

Core Outcome Measures in Effectiveness Trials

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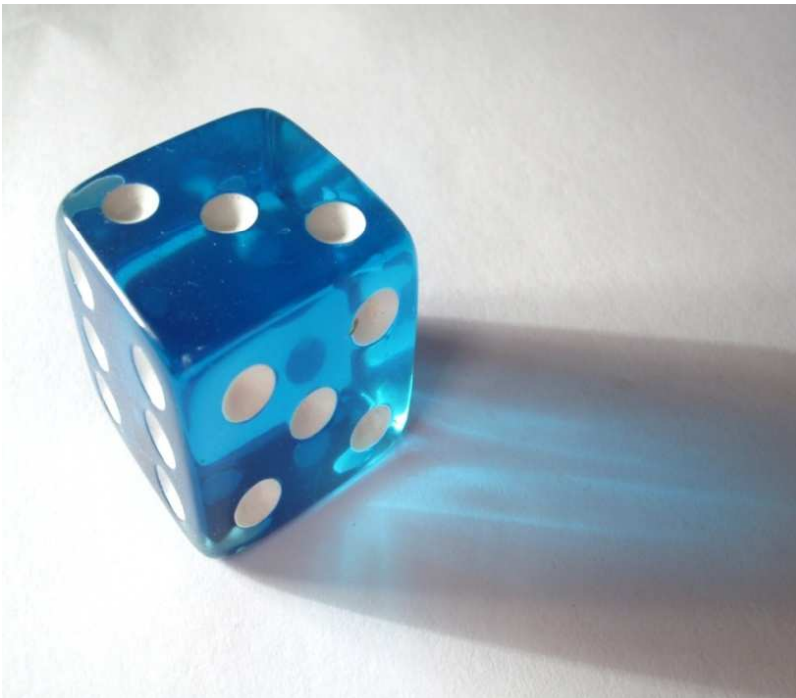
Overview

- Outcome measures, evidence & problems
- Core outcomes sets, OMERACT
- Core outcome sets in colorectal cancer

Outcomes

“...are events that are either present or absent after participants receive an intervention or exposure that can be measured and compared...”

Randomised controlled trials



- Primary outcome
- Secondary outcomes



✦ Systematic reviews and meta-analyses

- Combine RCTs to provide a summary result



Problems with outcomes

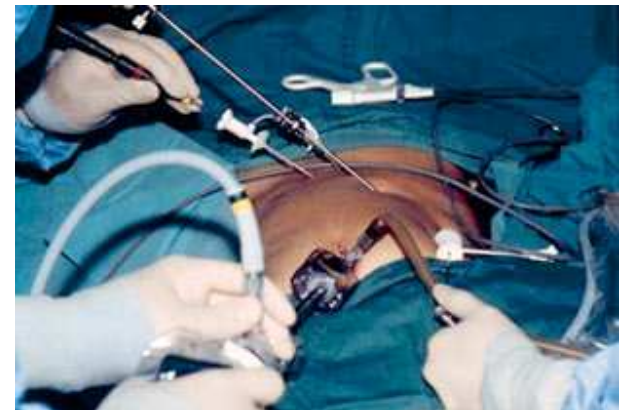
- Not all trials measure the same outcomes
- Outcomes are measured in different ways
- Outcome reporting bias



1. Many
different
outcomes

Laparoscopic versus open total mesorectal excision for rectal cancer (Review)

Breukink S, Pierie JP, Wiggers T



Different outcomes

Outcome	No. of studies reporting outcome (n=48)
Survival	17
Recurrence	31
Quality of life	0
Surgical mortality	37
Operative morbidity	36

Different outcomes

- Unable to perform meta-analysis.
- No firm conclusions could be reached
- More trials needed.

SAME SAME
BUT DIFFERENT

2. Outcomes
measured in
different
ways



Quality of life after rectal resection for cancer, with or without permanent colostomy. (Review)

Pachler J, Wille-Jørgensen P



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Different outcome measures

HRQL Questionnaire	Number of studies (n=26)
EORTC QLQ-C30/CR38	17
SF-36	4
FACT-C	1
EQ-5D	1
HADS	1
STAI	1
mCOP-QoL-Ostomy	1
FIQL	1
Spitzer's QLI	1
CRC-QoL	1

Different outcome measures

- 367 different items.
- Unable to perform meta-analysis.
- No firm conclusions could be reached



3. Outcome reporting bias

RESEARCH METHODS & REPORTING

The impact of outcome reporting bias in randomised controlled trials on a cohort of systematic reviews

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Objective To examine the prevalence of outcome reporting bias—the selection for publication of a subset of the original recorded outcome variables on the basis of the results—and its impact on Cochrane reviews.

Design A nine point classification system for missing outcome data in randomised trials was developed and applied to the trials assessed in a large, unselected cohort of Cochrane systematic reviews. Researchers who conducted the trials were contacted and the reason sought for the non-reporting of data. A sensitivity analysis was undertaken to assess the impact of outcome reporting bias on reviews that included a

Selective reporting bias in a study is defined as the selection, on the basis of the results, of a subset of analyses to be reported. Selective reporting may occur in relation to outcome analyses,¹ subgroup analyses,² and per protocol analyses, rather than in intention to treat analyses,³ as well as with other analyses.⁴ Three types of selective reporting of outcomes exist: the selective reporting of some of the set of study outcomes, when not all analysed outcomes are reported; the selective reporting of a specific outcome—for example, when an outcome is measured and analysed at several time points but not all results are reported; and

Outcome reporting bias

- 10% missing data in Cochrane reviews
- 30% reviews contained one trial with ORB
- Treatment effect over-estimated by 20%

Core outcome sets

“...are 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.”



- Provide guidance for core outcome sets
- Collate and maintain relevant resources
- Develop reporting standards
- <http://www.liv.ac.uk/nwhtmr/comet/comet.htm>

Paula Williamson, Northwest HTMR Hub (lead)

Jane Blazeby, ConDuCT HTMR Hub, Bristol

Doug Altman, Oxford

Mike Clarke, Cochrane

Core outcome set development

- Identify all potential domains of interest
- Reduce to shorter list & further reduce
- Ensure key stakeholder involvement

Commentary

Open Access

OMERACT: An international initiative to improve outcome measurement in rheumatology

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OMERACT – core outcome set

- tender joint count
- swollen joint count
- patient's assessment of pain
- patient's assessment of global well being
- physician's assessment of global well being
- physical function
- acute-phase reactant

What Outcomes From Pharmacologic Treatments Are Important to People With Rheumatoid Arthritis? Creating the Basis of a Patient Core Set

T. SANDERSON,¹ M. MORRIS,² M. CALNAN,³ P. RICHARDS,⁴ AND S. HEWLETT²

Objective. Function, patient global assessment, and pain are routinely measured in rheumatoid arthritis (RA) clinical trials. However, other patient-reported outcomes identified as important to patients in qualitative studies, such as fatigue and quality of life, are commonly not included, and modern treatment regimens may have changed patients' expectations of treatment outcomes. Our objective was to elicit patient priority treatment outcomes for pharmacologic interventions since the common use of anti-tumor necrosis factor (anti-TNF) therapy, which will form the basis of a core set of patient priorities to complement existing professional core sets.

Methods. In-depth interviews were conducted with 23 RA patients, purposively sampled for age, sex, medication (anti-TNF or other disease-modifying antirheumatic drugs), disease severity, and work status. Grounded theory guided iterative data collection and analysis. Coding of the data was peer reviewed. A patient research partner collaborated in the research design and analysis.

Results. Sixty-three different outcomes important to patients were generated from the interviews. Four major categories of patient outcomes from pharmacologic treatments were developed: "RA under control," "Doing things," "Emotional health," and "Coping with illness." The core category (or overall theme) was "Minimizing the personal impact of RA."

Conclusion. Although the routine outcomes of pain, function, and overall well-being were raised by the patients, they also generated a further 60 important outcomes that they look for from treatment. This difference in perspective may potentially influence treatment decisions. The next step is therefore to use these data to develop a patient core set.

🌿 Patient core outcome sets

- Patient perspective workshop 2002
- Patient interviews – 63 outcomes
- Patient focus groups – 23 prioritised
- Survey of patients



Patient core set

- pain
- activities
- joint damage
- mobility
- life enjoyment
- independence
- ***fatigue***
- valued activities

Clinical core set

- tender joint count
- swollen joint count
- patient's pain
- patient's global assessment
- physician's global assessment
- physical function
- acute-phase reactant



The development of a core outcome set for clinical trials of colorectal cancer surgery

Mr Robert N Whistance MRCS

NIHR Doctoral Research Fellow

University of Bristol

Aims



Methods

1. Identify all the outcomes we COULD measure
2. Agree on CORE outcomes

🔥 Methods

Systematic literature
review

Phases 1 & 2

Comprehensive outcome list

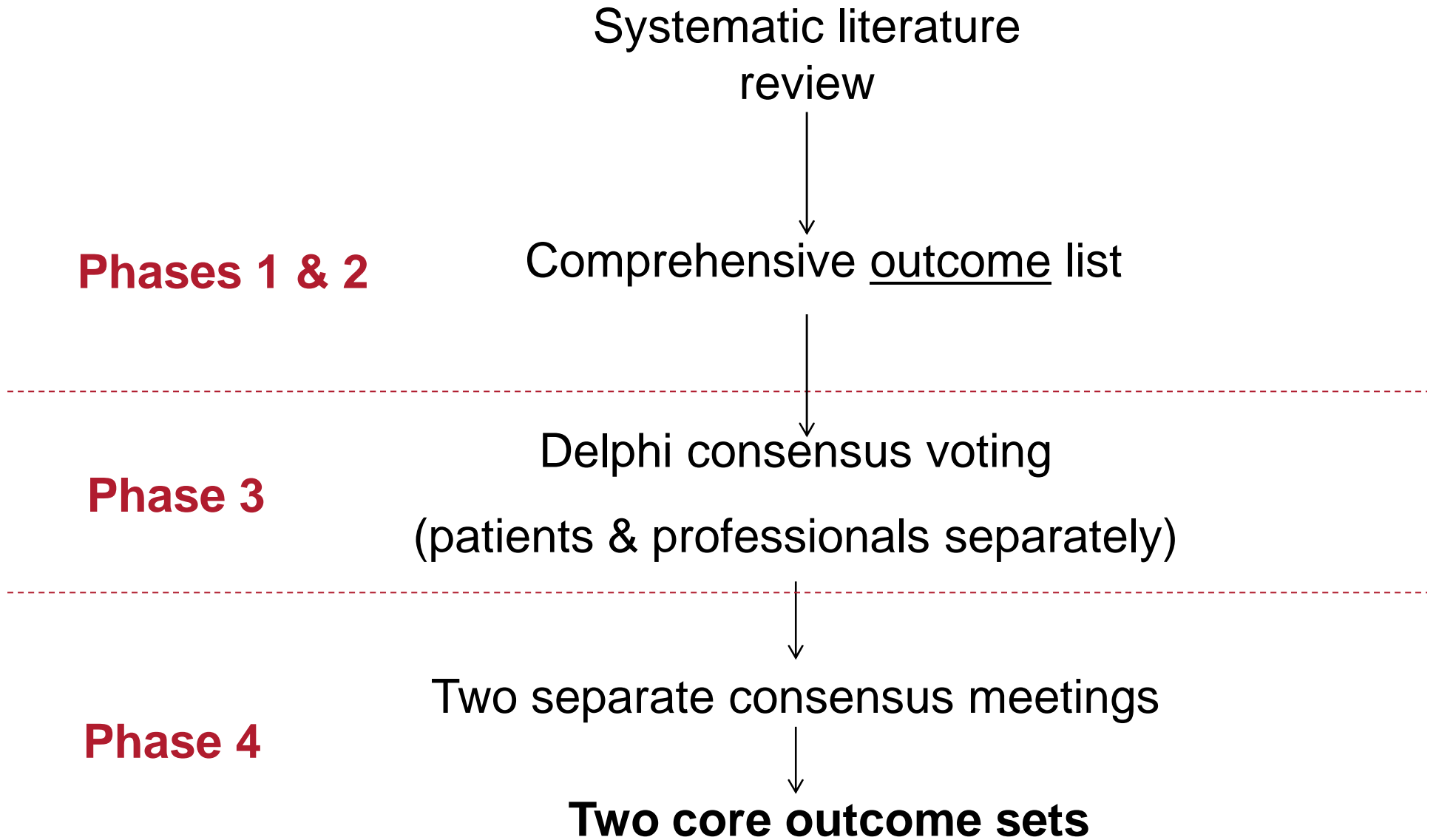
Phase 3

Delphi consensus voting
(patients & professionals separately)

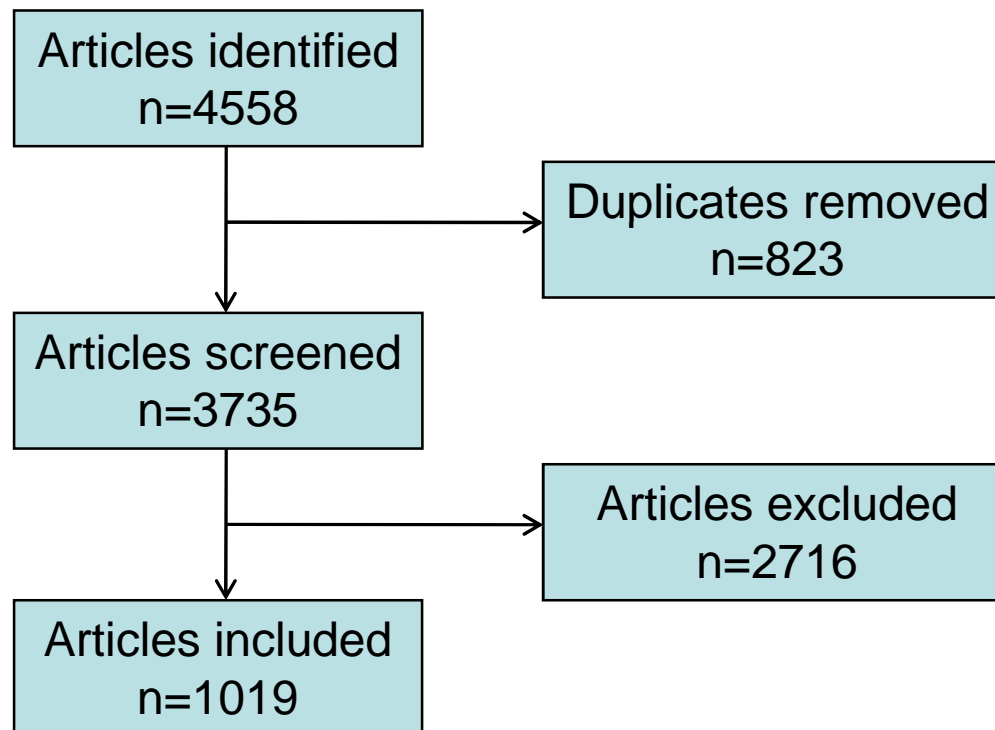
Phase 4

Two separate consensus meetings

Two core outcome sets



Systematic review



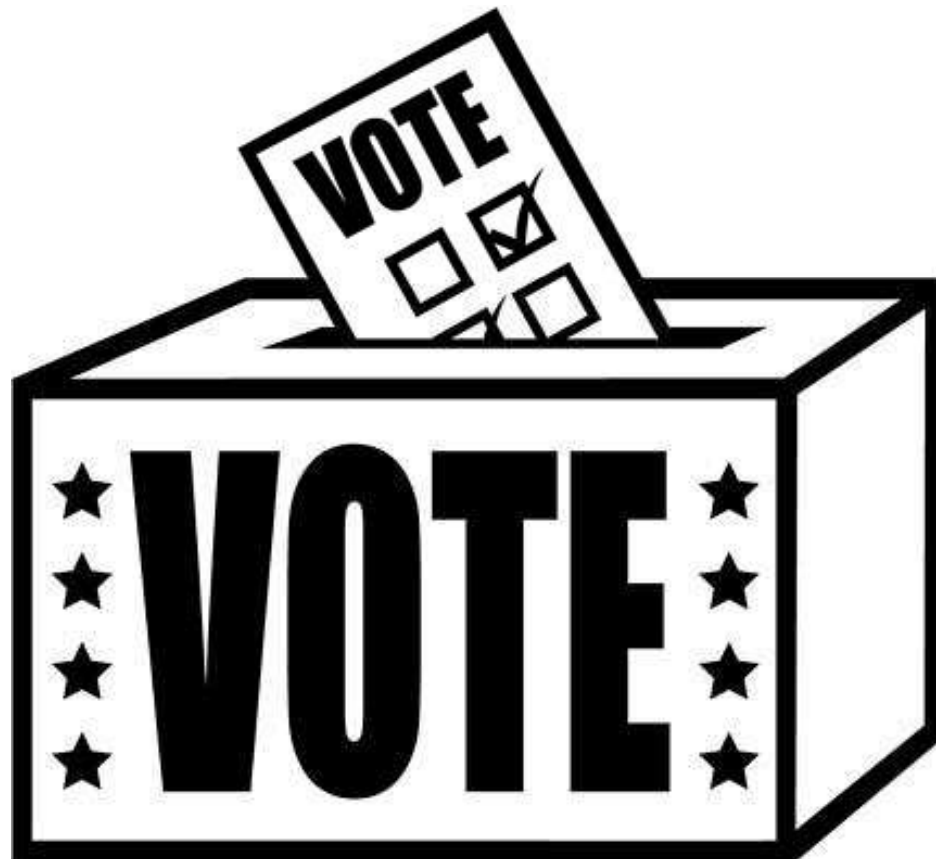
Inclusion criteria

- Surgery for CRC
- Neoadjuvant/adjuvant chemo/radiotherapy
- Palliative surgery

Exclusion criteria

- Palliative chemo/radiotherapy/stenting
- Non-biomedical interventions
- Screening
- Endoscopic treatment
- Review articles

Agree on CORE sets



Patient delphi process

Please rate the importance of measuring each of these outcomes in clinical trials of colorectal cancer.

	Irrelevant			Important
1. Survival after surgery	1	2	3	4
2. Presence of a stoma (bag)	1	2	3	4
3. Pain after the operation	1	2	3	4
4. Service satisfaction	1	2	3	4
5. Dry mouth after chemotherapy	1	2	3	4



Clinician delphi process

Please rate the importance of measuring each of these outcomes in clinical trials of colorectal cancer.

	Irrelevant			Important
1. Survival	1	2	3	4
2. Disease recurrence	1	2	3	4
3. Resection margin	1	2	3	4
4. Number of lymph nodes	1	2	3	4
5. Blood loss	1	2	3	4



To date

- NIHR Doctoral Research Fellowship award
- Ethics committee approval obtained
- Systematic review in progress

Impact of research

- Trials measure the same, minimum, outcome set
- Improved meta-analyses
- Reduced outcome reporting bias and cost

Summary

- Core outcomes improve trials
- Understanding service users views is central
- COMET initiative



Acknowledgements

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 - Paula Williamson, Northwest HTMR Hub (lead)
 - Jane Blazeby, ConDuCT HTMR Hub, Bristol
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