The COMET (Core Outcome Measures in Effectiveness Trials) Initiative

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www.liv.ac.uk/nwhtmr/comet/comet.htm

Background

Table 1: Review of therapeutic interventions for Burkitt's Lymphoma in children

Trial ID (author, date of publication)	Review primary outcome: Overall survival	Review Outcomes					Other Trial Outcomes	
		Event-free survival	Overall remission rate	Relapse rate	Toxicity and adverse events	Quality of life	Relapse site	Time to relapse
Anderson 1983	×	×	×	×	×	×	×	×
Brecher 1997	✓	✓	✓	×	✓	×	×	×
Cairo 2003a	×	O	×	×	×	×	×	×
Magrath 1973	×	×	×	✓	×	×	×	✓
Magrath 1976	✓	×	×	✓	×	×	✓	✓
Neequaye 1990	✓	×	×	✓	×	×	×	✓
Olweny 1976	✓	×	✓	✓		×	×	×
Olweny 1977	✓	×	×	✓	✓	×	×	×
Patte 1991	✓	✓	O	×	✓	×	×	×
Sullivan 1991	×	✓	×	×	×	×	×	×
Ziegler 1971	×	×	×	✓	×	×	×	×
Ziegler 1972a	✓	×	×	✓	×	×	O	O

✓= fully reported ; O = partially reported; × = not reported

Astonishingly, for most clinical areas, there is currently no general consensus on what outcomes should be reported in clinical trials. Achieving this is not straightforward, but it is not impossible.

One of the earliest examples is an initiative by the World Health Organisation in the late 1970s, relating to cancer trials. Meetings on the Standardization of Reporting Results of Cancer Treatment took place in Turin (1977) and again in Brussels two years later. More than 30 representatives from cooperative groups undertaking randomised trials in cancer came together and their discussions led to a WHO Handbook of guidelines on the minimal requirements for data collection in cancer trials (2, 3).

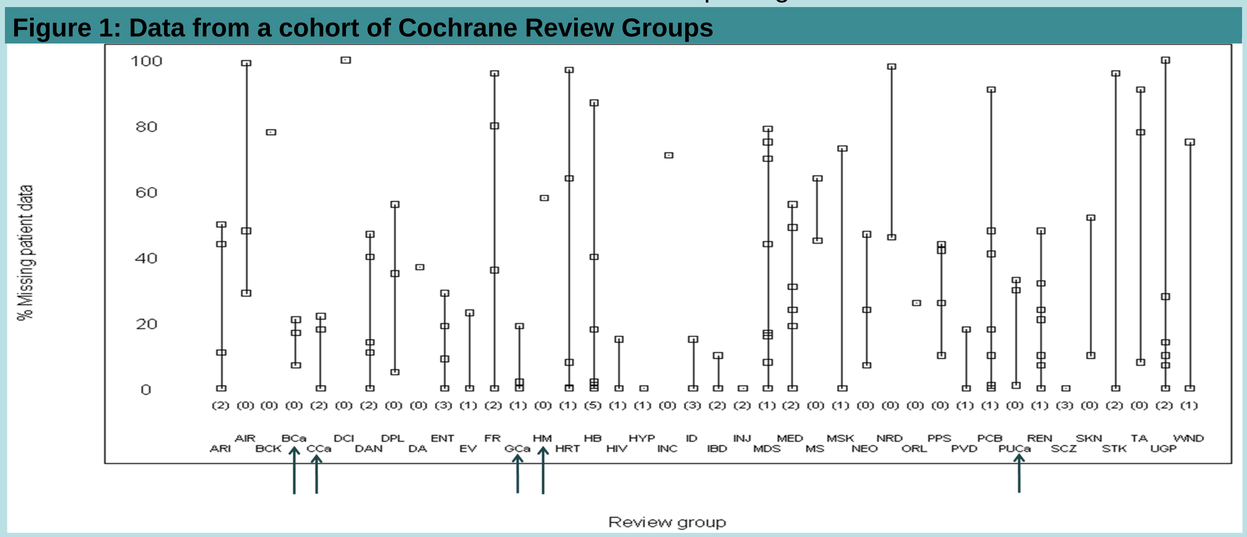
This small set of outcomes included acute toxicity, chronic or late toxicity, partial response (>50% decrease in tumour load), complete response (100% disappearance), date of first recurrence and date of death. These items may still reflect some of the needs of clinicians and patients today, but important outcomes may also be likely to have changed over the decades.

Systematic reviews of randomised trials are hampered by inconsistency in the patient outcomes assessed across the different studies. Many meta-analyses have to leave out key studies because the relevant outcomes were not reported. Table 1 demonstrates inconsistent reporting across studies in a review of therapeutic interventions for Burkitt's Lymphoma in children.

Figure 1 shows data from a cohort of Cochrane reviews (1) where the arrows on the x-axis indicate the cancer Collaborative Review Groups. Data displayed on the y-axis shows the % of patients across all trials in the review where the review primary outcome of interest was not measured and reported. Each box represents a separate review. The results suggest the lack of outcome data may be less of a problem for cancer reviews but there is clear room for improvement.

Much could be gained if each medical condition had an agreed minimum set of core outcomes that were measured and reported in all clinical trials. Systematic reviews and cross-study comparisons would be easier, the design of new trials would be simplified, and there would be reduced risk of bias from selective reporting of outcomes.

Figure 1: Data from a cohort of Cochrane Review Groups



COMET Initiative

The COMET Initiative was launched at a meeting in January this year. It is an international network bringing together individuals and organisations interested in the development, application and promotion of agreed standardised core outcome sets.

Objectives:

• to collate relevant resources (both applied and methodological) in a publically available searchable database

• to facilitate exchange of ideas and information

• provide guidance on methods for developing core outcome sets

• develop reporting standards for such studies

• advise on funding applications

What is a core outcome set?

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

Patient involvement

A notable initiative, established to identify appropriate outcomes for clinical trials in rheumatologic conditions in adults, is the OMERACT collaboration (4). It organises global consensus conferences in a 2 yearly cycle, where data driven recommendations are prepared and updated by expert working groups, including recommendations for core sets of measures for most of the major rheumatologic conditions.

Importantly, since 2002, patients have also been actively engaged in this process. This resulted in patients identifying an important outcome (fatigue) that had not been previously identified, demonstrating the important need to involve patients in the process of identifying appropriate outcomes to measure in clinical trials.

"As a parent you trawl through the literature on your child's condition and when you find relevant studies there is no way of comparing the information you find as many studies use such different outcome measurement tools. I am confused as a parent! Goodness knows how practitioners feel when they have to make clinical decisions based on incomparable data. I was overwhelmed by the positivity in the core outcome meeting and felt relieved as a consumer that such an essential issue is finally being addressed. The ground-breaking work of the international Rheumatology team was hugely inspiring and gave great direction to the meeting."

Heather Bagley, a parent attending the COMET Initiative launch meeting.

Examples of ongoing work to develop cancer core outcome sets

Oesophageal cancer surgery

AGK McNair, J Powell, S Whelan-Johnson, N Blencowe, D Titcomb, R Huxtable, JM Blazeby; University of Bristol

• A systematic review identified 77 papers reporting short-term outcomes of esophagectomy for cancer with or without neoadjuvant chemotherapy. 20 (26.0%) reported numbers of patients not progressing to surgery. Numbers of planned and completed operations were reported in 32 articles (28.1%). All papers reported post operative mortality but many different definitions for this term were used.

• Of 99 articles reporting morbidity, no single complication was reported in all studies. The most commonly reported complication was anastomotic leakage, reported in 76/99 (76.8%).

•Outcome reporting relating to oesophageal cancer surgery is inconsistent and lacks methodological rigour.

Head and neck cancer

Supervisors: Dr Terry Jones, Dr Catrin Tudur Smith. Research fellow: Aoife Waters, University of Liverpool

• Issues of biological heterogeneity, incidence of post-treatment functional deficits and relatively small numbers provide challenges when deciding on outcomes for RCTs in patients with SCCHN

Colorectal cancer surgery

Supervisors: Prof JM Blazeby, Dr ST Brookes, Dr K Avery, Mr A McNair. Research fellow: Robert N Whistance, University of Bristol

NIHR PhD Fellowship

• This project aims to develop a set of core outcomes for use in colorectal cancer RCTs, and to establish whether this is similar to the information required for core disclosure for informed consent for colorectal cancer surgery.

Breast cancer

L Kilburn, J Banerji & J Bliss on behalf of the NCRI Breast Clinical Studies Group

• A long term follow-up CRF and guidance notes have been developed to standardise the way long term follow-up data are collected in academic-led breast cancer trials. The aim is for these to be adopted by CTUs running breast cancer trials and then assess usage and feedback in 6-12 months time.

Breast reconstruction surgery

Paper in press: JNCI 'Reporting clinical outcomes of breast reconstruction; systematic review'. S Potter, A Brigic, SJ Cawthorn, KNL Avery, JL Donovan, JM Blazeby

• This systematic review shows that at present, the breast reconstruction literature is of insufficient quality to aid decision-making and well-conducted and designed studies are urgently needed. The rigorous development of 'core outcome sets' would dramatically improve study design and comparability and the potential value of research to patients and surgeons.

References

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COMET Initiative two day meeting,
11th - 12th July 2011, Ashton Court Mansion, Bristol, UK

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