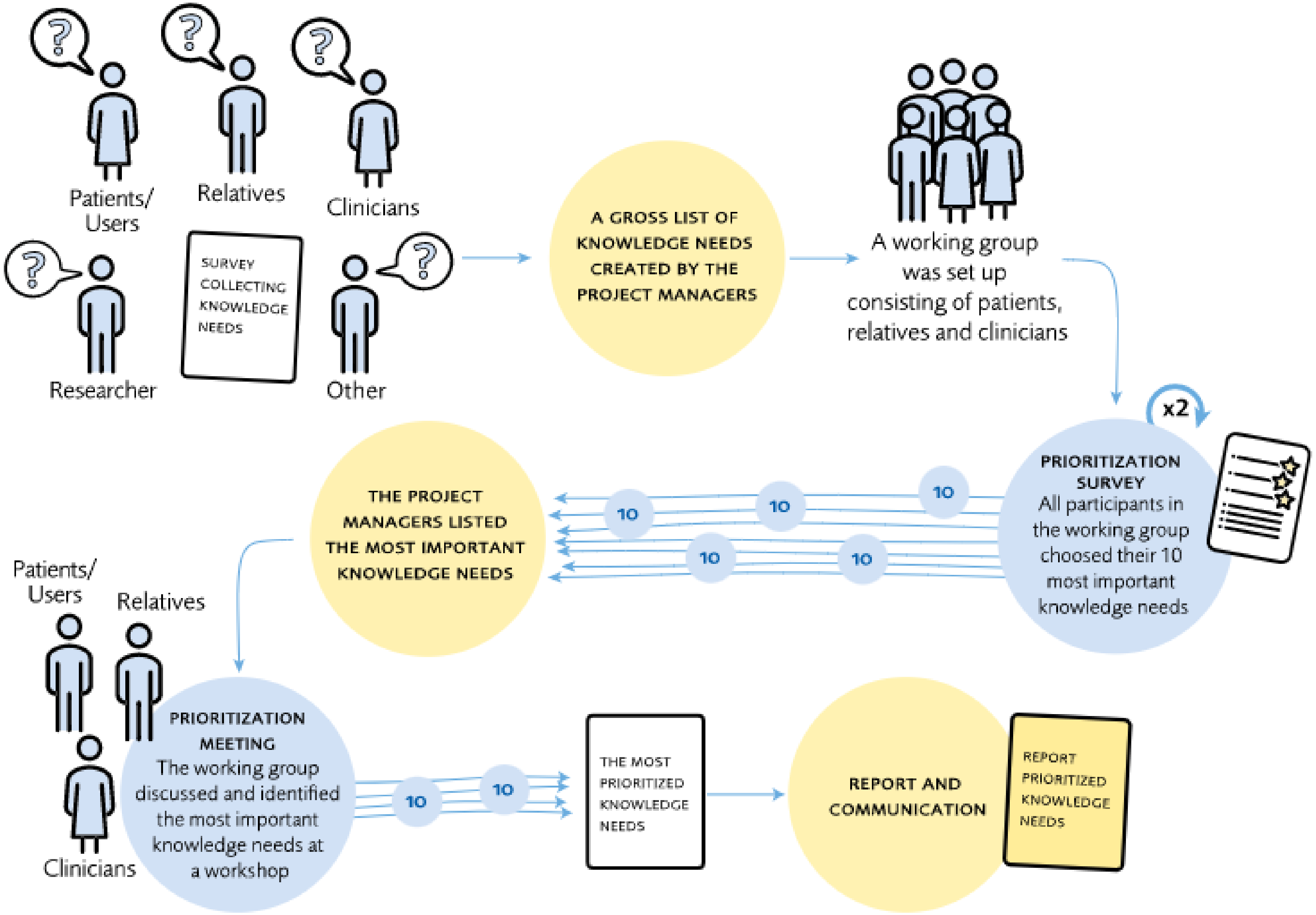
The priority setting project database provides a comprehensive overview of any projects in which researchers have worked together with stakeholders to define research priorities. The database serves both as a source of inspiration for future priority setting projects and as a research tool for unanswered research questions and under-researched topics.

799 projects

The James Lind Alliance Approach to Priority Setting for Prostate Cancer Research: An Integrative Methodology Based on Patient and Clinician Participation

AUTHORS
Lophatananon et al. (2011)
LINK
https://doi.org/10.1111/j.1464-410X.2011.10609.x
TOPIC
health, cancer
RESEARCH FOCUS
prostate cancer
COUNTRY
Europe, UK
STAKEHOLDER
academics/researchers, family/friends/carers,

Method



SURVEY COLLECTING KNOWLEDGE NEEDS

A GROSS LIST OF KNOWLEDGE NEEDS CREATED BY THE PROJECT MANAGERS

A working group was set up consisting of patients, relatives and clinicians

PRIORITIZATION SURVEY
All participants in the working group choosed their 10 most important knowledge needs

THE PROJECT MANAGERS LISTED THE MOST IMPORTANT KNOWLEDGE NEEDS

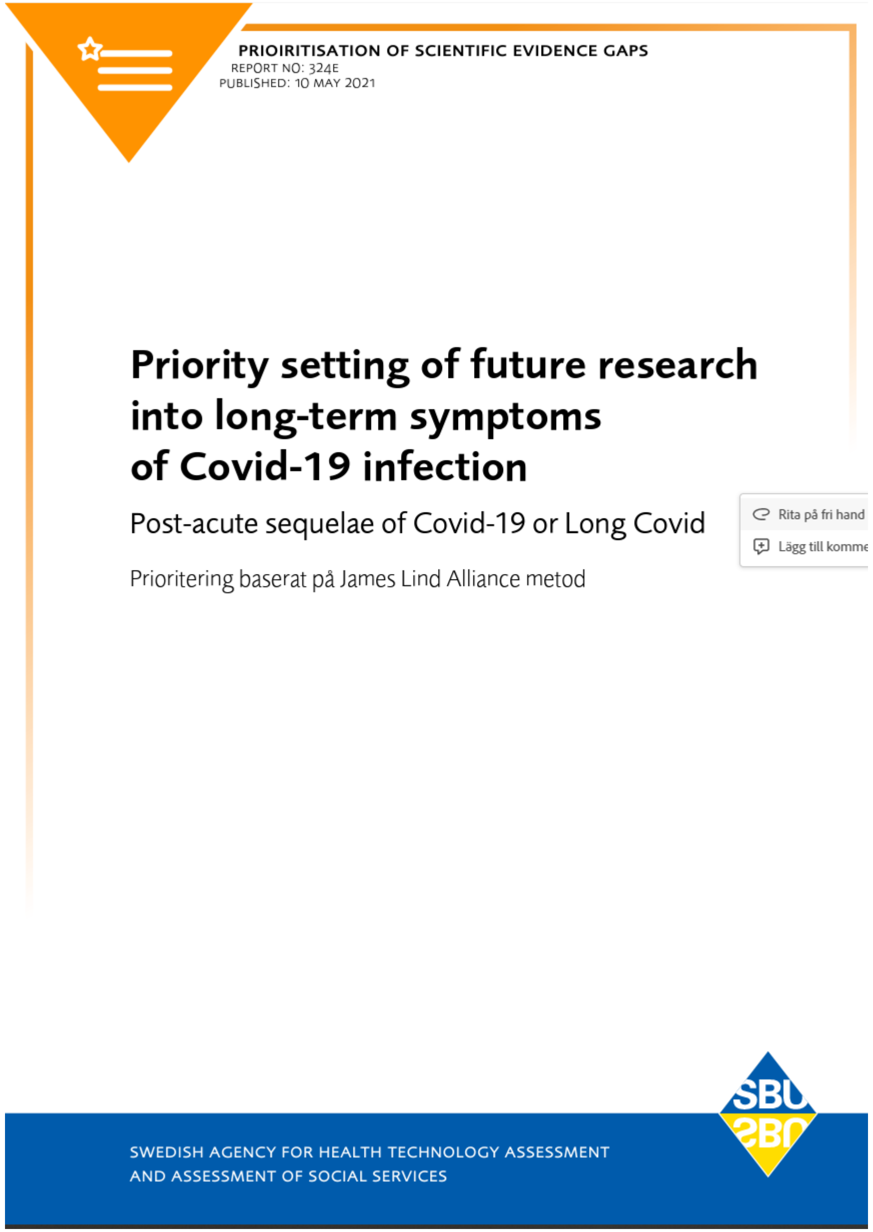
PRIORITIZATION MEETING
The working group discussed and identified the most important knowledge needs at a workshop

THE MOST PRIORITIZED KNOWLEDGE NEEDS

REPORT AND COMMUNICATION

REPORT PRIORITIZED KNOWLEDGE NEEDS

Example



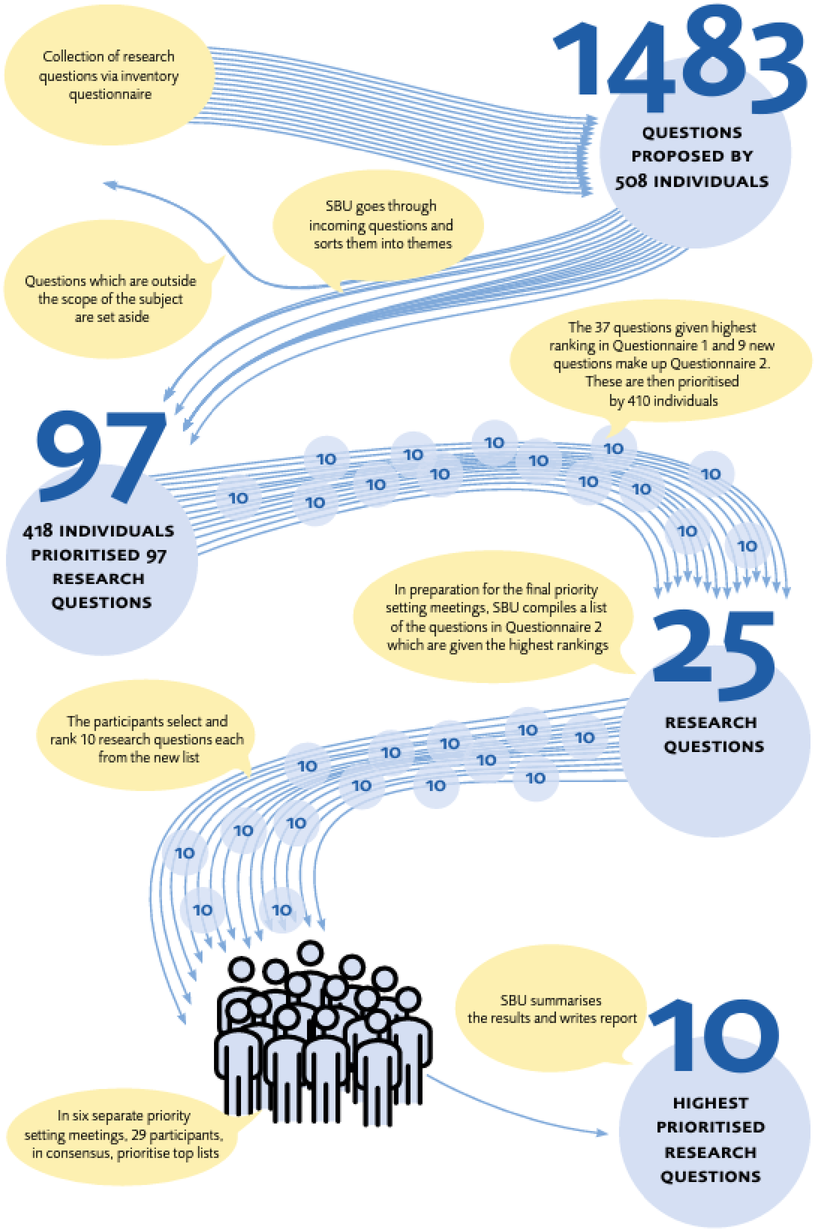
PRIOIRITISATION OF SCIENTIFIC EVIDENCE GAPS
REPORT NO: 324E
PUBLISHED: 10 MAY 2021

Priority setting of future research into long-term symptoms of Covid-19 infection

Post-acute sequelae of Covid-19 or Long Covid

Prioritering baserat på James Lind Alliance metod

SWEDISH AGENCY FOR HEALTH TECHNOLOGY ASSESSMENT
AND ASSESSMENT OF SOCIAL SERVICES



Collection of research questions via inventory questionnaire

1483
QUESTIONS PROPOSED BY 508 INDIVIDUALS

SBU goes through incoming questions and sorts them into themes

Questions which are outside the scope of the subject are set aside

The 37 questions given highest ranking in Questionnaire 1 and 9 new questions make up Questionnaire 2. These are then prioritised by 410 individuals

97
418 INDIVIDUALS PRIORITISED 97 RESEARCH QUESTIONS

In preparation for the final priority setting meetings, SBU compiles a list of the questions in Questionnaire 2 which are given the highest rankings

25
RESEARCH QUESTIONS

The participants select and rank 10 research questions each from the new list

SBU summarises the results and writes report

10
HIGHEST PRIORITISED RESEARCH QUESTIONS

In six separate priority setting meetings, 29 participants, in consensus, prioritise top lists

References

- The priority setting project database

  https://ois.lbg.ac.at/en/project-database

- The James Lind Alliance

  https://www.jla.nihr.ac.uk/

- JLA Guidebook

  https://www.jla.nihr.ac.uk/jla-guidebook/

- Reporting guideline for priority setting of health research (REPRISE)

  https://bmcmedresmethodol.biomedcentral.com/articles/10.1186/s12874-019-0889-3

  https://www.jla.nihr.ac.uk/news/reprise-reporting-guidelines/24495

What is a core outcome set (COS) and COMET?

The use of core outcome sets (COS) facilitates that more research can be combined systematic reviews

Endometriosis

Diagnosis, treatment and patient experiences

A systematic review and assessment of medical, economic, social and ethical aspects

SBU ASSESSMENTS | ASSESSMENT OF METHODS IN HEALTH CARE AND SOCIAL SERVICES

MAY 2018 | WWW.SBU.SE/277E

Conclusions

- GnRH-agonist and gestagen treatment seem to have similar pain-relieving effect, but GnRH-agonists decrease bone density.
- Postoperative treatment with gestagen and monophasic contraceptives seem to have similar pain relieving effect in women with chronic pelvic pain and dyspareunia. Hormonal intrauterine contraceptive devices may reduce dysmenorrhea in comparison to no treatment.
- Vaginal ultrasound has a clinical value in the diagnosis of endometrioma, and before operating for deep endometriosis. This applies to the identification of the spread of disease in women with well-established clinical suspicion of endometriosis. Vaginal ultrasound is inexpensive, easily accessible, has no contraindications and requires no preparation. Healthcare professionals conducting ultrasound examinations need to be experienced.
- During fertility treatment, the ultralong pretreatment with GnRH-agonist has a higher chance of resulting in pregnancy for women with endometriosis, compared to the short pretreatment.
- Women with endometriosis symptom experience that they are treated with ignorance about endometriosis in the non-specialised care. They experience delays in both their diagnosis and treatment, and feel that healthcare professionals do not take their problems seriously. In addition, it appears that increased expertise and improved attitudes among health care professionals could improve the life situation of women with endometriosis.
- Despite the large number of identified studies, there is a general lack of scientific evidence for most treatments. Future research should be more standardized regarding the length of treatment, follow up and evaluating the outcome/pain. More research is needed in the important areas of diagnostics, and evaluation of surgical treatment effect.

Background

Endometriosis is a chronic disease where the uterine mucosa (endometrium) grows outside the uterus. Women with endometriosis may be without symptoms or they may experience pain of varying degree. The most common types of pain are dysmenorrhea, dyspareunia and chronic pelvic pain. Endometriosis can also reduce fertility. The disease can affect quality of life, reduce the woman's ability to cope with work or study, and effect social relationships. It is estimated that around 10% of women of reproductive age have endometriosis. It takes five to seven years from the onset of symptoms until a diagnosis is set. There is currently no cure, but several treatments can relieve the symptoms.

Aim

The aim of this systematic review was to evaluate the scientific evidence with regards to diagnostic performance of different imaging methods for the diagnosis of endometriosis and to assess the ability of different treatments to reduce pain or improve fertility. In addition, qualitative studies regarding women's experiences with endometriosis health care were evaluated.

Method

Prospective peer-reviewed studies were included if they evaluated the ability of any imaging method to aid in the diagnosis of women presenting with clinical

"This report identifies many scientific uncertainties. This is in part due to study heterogeneity, that is, the inconsistent definitions of endometriosis in diagnostic studies, variations in the length of treatment or follow-up, and inconsistent evaluation and reporting of outcomes (dysmenorrhea, dyspareunia and pelvic pain) that make it difficult to reliably assess the body of evidence."

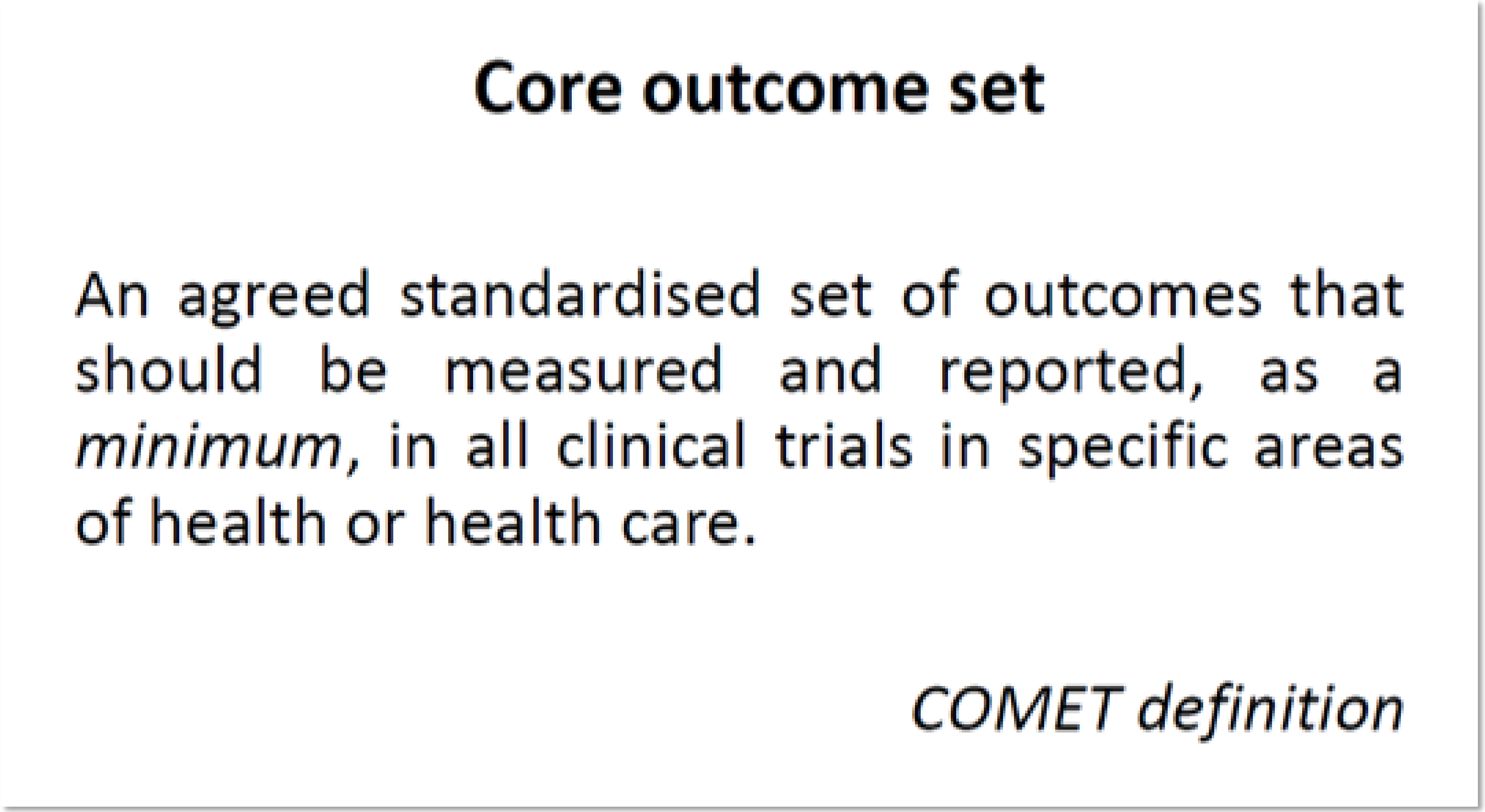
(1) We identified a body of late-stage trials in two clinical areas

(2) We identified the primary and secondary outcomes for these trials.

(3) We randomly ordered these outcomes and presented them to patients and healthcare professionals, and we asked them to rank the importance of the outcomes

1. *Breast cancer* — patients/patient representative and health professionals considered the primary outcome to be the most important outcome for 8/21 primary outcomes
2. *Nephrology* — patients and health professionals considered the primary outcome to be the most important outcome for 5/25 primary outcomes

Treweek S, Miyakoda V, Burke D, Shiely F. Getting it wrong most of the time? Comparing trialists' choice of primary outcome with what patients and health professionals want. Trials. 2022 Jun 27;23(1):537. doi: 10.1186/s13063-022-06348-z. PMID: 35761293; PMCID: PMC9235090.



Core outcome set

An agreed standardised set of outcomes that should be measured and reported, as a *minimum*, in all clinical trials in specific areas of health or health care.

COMET definition

WHAT
should be
measured?

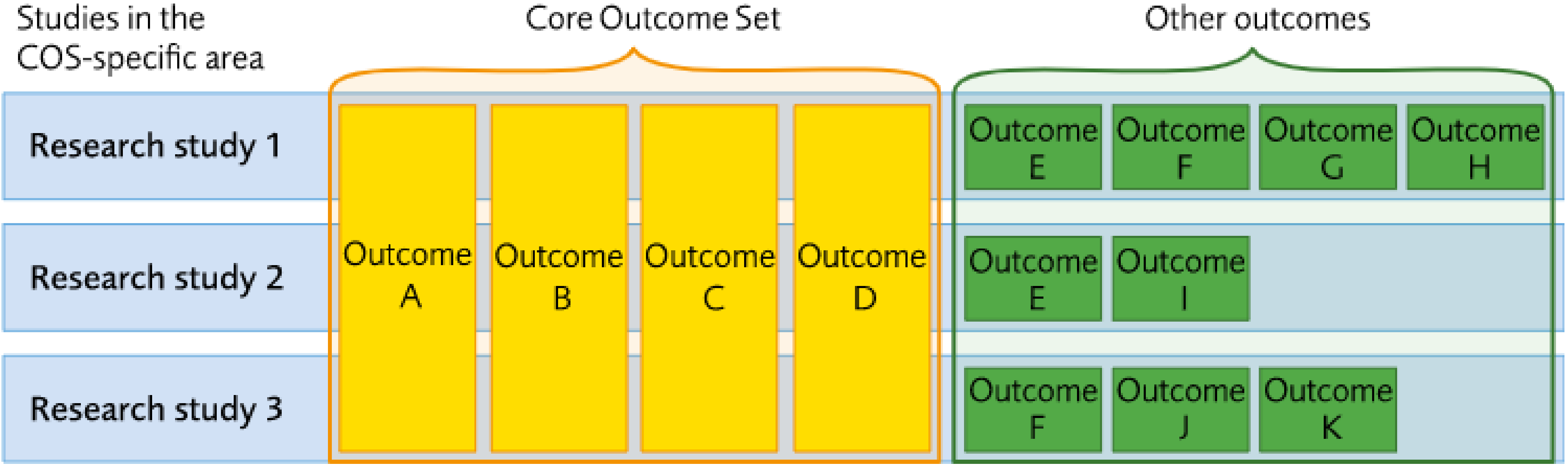
HOW
should it be
measured?

WHEN
should it be
measured?

Core outcome set

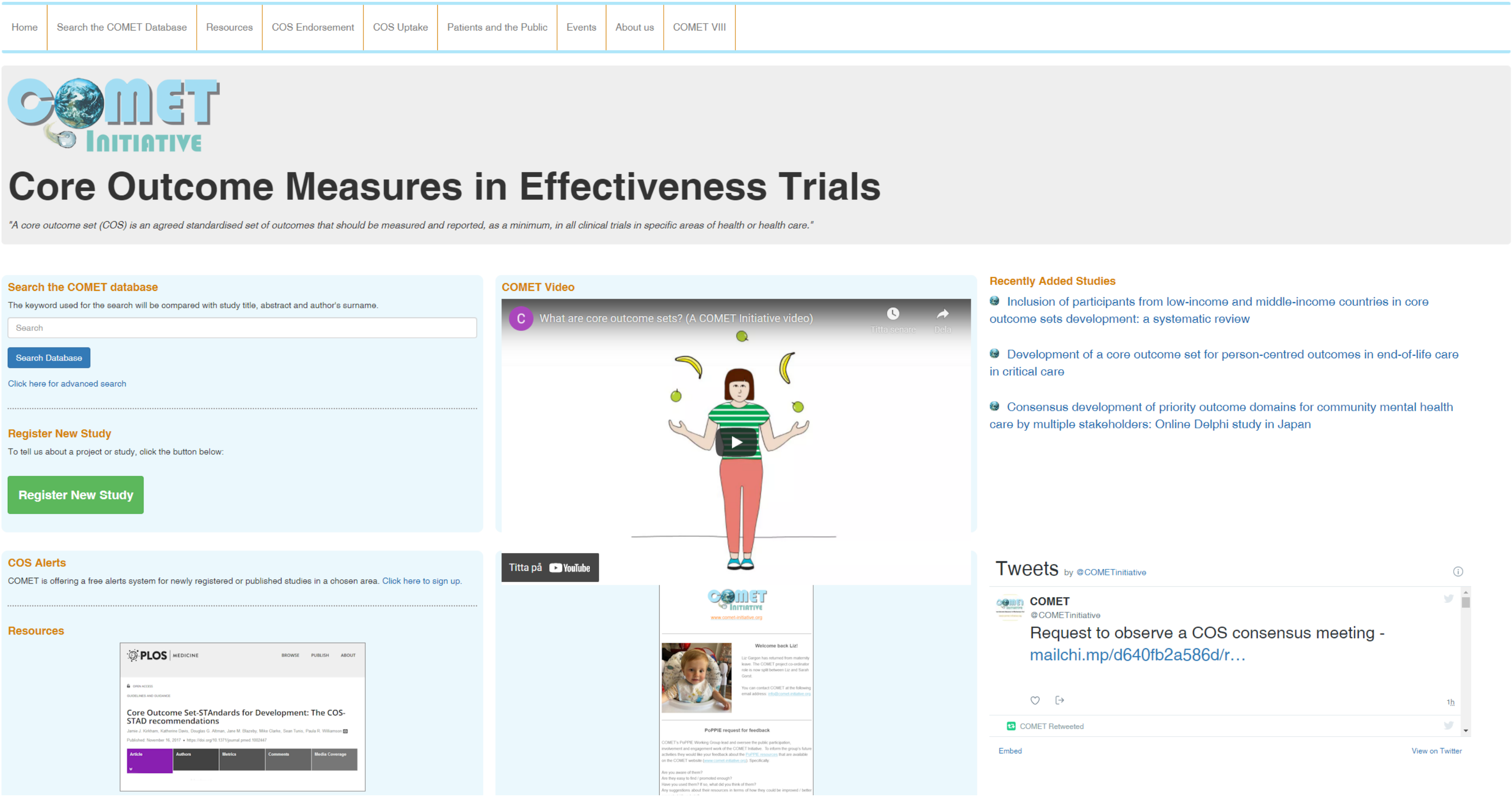
A few outcomes that should be measured in all future studies in a specific area

Video: https://www.youtube.com/watch?v=D0Q9vypSYeE



Published COS projects in
The COMET database

https://www.comet-initiative.org/



Core Outcome Measures in Effectiveness Trials

"A core outcome set (COS) is an agreed standardised set of outcomes that should be measured and reported, as a minimum, in all clinical trials in specific areas of health or health care."

Search the COMET database

The keyword used for the search will be compared with study title, abstract and author's surname.

Register New Study

To tell us about a project or study, click the button below:

COMET Video

What are core outcome sets? (A COMET Initiative video)

Recently Added Studies

- Inclusion of participants from low-income and middle-income countries in core outcome sets development: a systematic review
- Development of a core outcome set for person-centred outcomes in end-of-life care in critical care
- Consensus development of priority outcome domains for community mental health care by multiple stakeholders: Online Delphi study in Japan

COS Alerts

COMET is offering a free alerts system for newly registered or published studies in a chosen area. Click here to sign up.

Resources

Core Outcome Set-STAndards for Development: The COS-STAD recommendations

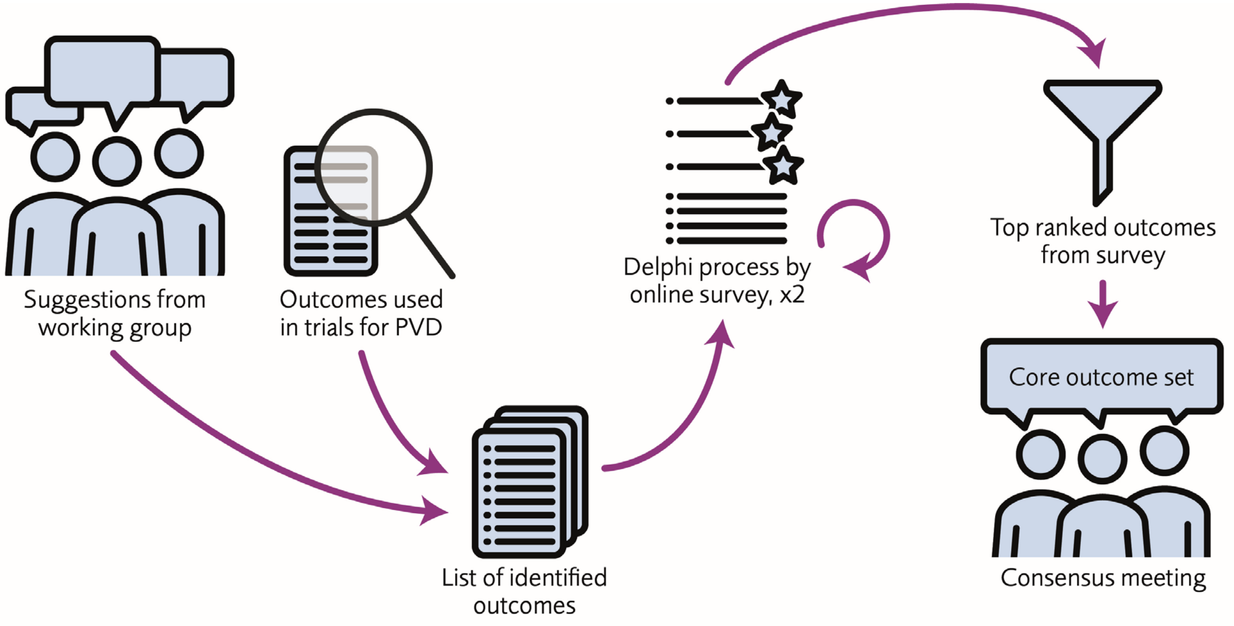
Tweets by @COMETinitiative

COMET
@COMETinitiative
Request to observe a COS consensus meeting - mailchi.mp/d640fb2a586d/r…
1h

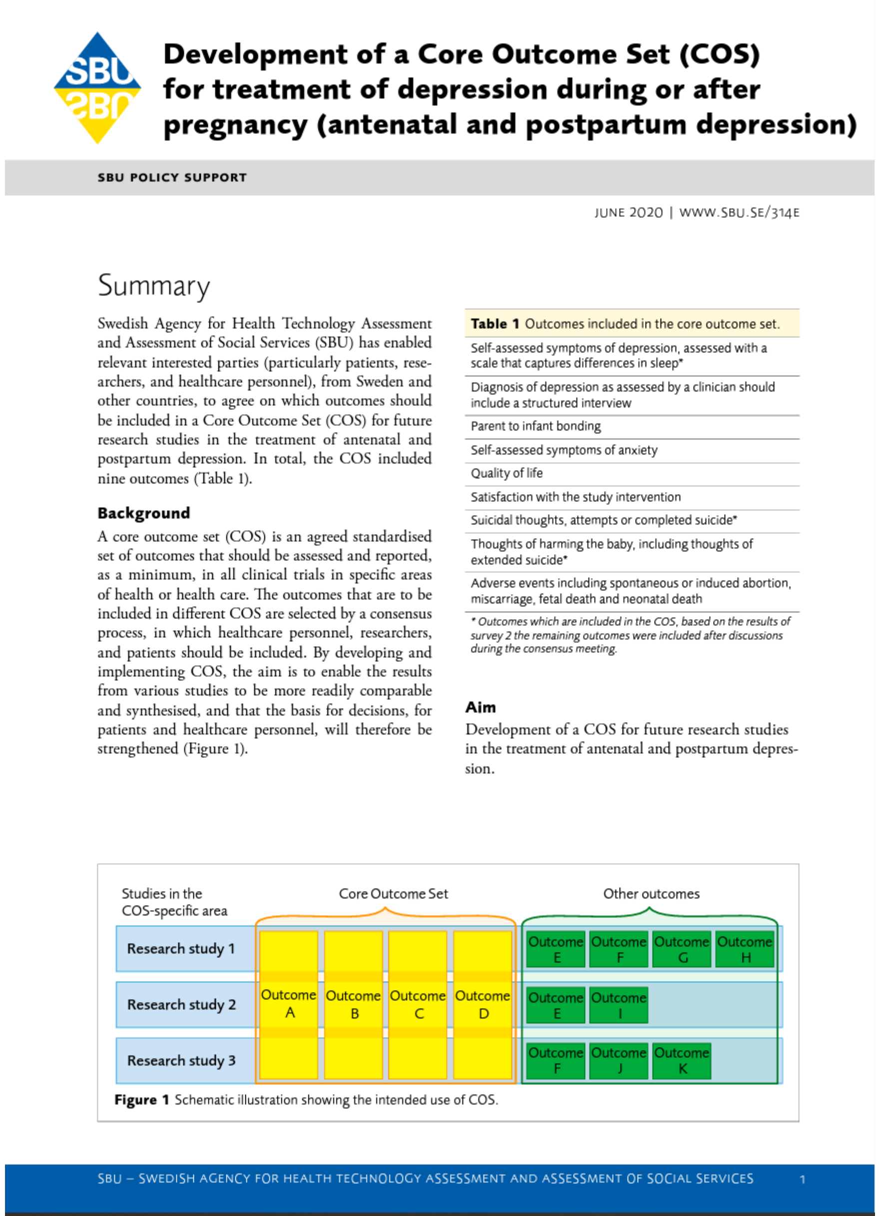
COMET Retweeted

Method

1. Ensure that a COS is needed
   - Check if one exists or is in the process of being developed
2. Specify
   - The population and the intervention
3. Identify outcomes
   - Which outcomes are used in the published research?
   - Which outcomes are important to patients/clients/professionals? (survey or qualitative study)
4. Prioritising
   - Delphi survey
   - Consensus meeting



Example



Development of a Core Outcome Set (COS) for treatment of depression during or after pregnancy (antenatal and postpartum depression)

SBU POLICY SUPPORT

JUNE 2020 | WWW.SBU.SE/314E

Summary

Swedish Agency for Health Technology Assessment and Assessment of Social Services (SBU) has enabled relevant interested parties (particularly patients, researchers, and healthcare personnel), from Sweden and other countries, to agree on which outcomes should be included in a Core Outcome Set (COS) for future research studies in the treatment of antenatal and postpartum depression. In total, the COS included nine outcomes (Table 1).

Background

A core outcome set (COS) is an agreed standardised set of outcomes that should be assessed and reported, as a minimum, in all clinical trials in specific areas of health or health care. The outcomes that are to be included in different COS are selected by a consensus process, in which healthcare personnel, researchers, and patients should be included. By developing and implementing COS, the aim is to enable the results from various studies to be more readily comparable and synthesised, and that the basis for decisions, for patients and healthcare personnel, will therefore be strengthened (Figure 1).

Table 1 Outcomes included in the core outcome set.

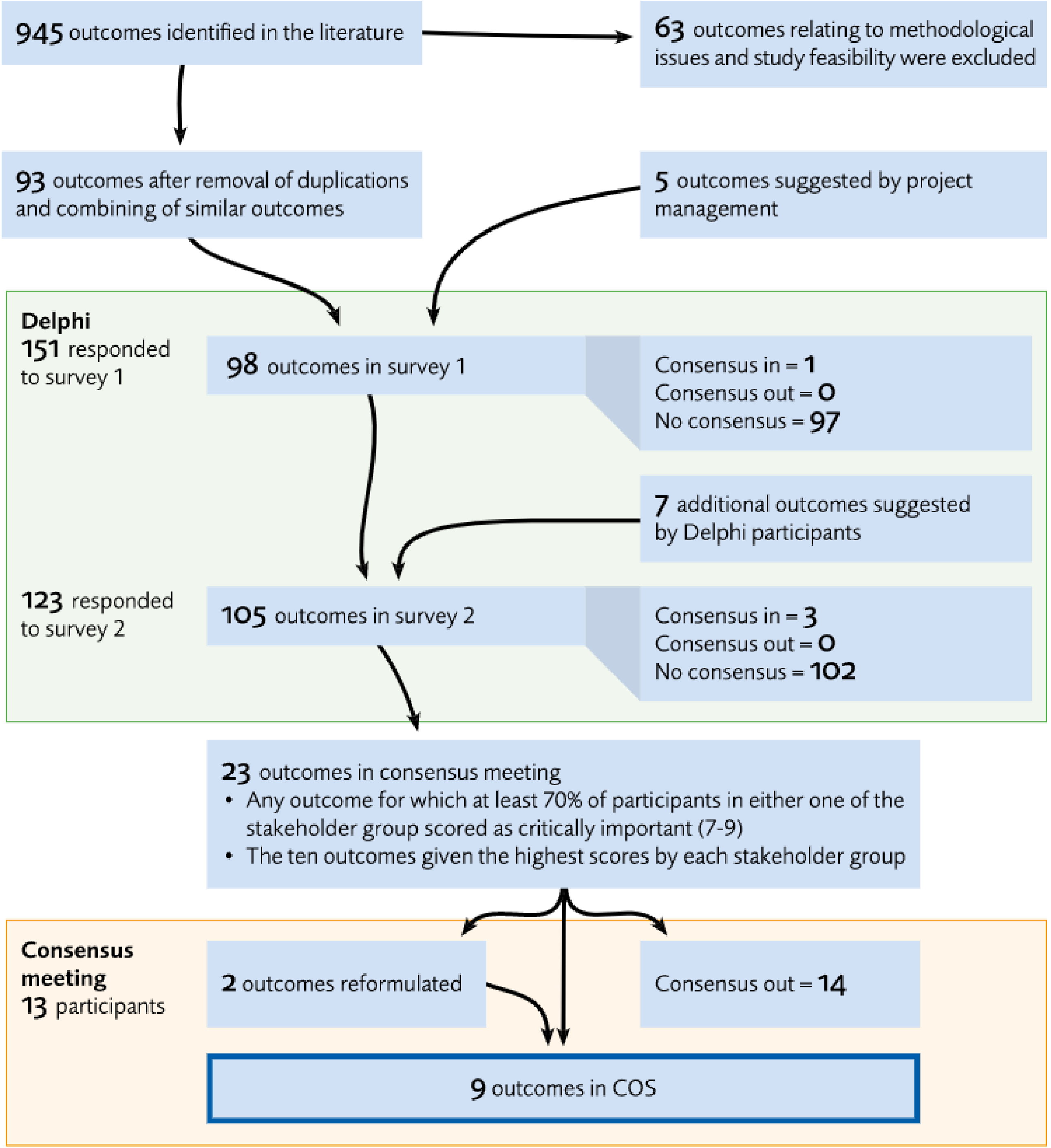
Self-assessed symptoms of depression, assessed with a scale that captures differences in sleep*
Diagnosis of depression as assessed by a clinician should include a structured interview
Parent to infant bonding
Self-assessed symptoms of anxiety
Quality of life
Satisfaction with the study intervention
Suicidal thoughts, attempts or completed suicide*
Thoughts of harming the baby, including thoughts of extended suicide*
Adverse events including spontaneous or induced abortion, miscarriage, fetal death and neonatal death

** Outcomes which are included in the COS, based on the results of survey 2 the remaining outcomes were included after discussions during the consensus meeting.*

Aim

Development of a COS for future research studies in the treatment of antenatal and postpartum depression.

Figure 1 Schematic illustration showing the intended use of COS.



945 outcomes identified in the literature

63 outcomes relating to methodological issues and study feasibility were excluded

93 outcomes after removal of duplications and combining of similar outcomes

5 outcomes suggested by project management

Delphi
151 responded to survey 1

98 outcomes in survey 1

Consensus in = 1
Consensus out = 0
No consensus = 97

7 additional outcomes suggested by Delphi participants

123 responded to survey 2

105 outcomes in survey 2

Consensus in = 3
Consensus out = 0
No consensus = 102

23 outcomes in consensus meeting

- Any outcome for which at least 70% of participants in either one of the stakeholder group scored as critically important (7-9)
- The ten outcomes given the highest scores by each stakeholder group

Consensus meeting
13 participants

2 outcomes reformulated

Consensus out = 14

9 outcomes in COS

References

- COMET Initative

  https://www.comet-initiative.org/

- COnsensus-based Standards for the selection of health Measurement Instruments (COSMIN)

  https://www.cosmin.nl/

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- The Core Outcome Set-STAndards for Development (COS-STAD)

  https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1002447

- The Core Outcome Set-STAndardised Protocol Items (COS-STAP)

  https://trialsjournal.biomedcentral.com/articles/10.1186/s13063-019-3230-x

  https://www.comet-initiative.org/Downloads/COS-STAP%20Reporting%20Checklist%20template.docx

- The Core Outcome Set-STAndards for Reporting (COS-STAR)

  https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1002148

  https://www.comet-initiative.org/Downloads/COS-STAR%20Reporting%20Checklist%20template.docx

More

- EVBRES https://evbres.eu/
- EVIR- Ensuring Value in Reserch https://evir.org/about-us/
- TranspariMED https://www.transparimed.org/
- Catalogue of Bias https://catalogofbias.org/
- Enhancing the QUAlity and Transparency Of health Research (reporting guidelines) https://www.equator-network.org/reporting-guidelines/
- Testing treatments http://www.testingtreatments.org/
- THAT'S A CLAIM! https://thatsaclaim.org/
- Students 4 best evidence https://s4be.cochrane.org/
- …

Thank you!

Website: [sbu.se/en](sbu.se/en)
Twitter: twitter.com/SBU_en
INSIA Twitter: twitter.com/INSIA_Official