Australian Clinical Trials Alliance

Improving impact of clinical trials through implementability

June 2020

ACTA gratefully acknowledges operational funding from the Australian Government's Medical Research Future Fund

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TABLE OF ABBREVIATIONS

ACTA	Australian Clinical Trials Alliance
ARC	Australian Research Council
AUD	Australian dollars
CTN	Clinical trial network
EIA	Engagement and impact assessment
ERA	Excellence of Research in Australia
FDA	Food and Drug Administration
FoR	Field of research
NHMRC	National Health and Medical Research Council
OECD	Organisation for economic co-operation and development
RACGP	Royal Australian College of General Practice
TGA	Therapeutic Goods Administration
UoA	Unit of assessment
UK	United Kingdom
US	United States
NZ	New Zealand

ACKNOWLEDGEMENTS

This document was created and developed by the Impact and Implementation Reference Group of the Australian Clinical Trials Alliance (ACTA). ACTA is funded by the Medical Research Future Fund (MRFF).

USE OF THIS DOCUMENT

ACTA requests that the following acknowledgement is included in any documents that are developed using knowledge gained from this document. This will assist ACTA in identifying the usefulness and impact of this document in relation to improving impact of clinical trials through implementability.

> '[Name of CTN] acknowledges the contribution of ACTA to improving impact of clinical trials through implementability (reference: *Improving impact of clinical trials through implementability*).'

DISCLAIMER

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EXECUTIVE SUMMARY

The Australian Clinical Trials Alliance (ACTA), with the expertise and knowledge of the Impact and Implementation Reference Group, has prepared this guidance document on Impact and Implementation of Clinical Trials. The objective of this document is to provide guidance on the optimising of impact of clinical trials by recommending improvement of the implementability characteristics of clinical trials.

Research impact is often measured in terms of social and/or economic effects that result from the study. The assessment of impact is now an important consideration for research, including application for funding. However, how we define research impact, and to whom we hope it should be applied, vary considerably between fields of science, funding agencies and recipients, other stakeholders, and end-users of the research. As such we report on key issues in the measurement of impact and the bearing this has on research funding proposals, particularly for clinical trials.

Current measurements of impact include metrics that are not always relevant to clinical trials including publication indices of lead investigators that often relate to academic impact and profile status rather than research impact specifically. Research impact can also be difficult to measure and there are many different types of impact including academic, social, economic, environmental, policy and health and wellbeing that can result but may be difficult to attribute to a single study.

Clinical trials are expensive and can take many years to complete. Impacts in terms of change in treatment, policy or behaviour can take many years following trial completion. The Impact and Implementation Reference Group of ACTA offers some recommendations for optimising impact of clinical trials through improved implementation and strongly encourage those involved in the planning, conduct and reporting of clinical trials, as well as the implementation of trial results, to consider improving the implementability characteristics of their trial in order to improve impact.

It is hoped that this document serves as a useful reference that enhances the impact of clinical trials through optimising their implementability characteristics. This document works best as a companion piece to the Implementability Guidance document. This guidance is intended to be iterative, and feedback to enhance and improve the document are welcomed to facilitate production of updated versions.

OBJECTIVE

The objective of this document is to provide guidance on improving the research impact of clinical trials through the adoption of implementability characteristics. This document provides recommendations that may facilitate in improved impact of clinical trials.

WHAT IS IMPACT AND WHY IS IT IMPORTANT?

Researchers are motivated by the hope that their research 'makes a difference'. This 'difference' should broadly be understood as the impact of their research on their field of science, on their community and economy, and on society. Assessment of this impact has become an important consideration of research, including the application of research funding. However, how we define 'difference', and to whom we hope it should be applied, varies considerably between fields of science, funding agencies and recipients, other stakeholders, and end users of the research. Herewith we report on key issues in the measurement of impact in research funding proposals.

Public funding of research prioritises the facilitation and promotion of the highest quality research that achieves demonstrable economic and societal benefits to the wider community.[1] Most funders around the world look to measures of impact (particularly economic and societal impact) to prioritise research activity and justify continued public spending on research – to direct the allocation of limited research resources, maximise research benefit and help minimise research waste.[2] In turn, researchers are expected to be accountable and produce value for money research.[3]

Research impact has many definitions but is generally conceptualised as beneficial change. A common feature of the varied definitions used by funding agencies (see Table 1) is that the influence of research is felt beyond academia, in the 'real world' of individuals, communities, culture, economies and society as a whole. From the funders' and researchers' perspective, the impact must be measurable; from the societal perspective the impact should be demonstrable and

intelligible, to make visible to the public the benefits of the research and thereby provide ongoing social licence to both researchers and funders. To this end, a combination of quantitative metrics and narrative accounts can be used to monitor impact (see 'Approaches to impact' on page 9).

In evaluating the impact potential of a research funding application, funding agencies will evaluate: 1) the application's description of prospective academic, societal, and/or economic significance; 2) the proposal for dissemination and implementation of study results; and 3) the track record of applicant researchers, and their previous contribution to their field. However, these criteria are potentially problematic because the success of implementation and eventual impact of concluded research cannot be known at the time funding decisions are made; publication profiles essentially measure academic impact rather than societal impact and the presumption that 'past performance is the best indicator of future performance (or impact)' may only encourage a limited focus and approach to research.

Furthermore, these are contributions assigned to single investigators, often leading the research, when many other types of research, such as clinical trials, involve networks of people or institutions, all important in the success of the trial.

There is, therefore, ongoing disquiet regarding the appropriate metrics for impact evidence[4] that can be recorded and reported. Greenhalgh, et al (2016)[5] have suggested the use of logic models, narrative accounts and case studies alongside more automated measures, but warn that alternative approaches to measuring impact may be required for different purposes and that some methods for measuring impact are labour-intensive, costly and inaccessible for some studies. Another strategy is the establishment of defined impacts, chiefly for mission-oriented settings, applied research or priority areas where researchers are focused on expected, intended and short-term impacts. However, such strategies may incentivise against conducting more complex, long-term impact studies.

Despite subtle differences between their definitions, each organisation acknowledges different types of impact and their respective benefits. The measurements of impact also differs. Generally, four types of impact (knowledge, health, societal/social and economic)[6] are accepted across funding and research organisations. However, an ongoing world-wide analysis of the impact of studies has led to the proposal for 10 types of impacts[7], namely:

1. **Understanding and awareness:** people understand an issue better than they did before, based on the research.
2. **Attitudes:** a change in attitudes, typically of a group of people who share similar views, towards a new attitude that brings them or others benefits.
3. **Economy:** monetary benefits arising from research, either in terms of money saved, costs avoided, profit, funding, or benefits to groups of people or the environment.
4. **Environment:** benefits from research to genetic diversity, species or habitat conservation, and ecosystems, including the benefits that humans derive from a healthy environment.
5. **Health and wellbeing:** research that leads to better outcomes for the health of individuals, social groups or public health, including saving lives and improving quality of life, and wider benefits for the wellbeing of individuals or social groups, including both physical and social aspects such as emotional, psychological, economic wellbeing and measures of life satisfaction.
6. **Policy:** the contribution that research makes to new or amended laws, regulations or other policy mechanisms that enable them to meet a defined need or objective that delivers public benefit.
7. **Other forms of decision-making and behaviour change:** whether directly or indirectly research can inform a wide range of individual, group and organisational behaviours and decisions leading to impacts that go beyond the economy, environment, health, wellbeing or policy.
8. **Culture:** changes in the prevailing values, attitudes, beliefs, discourse and patterns of behaviour, whether explicit or implicit in organisations, social groups or society that deliver benefits to the members of those groups or those with whom they interact.
9. **Other social:** benefits to specific social groups or society not covered by other types of impact.
10. **Capacity or preparedness:** research that leads to new or enhanced capacity that is likely to lead to future benefits, or that makes individuals, groups or organisations more prepared and better able to cope with changes that might otherwise impact negatively on them.

Descriptions of each type of impact are provided elsewhere[8] and are not repeated here. As can be seen, the requirements are more than just academic (creating or accumulating new knowledge), but must also include other means of measuring research impact that apply to the 'real world' and can be compared between research projects.

Table 1: Definitions of research impact

Organisation	Country	Link	Definition of research impact	Criteria	Measures
Economic and Social Research Council (ESRC)	UK	https://esrc.ukri.org/research/impact-toolkit/what-is-impact/	'The demonstrable contribution that excellent research makes to society and the economy'	Excellent research, advancing scientific method/theory/application, capacity building	Knowledge exchange, influencing practice and policy, collaboration, infrastructure
National Institutes of Health (NIH)	US	https://grants.nih.gov/grants/peer/guidelines_general/impact_significance.pdf	'The likelihood for the project to exert a sustained, powerful influence on the research field(s) involved'	Investigator(s), research approach, research environment, innovation, and research significance	Significant scientific contribution, research opportunities to students, strengthen research environment
Health Research Council (HRC)	NZ	https://www.hrc.govt.nz/sites/default/files/2019-09/2020%20Research%20Impact%20Slideshow%20with%20notes.pdf	'The direct and indirect influence of excellent research on individuals, communities or society as a whole, including improvements to health and equity, and other social, economic, cultural or environmental benefits for Aotearoa/New Zealand'	Development of human capital, value-add of research to 'real world benefits'	Communication, relationships, and collaboration
Netherlands Organisation for Scientific Research (NWO)	Netherlands	https://www.nwo.nl/en/common/about-nwo/organisation/nwo-divisions/wotro/the-impact-of-research	'The contribution that innovative research makes to understand and solve global issues, with a focus on sustainable development and poverty reduction'	Communication, stakeholder engagement, capacity building, evaluation	Knowledge and attitude change and exchange, changes in practice and policy
National Health and Medical Research Council (NHMRC)	Australia	https://www.nhmrc.gov.au/research-policy/research-translation-and-impact/research-impact	'The verifiable outcomes that research makes to knowledge, health, the economy and/or society, and not the prospective or anticipated effects of the research. Impact is the effect of the research after it has been adopted, adapted for use, or used to inform further research'	Value for money, investigator(s), commercialisation of discoveries/product development, improved health outcomes	Knowledge, health, economic and social impacts
Australian Research Council (ARC)	Australia	https://www.arc.gov.au/policies-strategies/strategy/research-impact-principles-framework	'The contribution that research makes to the economy, society, environment or culture, beyond the contribution to academic research'	Excellent research, stakeholder engagement, cost-effective and efficient approach	Knowledge, job creation, risk reduction in decision making, quality of life, changes in practice and policy, economic and health impacts

Table 1 shows the different definitions of research impact as described by various funding organisations around the world. All websites were accessed and viewed on 28 May 2020.

FRAMEWORKS FOR MEASURING RESEARCH IMPACT

Traditionally, evaluation of university research was based upon measuring academic impact and quality through peer review as evidenced by various publication metrics.[9] An example of this is the h-index, which incorporates the number of publications and citations assigned to the lead author. These bibliometrics measure knowledge creation and dissemination which are measures of academic impact within a research organisation or university and shared amongst an academic audience. Today, these metrics are used in combination with research income in the broader context of research impact as seen internationally, the Excellence Framework in the UK[10], the Excellence in Research for Australia (ERA)[11], and the Star Metrics in the USA[12]. However, these traditional bibliometrics only indicate impact and have a number of shortcomings.

First, knowledge creation and dissemination through academic publication does not provide evidence of knowledge uptake and change in behaviour, attitude, or policy in the broader community. Second, publication indices used are often assigned to a single author who is most likely the lead investigator, negating the valuable knowledge and essential skills of other team members, often across disciplines (e.g. health economics, implementation science and consumer engagements) involved in the research, particularly clinical trials. Third, publication indices only provide information on a researcher's academic record, not necessarily the impact of the research or clinical trial.

In the meantime, interest in developing broader socioeconomic impact measurement frameworks has increased considerably. Such frameworks are often adopted at an organisational level and used to measure the requirements specified by the organisation and its stakeholders.[13,14,15,16,17,18] A brief listing of some of the most popularly used frameworks is tabulated below. It should be noted that those frameworks designed to facilitate swift translation and impact of research, rather than just assessing impact, provide potentially greater contribution to the economic and social priorities compelling implementation.

There remains a number of issues with these frameworks, namely the attribution of research impact to mostly academic metrics and ascribing impact to specific types of research. Creating impact is largely about the approach an organisation takes before, during and after the completion of the study. For example, if the study is applicable to populations outside of the research institution (e.g. First Nations people, minority groups, patients with heart disease and so on), then effective knowledge transfer would include communications to audiences beyond academic circles. Furthermore, partnerships[19] with members of community, industry and government stakeholders would assist with community-level awareness and uptake of research results, product development and use and policy change. Time is also a factor to be considered particularly with regards to behaviour change and knowledge transfer and uptake in the wider community. How much time is required depends on the message delivered, changes (i.e. behaviour or policy) to be made and cost-benefit of the exercise itself (e.g. skilled resources for information delivery, training, consultation, and campaigns).

Table 2: Frameworks for measuring research impact

Framework	Authors	Principles	Evaluation of impact	Main indices of measurement
The Payback Framework	Buxton and Hanney[20]	Assesses outcomes of health science research in terms of impacts	Comprises two elements: a logic model of the seven stages of research from conceptualisation to impact, and five categories to classify the paybacks – knowledge, benefits to future research, benefits to policy, benefits to health and the health system, and broad economic benefits.	1. Academic publications, conference presentations, books, reports and other dissemination materials; 2. Training of research staff, students, PhD, Masters, career promotion; 3. Policy documents and guidelines, membership on advisory panels; 4. Cost saving to health services/systems, QALY, health outcomes 5. Patents, commercial spin-outs
Research Excellence Framework	https://www.ref.ac.uk/	Measure the quality of research through submissions of quality profiles to be assessed by a panel of experts.	Assess three distinct elements: research outputs (60%); impacts (on economy, society, culture, public policy or services, environment, or quality of life; 25%) and; environment (in terms of vitality and sustainability; 15%)	1. Publications, reports, patents, software, databases, citation data, etc 2. Reach, significance, case studies, and other forms of impact including on products, processes, behaviours, policies, practices and understanding; and avoidance of harm or the waste of resources in the widest sense 3. Context and structure, impact strategies, people, incomes, infrastructure, facilities, collaboration.
Excellence in Research for Australia	https://www.arc.gov.au/excellence-research-australia	Identifies and promotes excellence across the full spectrum of research activity	Divided into fields of research, each discipline submits impact case studies to be evaluated for research quality, research outputs and research application	1. Publishing profile, citations, peer reviewed research income 2. Profile of researchers, outputs 3. Research commercialisation income, patents, plant breeder's rights, registered design, etc
CAHS Impact Framework	Frank, et al[21]	Builds on the Payback Framework and adopts a systems approach to capture impacts	Advancing knowledge indicators and metrics, research capacity building and metrics, informing decision making, health impacts, broad economic and social impacts	1. Publication profile, citation, research quality etc 2. Research funding and infrastructure, personnel 3. Healthcare, public health, social care, research decision making, industry decision making, products, media citation, public policy 4. Improved healthcare, QALY 5. Commercialisation, health benefit and cost savings, socio-economic benefits
Engagement and Impact	https://www.arc.gov.au/engagement-and-impact-assessment	Assess engagement with end users of research and translation of research into economic, social, environmental, cultural and other impacts	Divided into fields of research, each discipline submits impact case studies to be evaluated for engagement, impact, approach to impact and research outputs	1. Interactions between researchers, interactions between researchers and end-users outside of academia, knowledge transfer, technologies, methods, or resources 2. Significant contribution made outside academia (society, economy, culture, environment) 3. Strategies implemented to create impact including publication, citation, other forms of dissemination, etc

All websites were accessed on 3 June 2020

APPROACHES TO IMPACT

The Engagement and Impact Assessment (EIA) conducted by the Australian Research Council (ARC)[22] specifically looked at approaches to impact – as part of the measurement for research impact of quality research in Australia. The national report served as a companion to the Excellence in Research for Australia (ERA)[23], and culminated from the National Innovation and Science Agenda of 2015[24]. The ERA was a far larger exercise, that comprehensively evaluated the quality of research undertaken in Australian universities and compared these against international benchmarks of research excellence.

The purpose of the EIA was primarily to improve university 'engagement' with industry as Australia rated poorly against other OECD countries and the government of the day was keen to see return-on-investments with regards to research funding from public monies. The EIA exercise looks to identify what tangible benefits have been achieved beyond academia through investments in university research, the processes and infrastructure that enable research engagement, and how these institutions translate and promote translation of research into impact for the benefit of Australia.

With strong interest in impact and the mechanisms by which impact is enabled, the ARC designed a framework that would evaluate three separate areas: engagement, impact, and approach to impact. The engagement component was assessed using a suite of quantitative indices of engagement as well as a short narrative explaining the interaction between researchers and research end users, knowledge transfer, technologies and methods and resources. Impact and approach to impact were assessed based on qualitative impact case studies that detailed the impact, the research associated with the impact and the methods by which the institutions achieved impact. Panels of experts assessed these submissions and rated them on a three-tiered rating scale of low, medium, or high.

For 2018–19, the EIA assessed 626 individual research submissions for engagement, 637 case study submissions for impact and 159 case study submissions for approach to impact. Of these, 85% of engagement, 88% of impact and 76% of approach to impact submissions rated medium or high across the university sector. When matched to ERA findings, it appears there is a positive correlation between those studies that rated above world standards (in ERA) and also rated medium or high as assessed by the EIA. This indicates that locally-conducted, world-class research is likely to have greater local uptake and impact.

Many have debated the purpose and methods of such assessments. For example, the interactions between universities and industry or business, engagement is measured in terms of flow of money and there are no indicators for societal benefits or non-commercial engagement activities.[25] Others have asked what the results truly mean with a high rating simply being the result of impressive storytelling in the case study or narrative.[26]

Additional concerns included that the EIA assessments have thus far been restricted to academic research conducted through universities and that measurements of engagement and impact may vary widely between research disciplines whilst not necessarily being reflected in the measurement criteria (e.g. disciplines such as astrophysics and climate science may have greater difficulty demonstrating impact compared to nanotechnology or fossil fuel research). Further, the research outputs still include publication profiles (which as noted above, provides information about researcher publication history and not research impact), and this assessment favours applied over pure research.

When looking across those research studies that rated high on approach to impact, despite the diversity of methods adopted, there are common features associated with success:

- **Stakeholder collaboration in trial design and implementation**
  University support for ongoing collaboration between researchers and industry and other external partners was instrumental in successful translation beyond academia (various stakeholders and partnerships in industry and government, agreements/contracts).
- **Provision for infrastructure**
  Investment in infrastructure was vital in supporting research collaboration that lead to successful outcomes beyond academia (state of the art equipment, technological support, building and workspace infrastructure, administrative support).
- **Support mechanisms for knowledge transfer**
  Two-way knowledge transfer between researchers and external partners. (training, mentoring of students and early career researchers, strengthening skills and knowledge of research team, dissemination of research and networking activities).

WHAT DOES THIS MEAN FOR CLINICAL TRIALS?

Clinical trials have a number of associated benefits and risks.[27] In addition to being the only method of proving causal relationships between interventions and outcomes, the benefits of clinical trials include:

- Finding and developing better treatments, therapies, and diagnostic tools,
- Access to new interventions with potentially fewer side-effects and better outcomes, before they are made available to the general public,
- Opportunity for the patient to play an active role in their own health,
- Advice, care and support from trained clinical staff who understand the disease or condition,
- Closer monitoring of the condition, healthcare and treatment, and
- Potential value to those with rare or difficult-to-treat conditions for which there may be limited evidence on how best to treat or manage.

Clinical trials have facilitated development and testing of vaccines, medical drugs, medical products and services, improved healthcare services and delivery, reduced infectious disease death tolls and most importantly, improved life expectancy.[28]

The economic return-on-investment of clinical trials is well documented. In a report that evaluated the potential health and economic benefits generated by investigator-initiated clinical trials conducted in Australia[29], 25 high impact clinical trials were selected and analysed from three well established Australian Clinical Trial Networks (CTNs) that collectively have overseen more than 460 individual trials): Australasian Stroke Trials Network (ASTN), Interdisciplinary Maternal Perinatal Australasian Collaborative Trials (IMPACT) and Australian and New Zealand Intensive Care Society Clinical Trials Group (ANZICS CTG). Assuming results were implemented in 65% of the eligible Australian patient population for one year:

- Gross benefit would be approximately AUD$2 billion measured through better health outcomes and reduced health service costs
- Reductions in health service costs would account for 30% (AUD$580 million) of the gross benefit, and this alone would exceed the total costs for the CTNs and all their research activity from 2004 to 2014
- Overall return-on-investment was AUD$5.80 for every AUD$1 invested
- Results of the 25 trials only needed to be implemented in 11% of the eligible patient population for benefit to exceed cost
- For every AUD$1 awarded in National Health and Medical Research Council (NHMRC) funding to the 25 trials, a return of AUD$51.10 was achieved.

When we examine the characteristics of these successful clinical trials[30], they generally include the following:

- Research that is clinically relevant to clinicians and their patients
- Identified the best intervention irrespective of commercial relevance
- The clinical trials were conducted by investigators that were independent of any commercial organisation (that may be influenced by the results)
- The trials were embedded within routine clinical practice (primarily through connections with healthcare facilities)
- Were part of a Clinical Trial Network (CTN; which enabled access to people with multi-disciplinary skillsets and experience, provided shared infrastructure and facilitated funding for the successful completion of the trial)
- Were able to successfully recruit a large sample of the required patient population
- Could rapidly translate the findings to ‘real world’ (although the methods are not clearly understood).

Others[31,32,33] have suggested additional key factors that would contribute to the successful execution of clinical trials including well written protocols (these have to be rigorous, detailed and contain contingency plans for when things go wrong), risk assessment and management, commitment and dedicated time to the clinical trial by clinician-researchers, statistician consultation before trial commencement (to assess the feasibility of the study design and analyses, and estimate the sample size to power the study), transparency (in trial processes and communication with participants) and honest and regular reporting and monitoring, high quality data collection and safe, confidential storage, and collaboration (with consumer groups, colleagues with required skillsets and other stakeholders).

Further to the above, effective, quality implementation is crucial to impact. ACTA (https://clinicaltrialsalliance.org.au/about-acta/), particularly the Impact and Implementation Reference Group, has defined impact as “the change in health outcomes or health system productivity or both that arises from the implementation of evidence, including clinical trials.”[34]

When we superimpose the features determined to produce impactful research as determined by the Engagement and Impact framework onto clinical trial research, we find these features can be applied to clinical trials using different scope and definitions according to the implementability characteristics of trials as defined in the Implementability Guidance[35] document produced by ACTA.

APPROACH TO IMPACT, IMPLEMENTATION, AND CLINICAL TRIALS

STAKEHOLDER COLLABORATION IN TRIAL DESIGN AND IMPLEMENTATION:

Cooperation among a diverse group of stakeholders, including research sponsors (industry, academia, government, non-profit organisations, and patient advocates), clinical investigators, patients, payers, physicians, and regulators, is necessary when conducting a clinical trial. Each stakeholder offers a different set of tools to support the essential trial components. However, the ACTA Implementability Guidelines emphasise that these relationships should be formed as early as possible during a clinical trial's planning stage, especially during the stage of research priority setting.

It is estimated that around 20% of medical treatments and recommendations delivered today are supported by evidence[36], even then, compliance with evidence-based clinical practice guidelines is often poor[37,38,39]. These data emphasise the need to prioritise research to fill the gaps in healthcare and to have partnerships with stakeholders to ensure the success and uptake of the evidence. Consumers and vulnerable populations, such as the First Nations people, and ethnic groups must be consulted so that their health needs are not overlooked and that the beneficial impact of research is felt by those with the greatest need. Engagement means not just forming relationships but also having a deep understanding of the issues related to the populations studied, to hear their concerns and advice/recommendations for approach to research design and conduct, engaging other community members, impact (knowledge dissemination and transfer, uptake of evidence, and reach) and sustainability.

Building stakeholder relationships and consumer collaboration can take time and can be laborious and time-consuming. Time is needed to encourage participation and recruitment of stakeholders with appropriate skillsets and knowledge. Time is also needed for participant recruitment particularly for First Nations people – who may require consultation with their elders and community. Community consultations may also require considerable time and expense. In this context, equity must always be a part of the research, to ensure benefit are appropriately distributed. Transparent communication is key to ensuring that the process is easily understood and not burdensome for patients or consumers.

Time is also important after trial completion. Time and expense are needed for knowledge dissemination and will require human resources delivering training, workshops and consultations, media and other campaigns. It is also expended in measuring the uptake of the information in terms of behaviour and policy change, creating procedures and guidelines, and providing these to the appropriate stakeholders. For example, providing information on evidence-based medical procedures to the Royal Australian College of General Practitioners (RACGP) or publication in medical journals and newsletters or delivery of training of services and/or medication delivery.

Additionally, the type of stakeholder involved in collaboration is important and can have an influence on research design. For example, when working with industry, the prioritisation of clinical research questions for companies seeking regulation (of drugs or devices) may be very different to the research priorities of society in general. Consumer engagement may override the integrity of research processes and government stakeholders may be involved in developing research that creates new or confirms previous policies.

Impact of clinical trial results may also be dependent on whether the trial data are meaningful and can be easily delivered. For example, some trials may be difficult to implement as the procedures are complex and costly and cannot be delivered to patients outside of a hospital setting. Implementation will also be difficult when the only clinical staff with the appropriate skills are those that work within the trial. Embedding is important for generalisability to ensure the efficacy and effectiveness of the trial.

PROVISION FOR INFRASTRUCTURE

The various stakeholders of clinical trials, as described above, make up the different skillsets and knowledge that are vital for conducting a successful clinical trial. These resources form part of the infrastructure. Time, money, personnel, materials, support systems (informatics as well as manpower), and a clear plan for completing the necessary steps in a trial are all part of the clinical research infrastructure.

Embedding research into routine clinical care is also important in providing for infrastructure. The clinical staff that often have the appropriate skills are those involved in the clinical trials. To ensure necessary infrastructure remains available following clinical trial implementation, hospital staff, community health staff and healthcare staff should be trained in the trial processes within the appropriate healthcare setting. This would be facilitated by trial protocols that are easily translated into community healthcare systems and are easily accessible by patients and consumers who would benefit greatly from trial implementation. Successful implementation should also include functioning equipment and appropriate and non-onerous governance to streamline processes for implementation.

Current frameworks measure impact through the training of academic staff and students and trial researchers. However, it is also valuable to train those outside of academia who may serve in the dissemination of knowledge to community.

The make-up of the trial team is also important to implementation. Incorporating health economists and implementation scientists into the trial team is valuable for translating research to community and in evaluating the return-on-investment of the trial itself.

SUPPORT MECHANISMS FOR KNOWLEDGE TRANSFER

Knowledge transfer can be done in a number of ways. Current impact frameworks look to academic publication and academic dissemination methods such as conferences, workshops and seminars. However, this only disseminates the information to a largely academic audience. The successful implementation of the trial would most likely involve those outside of academia. Trialists and researchers must consider other means of knowledge transfer and culturally safe approaches when engaging stakeholders from diverse groups. Community workshops and consultation, collaboration with community leaders and champions who can facilitate community awareness and knowledge uptake and social media campaigns are some approaches to information delivery to the public. Even small presentations and animations delivered through webinars or videos, or public-friendly stories presented in flyers and posters translated into multiple languages and displayed in cultural centres, general practice offices, schools, and radio and other media would give greater reach, leading to greater impact.

These three mechanisms of approach to impact must be included in the original trial planning. All aspects of implementation must be planned and accounted for prior to undertaking the trial including research proposals considering the impact and benefit of the research. Not all research is funded through government, who typically focus on flagship-type work that benefits the whole population (e.g. colorectal or breast cancer research) and has short-term impacts such as the development and uptake of diagnostic instruments.

It has been argued that current peer-review processes of funding bodies and funding programs are inherently conservative failing to reward innovative research they know little about or that do not follow the same processes and measures of impact.[40] It is believed that this approach has resulted in serious gaps in knowledge and skills in areas of research such as mental health, astronomy, and climate sciences.

Industry-sponsored trials are conducted to gain FDA or TGA regulatory approvals to market a new drug or device, or a previously approved therapy for new indications. Such trials are frequently narrow in scope and follow a simple protocol (i.e., ask a limited number of questions) designed to test therapies in a highly selected patient group and provide evidence on benefits and risks that is sufficient to satisfy regulatory requirements. Conversely, governments are not constrained by the same financial imperatives and can fund large clinical trials to answer questions unrelated to gaining regulatory approval for a new drug or therapy. These studies can involve a wide range of patients and seek to answer clinically relevant questions. Alternatively, government can fund research in niche populations where industry may find it difficult to attract the interest. For example, the type-1 diabetes patient population is relatively small compared to the considerably larger type-2 diabetes population.

RECOMMENDATIONS FOR CLINICAL TRIALS

The recommendations that ACTA and the Impact and Implementation of CTN trials Reference Group propose to improve the impact of clinical trials include that:

- Impact is the result of quality implementation of trial results
- Quality implementation includes:
  - Prioritising research that fills gaps in knowledge and is relevant to clinicians and patient alike
  - Developing a comprehensive scope for the clinical trial that researches the needs of the target population and any underlying issues
  - Developing respectful relationships with stakeholders that would assist in the implementation and reach of the research
  - Transparent communication that works both ways; integrity of research is maintained while listening to the needs and priorities of stakeholders with regards to health outcome
  - Ensuring trial team make-up that includes a variety of skillsets and knowledge that can be applied to facilitate effective and efficient translation of trial results
  - Ensuring that methods of knowledge dissemination and transfer include those outside of academic circles such as consumers, community leaders and champions of evidence-based research
  - Embedding the intervention in clinical practice
  - Ensuring equity when engaging participants/patients/consumers who are of First Nations, ethnic and other social groups and vulnerable people
  - Considering pre-trial pilots to ensure the characteristics of the full trial are implementable with simple protocols that are executable, translatable, and accessible.
- Expenses and time that enable approach to impact through support of collaborations, knowledge transfer and embedding and implementation of trials in community are considered in funding proposals:
  - Measuring all the resources and costs of the intervention and comparator so that a full economic analysis and budget impact can be undertaken on completion of the trial
  - Inclusion of plans to seek government reimbursement for effective new interventions and models of care (e.g. through Medicare/MBS, or through getting new procedure/ICD-10/AR-DRG codes).

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ACTA gratefully acknowledges operational funding from the Australian Government's Medical Research Future Fund