Sustaining Australian research through clinical trials and investigator networks

Australians should continue to benefit from a health system based on clinical trials evidence

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doi: 10.5694/mja13.10066

In mid 2012 the *MJA* convened a summit on improving the landscape of clinical trials in Australia, where researchers from investigator networks and trial coordinating centres met with government policymakers, industry representatives, consumer groups and health professionals. The difficulties Australia faces in relation to research and health care and the practical solutions that emerged from the summit are the subject of a series of forthcoming articles in the *MJA*, including one in this issue.[1]

Health care expenditure in Australia is growing faster than the gross domestic product supporting it, having increased from $72 billion to $121 billion per year in the past 10 years.[2] According to Treasury projections, the current annual cost to the Australian Government of $50 billion will triple over the next 30 years, predominantly on account of increases in the costs of treatments and, to a lesser extent, the changing age structure of the population.[3]

While clinical trial evidence for new treatments is clearly needed, many therapies currently used in clinical practice are not based on reliable trial evidence;[4] or are based on evidence only within limited clinical settings.[5] Some, when properly evaluated within a randomised controlled trial (RCT), have been shown to be ineffective[6] or even harmful.[7,8] A rational approach to sustaining health care would be to conduct pragmatic clinical trials so clinicians and policymakers could use effective, affordable therapies and abandon therapies that are ineffective or harmful.

Although clinical trials have the potential to save several hundred million dollars per year in Australia through better evidence, large trials that are directly relevant to public health are expensive, so the National Health and Medical Research Council (NHMRC) and other public funding bodies must choose from among many worthwhile projects those that will receive funding. Since 2008, the number of larger Phase III trials, both commercial[9] and investigator-led, has declined by 30% to 50% (Associate Professor Lisa Askie, Australian New Zealand Clinical Trials Registry, personal communication, 2012). Reducing clinical trial activity when resources are scarce is a false economy and fails to recognise the opportunity costs of loss of evidence and the degradation of clinical trials infrastructure.

A new funding model to enhance existing research could incorporate additional clinical trials research in the health care budget. There is notional funding for research within the existing health care budget, but it is often subsumed within operational budgets or allocated for research in an ad-hoc and poorly coordinated way. A target of 0.5% to 1% of the health care budget, phased in over several years, could be used to support clinical trials and provide evidence to guide future practice and policy. Other knowledge-based industries typically allocate more turnover to research and development.

This funding would include support for clinical trials within hospitals, trial networks and coordinating centres, and some specific trials. It would complement rather than replace NHMRC and other research funding, and could be made cost-neutral by adjusting the decision thresholds for new interventions. For example, RCTs of promising new drugs funded by the Pharmaceutical Benefits Scheme (as proposed by Glasziou[10]) or new health technologies funded through Medicare should be considered where there is potential benefit of new treatment but not sufficient evidence to recommend funding as part of standard care. The Second Australian National Blood Pressure Study, among over 6000 patients, provided such evidence for the choice of antihypertensive drug therapy in elderly patients, using government funding of the drugs in the trial.[11] Further, when clinical trial evidence is implemented with tangible cost savings to government and insurers, a portion of the savings could be made available competitively to support more clinical research.

In the United Kingdom, adoption by the National Institute of Health Research (NIHR) of a model for allocating funds derived from the health care budget has revolutionised clinical trials. The NIHR receives funding identified as being for research in the National Health Service budget (currently 1% of the total budget) and centrally allocates this for infrastructure support and project funding.[12] Similar schemes to evaluate health care using comparative-effectiveness research have been established in the United States.[13]

Organisations that license or subsidise drugs and procedures in Australia can only approve or reject applications. Sometimes, however, when evidence of efficacy may be incomplete, an alternative strategy would be to approve these therapies only for use within an RCT while further evidence is obtained. If only half the patients received a new therapy, the cost savings to the government (compared with funding therapy for all) would usually be more than sufficient to cover the costs of the trial. Similarly, new health care policies, too, could be better evaluated by being implemented in trials with robust designs, such as stepped wedge or cluster randomised trials.

Australia needs many more clinical trials, and this requires much closer integration of clinical trials within routine clinical care. As well as providing more reliable evidence for future care, this may improve the quality of health care indirectly, as patients in trials and their hospi-

Perspective p 136

Examples of outcomes of work by Australian investigator-led networks or trial coordinating centres

Major advances

- Survival gains from cholesterol-lowering treatments[14]
- Cardiovascular events avoided with antihypertensive treatments
- Improvements in quality of life and survival for patients with cancer

Expensive therapies negated by clinical trials

- Intensive care treatments with starch-based colloids[15]
- Decompressive craniectomy for patients with traumatic brain injury[8]
- Tight glycaemic control in critically ill patients[16]
- Nitrous oxide anaesthesia[17]
- Immunoglobulin for preventing neonatal sepsis[6] ◆

tals often have better outcomes. Clinical trials research should be regarded as a core component of the health care system, and research participation should be a performance indicator for senior health care managers.

A particular role for publically funded trials exists where there is variation in standard care because of insufficient evidence. For trials testing two or more types of recognised standard care, opt-out consent should be considered and coupled with the process of providing information to prospective participants.

Investigator-led trials are more likely than commercial trials to generate evidence that improves health and reduces costs, particularly in finding new uses for old therapies or identifying ineffective therapies.[4] The NHMRC has a register of over 80 Australian investigator-led networks or trial coordinating centres. The work of these networks and centres has made Australia a world leader in the conduct of large trials for the public good in areas of medicine including cancer, cardiovascular disease, neonatology, diabetes, intensive care, nephrology, stroke and neurosciences, and anaesthesia, and many examples were presented at the summit (see Box).

Greater engagement, dialogue, and partnership between policymakers and the clinical trials networks offers the potential to improve the evidence base for new clinical practices and policy and to do so at low marginal cost or with cost savings. Clinical trial networks can:

- assist policymakers and clinicians to better understand the value of information that comes from trials
- share best practices for creating sustainable networks
- share infrastructure
- develop and adopt standardised study tools and metrics
- promote formation of new networks so that all areas of clinical medicine are covered
- contribute to the implementation of the results of trials in clinical practice
- promote common processes for accessing e-health information for trial purposes
- promote the safety, importance, and morality of participation in clinical trials.

A coherent strategy (possibly, the only viable strategy) for ensuring the sustainability of the health care system is to conduct more clinical research, as is now occurring in the UK and the US. The contribution that the trials networks can make to improving public health is substantial, but we need a revolution in research and health care models that leads to integration of clinical trials research as a routine activity within clinical care.

Acknowledgements: Steven Webb receives funding from a Royal Perth Hospital Medical Research Foundation Practitioner Fellowship.

Competing interests: The NHMRC Clinical Trials Centre and the Australian and New Zealand Intensive Care Society Clinical Trials Group receive research grants from the NHMRC.

Provenance: Commissioned; externally peer reviewed.

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