

## W Avoidable waste in the production and reporting of research evidence

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Lancet 2009; 374: 86–89

Published Online  
June 15, 2009

DOI:10.1016/S0140-  
6736(09)60329-9

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Without accessible and usable reports, research cannot help patients and their clinicians. In a published Personal View,<sup>1</sup> a medical researcher with myeloma reflected on the way that the results of four randomised trials relevant to his condition had still not been published, years after preliminary findings had been presented in meeting abstracts:

“Research results should be easily accessible to people who need to make decisions about their own health... Why was I forced to make my decision knowing that information was somewhere but not available? Was the delay because the results were less exciting than expected? Or because in the evolving field of myeloma research there are now new exciting hypotheses (or drugs) to look at? How far can we tolerate the butterfly behaviour of researchers, moving on to the next flower well before the previous one has been fully exploited?”

This experience is not unusual: a recently updated systematic review of 79 follow-up studies of research reported in abstracts estimated the rate of publication of full reports after 9 years to be only 53%.<sup>2</sup>

Worldwide, over US\$100 billion is invested every year in supporting biomedical research, which results in an estimated 1 million research publications per year. Much of this investment has supported basic research. For example, over two-thirds of government and charitable investment in biomedical research in the UK has been for basic research, with less than 10% for treatment evaluation. The relative lack of support for applied research and the bureaucracy that regulates

research involving patients have been powerful disincentives for those who might otherwise have become involved in research in treatment evaluation. In recent years, there has been recognition of the need to address both of these disincentives. In the UK, the Cooksey enquiry concluded that government support for applied research should be increased,<sup>3</sup> and the National Institute for Health Research (NIHR) has responded rapidly to this policy (its funding for clinical trials will soon be £80 million a year).<sup>4</sup> In the USA, a bill currently before Congress calls for federal support for evaluations of treatments independent of industry, and in Italy and Spain, independent research on the effects of drugs is being supported with revenue from a tax on pharmaceutical company drug promotion.<sup>5</sup>

This increased investment in independent treatment evaluation is laudable. Irrespective of who sponsors research, this investment should be protected from the avoidable waste of inadequately producing and reporting research. We examine the causes and degree of waste occurring at four successive stages: the choice of research questions; the quality of research design and methods; the adequacy of publication practices; and the quality of reports of research (figure).

### Choosing the wrong questions for research

An efficient system of research should address health problems of importance to populations and the interventions and outcomes considered important by patients and clinicians. However, public funding of research is correlated only modestly with disease burden, if at all.<sup>6–8</sup> Within specific health problems there is little research on the extent to which questions addressed by researchers match questions of relevance to patients and clinicians. In an analysis of 334 studies, only nine compared researchers' priorities with those of patients or clinicians.<sup>9</sup> The findings of these studies have revealed some dramatic mismatches. For example, the research priorities of patients with osteoarthritis of the knee and the clinicians looking after them favoured more rigorous evaluation of physiotherapy and surgery, and assessment of educational and coping strategies. Only 9% of patients wanted more research on drugs, yet over 80% of randomised controlled trials in patients with osteoarthritis of the knee were drug evaluations.<sup>10</sup> This interest in non-drug interventions in users of research results is reflected in the fact that the vast majority of the most frequently consulted Cochrane reviews are about non-drug forms of treatment. The current emphasis on drugs is not simply a feature of commercial research: controlled trials funded by the UK

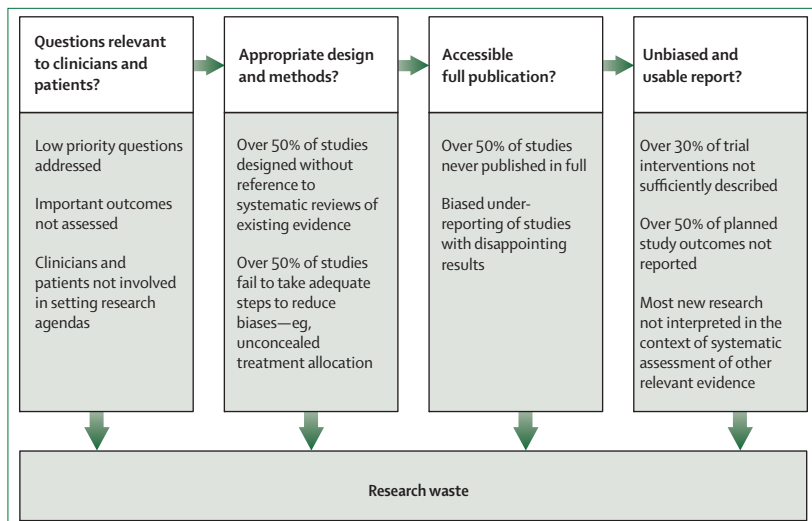


Figure: Stages of waste in the production and reporting of research evidence relevant to clinicians and patients

Medical Research Council and British medical research charities between 1980 and 2002, for example, were substantially more likely to be drug trials than were trials commissioned by the National Health Service Research and Development Programme (now the NIHR).<sup>11</sup> Furthermore, the outcomes that researchers have measured have not always been those that patients regard as most relevant. The exemplary involvement of patients by researchers assessing treatments for rheumatoid arthritis showed that, for most patients, fatigue was the dominant symptom of concern, rather than pain, as researchers had assumed.<sup>12</sup>

Many researchers remain dismissive of suggestions that patients, carers, and clinicians should help to prioritise research, but there are some signs of change. For example, the James Lind Alliance has been established to bring together patients, carers, and clinicians to prioritise unresolved questions about the effects of treatments. In the case of asthma, unaddressed uncertainties about possible adverse effects of long-term use of steroids and other powerful treatments emerged as their principal shared concern.

### Doing studies that are unnecessary, or poorly designed

New research should not be done unless, at the time it is initiated, the questions it proposes to address cannot be answered satisfactorily with existing evidence. Many researchers do not do this—for example, Cooper and colleagues<sup>13</sup> found that only 11 of 24 responding authors of trial reports that had been added to existing systematic reviews were even aware of the relevant reviews when they designed their new studies. About 2500 systematic reviews of research are now being published every year, with roughly a quarter of them in the *Cochrane Database of Systematic Reviews*. Systematic reviews are now the most frequently cited form of clinical research<sup>14</sup> (the citation frequency of the *Cochrane Database of Systematic Reviews* ranks seventh among general medical publications), but there is still a long way to go before we will know what number and proportion of the many questions of importance to patients and clinicians can be answered with systematic reviews of existing evidence. It has been estimated that at least 10 000 systematic reviews would be required to cover the issues that have been addressed in over half a million reports of controlled trials.<sup>15</sup>

New research is also too often wasteful because of inadequate attention to other important elements of study design or conduct. For example, in a sample of 234 clinical trials reported in the major general medical journals, concealment of treatment allocation was often inadequate (18%) or unclear (26%).<sup>16</sup> In an assessment of 487 primary studies of diagnostic accuracy, 20% used different reference standards for positive and negative tests, thus overestimating accuracy, and only 17% used double-blind reading of tests.<sup>17</sup>

### Failure to publish relevant research promptly, or at all

Biased under-publication and over-publication of research are forms of unscientific and unethical misconduct about which the public has become increasingly aware, particularly because of several exposés of suppressed evidence about serious adverse effects of treatments.<sup>18</sup> More generally, studies with results that are disappointing are less likely to be published promptly,<sup>19</sup> more likely to be published in grey literature, and less likely to proceed from abstracts to full reports.<sup>2</sup> The problem of biased under-reporting of research results mainly from decisions taken by research sponsors and researchers, not from journal editors rejecting submitted reports.<sup>20</sup>

Over the past decade, biased under-reporting and over-reporting of research have been increasingly acknowledged as unacceptable, both on scientific and on ethical grounds. Calls for prospective, public registration of all clinical trials have been issued by influential organisations—eg, WHO and the World Medical Association (through the latest revision of the Declaration of Helsinki) and the International Committee of Medical Journal Editors—and some progress has been made. WHO's International Clinical Trials Registry Platform has been developed to improve transparency and social involvement in research, and there has been progress, especially in the USA, where publication of the results of research is now required. Although these developments are welcome, public access to the full results of all research remains an aspiration, and one that continues to be resisted by some research sponsors and researchers.

### Biased or unusable reports of research

Although their quality has improved, reports of research remain much less useful than they should be. Sometimes this is because of frankly biased reporting—eg, adverse effects of treatments are suppressed, the choice of primary outcomes is changed between trial protocol and trial reports,<sup>21</sup> and the way data are presented does not allow comparisons with other, related studies. But even when trial reports are free of such biases, there are many respects in which reports could be made more useful to clinicians, patients, and researchers. We select here just two of these.

First, if clinicians are to be expected to implement treatments that have been shown in research to be useful, they need adequate descriptions of the interventions assessed, especially when these are non-drug interventions, such as setting up a stroke unit, offering a low fat diet, or giving smoking cessation advice. Adequate information on interventions is available in around 60% of reports of clinical trials;<sup>22</sup> yet, by checking references, contacting authors, and doing additional searches, it is possible to increase to 90% the proportion of trials for which adequate information could be made available.<sup>22</sup>

For more on the James Lind Alliance see <http://www.lindalliance.org>

For more on WHO's International Clinical Trials Registry Platform see <http://www.who.int/ictrp/en/>

**Panel: Stages of waste in the production and reporting of research evidence—barriers (in italics) and recommendations (bullet points)**

**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

*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

**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-care 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

**Accessible full publication**

*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

**Unbiased and usable report**

*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 (<http://www.equator-network.org>)

*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

*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

CONSORT=Consolidated Standards of Reporting Trials. STARD=Standards for the Reporting of Diagnostic Accuracy Studies.

For more on the Health Technology Assessment Programme see <http://www.ncchta.org/funding/clinicaltrials/index.shtml>

Second, unless new evidence is set in the context of updated systematic reviews, readers cannot judge its relevance. Yet among the world's major general medical journals, *The Lancet* is alone in requiring reports of new research to be preceded by and to conclude with reference to systematic reviews of other relevant evidence. In 2005, the editors wrote: "...we will require authors of clinical trials submitted to *The Lancet* to include a clear summary of previous research findings, and to explain how their trial's findings affect this summary. The relation between existing and new evidence should be illustrated by direct reference to an existing systematic review and meta-analysis".<sup>23</sup>

This principle will remain challenging while the need for up-to-date, reliable systematic reviews of research findings remains insufficiently recognised and supported. Although the Cochrane Collaboration aspires to maintain its reviews by adding new evidence to them, presenting more detailed analyses, and correcting any mistakes identified, many Cochrane reviews are not being updated in a timely manner, and the organisation is struggling to deal with this deficiency. The challenge of keeping existing systematic reviews up to date has not been solved by any other organisation in the world.

**Conclusions and recommendations**

Although some waste in the production and reporting of research evidence is inevitable and bearable, we were surprised by the levels of waste suggested in the evidence we have pieced together. Since research must pass through all four stages shown in the figure, the waste is cumulative. If the losses estimated in the figure apply more generally, then the roughly 50% loss at stages 2, 3, and 4 would lead to a greater than 85% loss, which implies that the dividends from tens of billions of dollars of investment in research are lost every year because of correctable problems. Although we have mainly used evidence about the design and reporting of clinical trials, we believe it is reasonable to assume that the problems also apply to other types of research.

Because there are problems within each stage of production and reporting, there is no single, simple solution. But even modest efforts to understand and improve production and reporting of research are likely to yield substantially increased dividends for patients and the public. Enough is known to justify some specific suggestions for the attention of the research community, and for action related to each of the stages of design and reporting. These recommendations are shown in the panel. Some elements of these recommendations reflect policies already implemented by some research funders in some countries. For example, the NIHR's Health Technology Assessment Programme routinely requires or commissions systematic reviews before funding primary studies, publishes all research as web-accessible monographs, and, since 2006, has made all new protocols freely available.

Even though there is more to learn about the "epidemiology" and "treatment" of waste in the production and reporting of research evidence, we believe that all of our recommendations are justified on the basis of the evidence we have cited. Action to address this waste is needed now because it has human as well as economic consequences, as illustrated by the quotation with which this Viewpoint began.<sup>1</sup>

**Contributors**

The coauthors contributed equally to the background research and text of the manuscript.

**Conflicts of interest**

We declare that we have no conflicts of interest.

**Acknowledgments**

We are grateful to Doug Altman, Luis Gabriel Cuervo, John Kirwan, Marie Claude Lavoie, Sally Davies, Tom Walley, and an anonymous referee for helpful comments on an earlier draft of this paper.

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