An opportunity to maximise the impact of funding: reducing the 85% avoidable "waste" in research

NOTE: This submission is aimed at addressing the fourth term of reference: "opportunities to maximise the impact of funding" but is also relevant to the other three.

In 2009, we estimated that 85% of all health research was being avoidably "wasted" [Chalmers & Glasziou, 2009] due to non-publication, poor reporting, or avoidable design flaws. Given that around \$200 billion per year is spent globally on health and medical research, it implied an annual waste of \$170 billion. That amount ranks somewhere between the GDPs of Kuwait and Hungary. It seems a problem worthy of serious analysis and attention. But how can we estimate the waste?

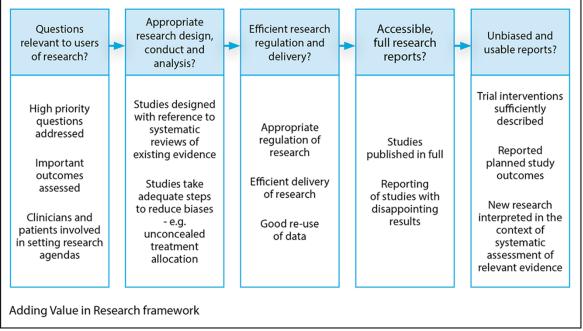


Figure: Stages of waste in research (from Lancet series, 2014 - http://rewardalliance.net/documents/articles/)

Unpublished research cannot have impact (Stage 3). Yet we know from follow up of registered clinical trials that about 50% are never published in full, a figure which varies little across countries, size of study, funding source, or phase of trial [Ross, 2014]. If the results of research are never made publicly accessible – to other researchers or to end-users - then they cannot contribute to knowledge. The time, effort, and funds involved in planning and conducting further research without access to this knowledge is incalculable. Though the 50% non-publication rate for clinical trials is well established, rates of non-publication for other types of research appear worse but less well documented. For example, in psychology one survey found 50% researchers admitted not reporting studies that didn't "work" and 66% admitted selective reporting of outcomes[Johns, 2012].

Published reports of research must also be **sufficiently clear**, **complete**, **and accurate** for others to interpret, use, or replicate the research correctly(Stage 5). But again, at least 50% of published reports do not meet these requirements [Glasziou, 2014]. Measured endpoints are often not reported, methods and analysis poorly explained, and interventions insufficiently

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described for others – researchers, health professionals and patients - to use. All these problems are avoidable, and hence represent a further "waste".

Finally, new research studies should be designed to take systematic account of lessons and results from previous, related research, but at least 50% are not (Stage 2). New studies are frequently developed without a systematic examination of previous research on the same questions, and they often contain **readily avoidable design flaws** [Yordanov, 2015]. And even if well designed, the execution of the research process may invalidate it, for example, through poor implementation of randomization or blinding procedures.

Research waste also occurs in Stage 1 and 3, but is less readily quantifiable. Given the three quantifiable and essential elements – accessible publication, complete reporting, good design — we can estimate the overall percent of waste. Let us first consider what fraction of 100 research projects DO satisfy all these criteria? Of 100 projects, 50 would be published. Of these 50 published studies, 25 would be sufficiently well reported to be usable and replicable. And of those 25, about half (12.5) would have no serious, avoidable design flaws. Hence the percent of research that does NOT satisfy these stages is the remainder, or 87.5 out of 100. In our 2009 paper, we rounded this down to 85%.

Although the data on which our estimates were based came mainly from research on clinical research, particularly controlled trials, the problems appear to be at least as great in preclinical research [Macleod. 2014]. Additionally, our 2009 estimate did not account for waste in deciding what research to do and inefficiencies in regulating and conducting research. These were covered in the 2014 Lancet series on waste, but it is harder to arrive at a justifiable estimate of their impact.

The "good news" is that there is vast potential gain from reductions in this avoidable waste. A few percent of the current budget could be used to recover lost and poorly reported research. However, we need to press on with that salvage: data from studies are being lost forever at a rate of perhaps 7% per year [Vines, 2014]. We certainly should, and must, attend to that – indeed it seems both an economic and an ethical imperative – but we also need to improve the processes and incentive systems in research. This is the motive that led to the launch of the REWARD Alliance, which held its first conference in Edinburgh in September 2015 (www.rewardalliance.net/). The Alliance is currently working with funders, regulators, publishers, organisations, and others to reduce waste and add value.

In order to increase the value of health related research, several organisations around the world are now working together to advance the practices of health related research and research funding. In particular, the *Ensuring Value in Research (EViR) Funders' Collaboration and Development Forum* started in 2017 by NIHR (UK), ZonMw (Netherlands), and PCORI (USA), with meetings in London, Den Haag and Washington DC. (see https://sites.google.com/view/evir-funders-forum/guiding-principles). The Funders' Forum have developed and posted a set of Guiding Principles, based around the Lancet series 5-stage model (Figure) and recommendations:

1. Justifiable research priorities

Principle 1: Health-related research agendas and priorities should be set with the meaningful involvement of those who will use and be affected by health-related research.

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2. Robust research design, conduct and analysis

Principle 2: Research should only be funded if set in the context of one or more existing systematic reviews of what is already known or an otherwise robust demonstration of a research gap.

Principle 3: Funders should take into account advances in research methodology and fund new research only if adequate steps have been taken to reduce bias.

3. Regulation and management of research conduct proportionate to risks

Principle 4: Selection and conduct of research should be actively managed in a risk proportionate way, consistent with applicable human subjects research laws, regulations, and ethical guidance.

4&5. All information on research methods & findings accessible and all reports are complete and usable

Principle 5: Studies should be registered in an appropriate, design-relevant publicly accessible registry at study inception whenever possible.

Principle 6: Research questions, methods, materials, analysis plans or sequence of analytical choices for all studies should be made available as early as possible and preferably near or before the start of the study or analysis. Any deviation from the original plans should be documented.

Principle 7: All studies should report methods and findings in full, following credible and justifiable reporting guidelines. This applies irrespective of the nature of the findings and whether the study completed as planned.

Principle 8: When appropriate and when it will add value to evidence users, replication, reanalysis, and reuse of data from studies should be supported and facilitated.

Principle 9: New evidence should be placed in the context of existing knowledge to inform appropriate interpretation and use of findings. When appropriate and when it will add value to evidence users, systematic reviews should be updated following primary research.

Principle 10: Research knowledge that can lead to benefit should be effectively disseminated to end users. Where appropriate, the usage of new knowledge should be supported and facilitated.

The forum recognizes that the necessary actions, if any, required to work towards these guiding principles will be different for different funders, and provide both implementation mechanisms and specific examples (see https://sites.google.com/view/evir-funders-forum/implementation-of-guiding-principles). Application of these principles would help guide a stepwise reduction in the 85% research waste, and has the potential to improve the value and efficiency from Australia's research investment.

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