Measuring the impact of clinical trials: developing and applying a set of impact metrics

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Abstract

There is increasing interest in the so-called "impact" of clinical trials, with many funders requiring researchers to demonstrate this. It is unclear what researchers should be measuring as 'impact', and how.

We have developed a set of metrics to capture what we believe are the most important types of impact of clinical trials, specifically, effects on: future patients; health policy and society; and scientific knowledge. These metrics focus on the wider implications of a trial, rather than logging trial activities or outputs. Not every metric is relevant for every study.

Using these metrics, we developed 16 case studies of the impact of our past cancer and infectious diseases trials. Two examples are below.

Study A was a tuberculosis trial that reported in 2004. Impact was assessed in 2013 by interview with a key individual from the trial, guideline searches, citation search and routine data. Routine data collected by WHO reveal 196/206 countries used the Study A recommended regimen in 2011, equating to almost 7.9million TB cases. Cost-effectiveness analysis showed the Study A regimen was cost-saving compared to the previously recommended regimen, which may have saved health systems globally up to US$19m in 2011 alone.

PR07 was a prostate cancer trial. Impact was measured through guideline search, survey of clinicians and modelling. The PR07 results have influenced guidelines, practice and subsequent trials. 44% of UK and 21% of Canadian survey respondents reported changing practice due to these results. This change in practice could result in around 3730-5177 extra life-years at 15 years after diagnosis from a cohort of 7930 men diagnosed in any single calendar year.

Our metrics provide a practical framework for systematically assessing a range of impacts. Trial teams should routinely measure the impact of their results and funders should cover the costs of this activity.

Background

- There is increasing interest in the 'impact' of clinical trials, particularly from research funders, for example:
  - The UK Medical Research Council require 'Pathways to Impact' as part of grant applications
  - The European & Developing Countries Clinical Trials Partnership grant application form includes a section on impact
  - The UK Department for International Development require case studies of impact from funded research
  - The Research Excellence Framework (for assessing quality of UK higher education institutes) requires impact case studies
- Demonstrating impact is important to help justify public / charitable funding of clinical trials, and to show potential trial participants the importance of trials
- Little clarity on what sorts of things can be counted as impact, or how they are measured
- We developed a set of metrics to assess the impact of phase III clinical trials
- We applied these metrics to a number of our past studies, to assess their impact and the feasibility of the metrics

Methods

- Metrics were selected based on our experience and practice of designing, conducting and analysing clinical trials
- We shared the draft metrics with colleagues to get their feedback, and revised the metrics in the light of these comments
- To assess the impact of our past studies, we:
  - Interviewed lead researchers
  - Searched the literature & relevant clinical guidelines for citations, meta-analyses & cost-effectiveness studies
  - Searched for routine data about the relevant clinical practice
  - For PR07, we surveyed clinicians in the UK and Canada about the impact, and modelled improvements in survival based on uptake scenarios

Results

Table 1: Impact of Study A and PR07 trials

Impact Upon	Metric	Study A	PR07
Future Patients	Number of life-years saved by the intervention if universally adopted	N/A (primary outcome was relapses or treatment failures)	There are no good figures on how many men with locally-advanced prostate cancer are treated with hormone therapy alone each year, globally.
	Number of life-years saved by actual adoption of the intervention	N/A (primary outcome was relapses or treatment failures)	In the UK, current uptake of RT + hormone therapy will result in ~3730–5177 extra life-years at 15 years post treatment from a cohort of 7930 men diagnosed in a calendar year, compared to if all were treated with ADT alone.
	Improvements in QoL and/or reductions in toxicity (including QALYs or DALYs)	N/A	Toxicity increase was acceptable and patients recovered.
	Changed adherence to intervention as a response to trial results	Study A did not look at this, but reduction in treatment time may also help people who find it less easy to access health facilities (eg. those living far from nearest clinic) to complete treatment course.	N/A
	Increased access to an intervention as a result of the trial	N/A	N/A
	Changes in clinical practice that occur as a result of a trial being undertaken or results published	Routine data collected by WHO (2011) showed 196/206 countries reported using the 6-month regimen with rifampicin throughout for new TB patients. The number of new TB cases (excluding MDR TB) in these 196 countries totalled 7,883,245 in 2011. Treating these cases with the 6-month regimen rather than the previously recommended 8-month regimen will have prevented ~450,000 relapses and failures in 2011 alone. However, not all these countries were previously using the 8-month regimen, so this figure gives an idea of the maximum impact of Study A. The reality is likely somewhat less.	Use of RT plus hormone therapy increased from ~17% prior to the results being released (National Prostate Cancer Audit figures) to ~72% (survey data) for UK men with locally-advanced disease. Use of RT + hormone therapy was already high in Canada, so there was less increase. 44% of UK survey respondents and 21% of Canadian survey respondents reported changing their practice due to the trial results.
Health Policy and Society	Trial cited as a basis for guideline(s) recommendation or change in policy(ies)	Trial cited in many guidelines, including the World Health Organisation's, which influences national TB programme guidelines: • World Health Organisation, Tuberculosis care and control in refugee and displaced populations: An interagency field manual, second edition. 2007. • World Health Organisation, Treatment of Tuberculosis guidelines, fourth edition. 2010. pp.32	RT + hormone therapy is now recommended by major guidelines including: • European Association of Urology, 2014 • National Institute for Health and Care Excellence (NICE), UK, 2014 • National Comprehensive Cancer Network, USA, 2014
	Widespread implementation of an intervention in a standardised way	N/A	N/A
	Incremental cost-effectiveness ratio	"The expected cost savings associated with 4HR were $2.42 per patient." doi: 10.1371/journal.pone.0039187	N/A
	Financial costs saved as a result of the trial	Based on cost savings from the Ugandan cost-effectiveness study, and estimate of numbers treated with the 6-month regimen, the widespread use of the 6-month regimen will have saved US$19,077,453 in 2011 alone, compared to if all those patients had been treated with the 8-month regimen.	N/A
	Trial cited as a basis for drug licensing decision	N/A	N/A
Scientific Knowledge	Novel trial design or methodology adopted by future trials	Study A was the first non-inferiority trial in TB. This approach was subsequently used in Study C.	N/A
	Correlative research increasing the utility of the intervention and/or indicating mechanisms of action	N/A	N/A
	Intervention arm of trial is adopted as the control arm of subsequent trials	6-month regimen is viewed as the gold standard, so used as control arm in many trials. (It was already viewed as gold standard, but Study A reinforced this).	STAMPEDE trial was updated in 2011 following the PR07 results
	Generation of new hypotheses	N/A	N/A
	Contribution to meta-analyses	3 meta-analyses (doi: 10.1371/journal.pmed.1000146; 10.1086/651686; 10.1093/cid/cis630)	None yet.
	Impact factor of journal and/or the subsequent number of citations	First paper: Lancet IF=39.06 → 139 citations Long-term results: International Journal of Tuberculosis and Lung Disease IF=2.61 → 5 citations	First paper: Lancet IF=39.06 → 188 citations Long-term results: Journal of Clinical Oncology IF=18.44 → 34 citations

Study A

Study A was an RCT for TB testing the WHO-recommended 8-month regimen (with rifampicin for only 2 months) against a 6-month regimen (containing rifampicin throughout). Patients on the 6-month regimen did much better than those on the 8-month regimen; they were about half as likely to have an unfavourable outcome. Results were published in 2004 for 12-month outcomes.

PR07

PR07 was a trial comparing hormone therapy plus radiotherapy against hormone therapy alone for men with locally-advanced prostate cancer.

PR07 found clear evidence that adding radiotherapy to hormone therapy improves outcomes, increasing overall survival and halving deaths from prostate cancer.

Recommendations

- Our metrics provide a practical framework for systematically assessing a range of impacts
- Trial teams should routinely measure study impacts
- Funders should cover the costs of this activity

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