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Explainer:
Clearing the pathway for global clinical trials

Australia has the opportunity to become a global leader in clinical trials, giving Australians access to the most innovative health solutions and building local health industries. Our low COVID-19 infection rates, world-class research community and strong health system should be a beacon, positioning Australia as the preferred global destination for clinical trials.

Improving the environment for clinical trials enables Australian patients to benefit from the latest medicines and technologies developed both in Australia and overseas while also helping Australian health and medical research to flourish in a competitive and lucrative world market. Clearing the pathway for clinical trials will help us meet the twin objectives of improving Australians' health and prosperity.

Much has been done to facilitate increased clinical trial activity in Australia including work to reform the system underpinning clinical trials. However, our golden opportunity to capitalise on Australia's clinical trial potential is challenged by state-based systems, which are not coordinated, and inefficient processes that drive up the already expensive cost of clinical trials.

This explainer provides a summary of the barriers facing clinical trials and provides viable solutions to these issues.

The barriers and opportunities identified in this explainer are largely focused on commercial clinical trials, though many of these improvements will benefit both commercial and non-commercial clinical settings.

About Research Australia

Research Australia is the national alliance representing the entire health and medical research pipeline from the laboratory through to the patient and the marketplace and was established by the Australian Government 20 years ago to advise on the policy settings for health and medical research.

Clearing the pathway
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1. The first country in the world to have a national approach to decentralised clinical trials

A national framework for decentralised clinical trials would open up and enhance clinical trial access to broader communities while delivering a streamlined and efficient approach. These trials enable some or all study-related procedures to take place away from the investigator site; either via telemedicine or through local healthcare providers, such as primary care physicians, pharmacists, clinics, home based care or even a regional hospital.[1] The potential benefits of decentralised trial models to clinical sponsors and sites include: broader patient access and demographics; opening trial participation to patients in remote areas and reducing the geographic barriers; assisting with recruitment and patient retention; and increasing access to patients with rare diseases.[2]

Australia is already taking a contemporary approach to delivering healthcare via teletrials, telehealth and mobile healthcare[3], especially since COVID-19 and the 2020-21 Federal Budget included $125 million aimed at addressing the rural and regional disparity in access to clinical trials. Other initiatives underway include the Australasian Tele-trial Model[4] developed in 2016 by the Clinical Oncology Society of Australia (COSA) and the recent inclusion of teletrials into the National Standard Operating Procedures for Clinical Trials.[5] These initiatives are welcomed. With increased national support and coordination, Australia could become the first country in the world to have a national approach to supporting decentralised trials. It also offers an opportunity for greater international collaboration.

2. Developing a 'one-stop-shop' for clinical trial approvals

Reducing clinical trial approval red tape and improving start up times will provide easier access to Australian clinical trials whilst maintaining Australia's strong reputation as a safe place to conduct clinical trials. Various national initiatives have been developed in Australia, including National Mutual Acceptance (NMA) and NHMRC national certification of ethics for multi-centre research. These initiatives have had limited success in shortening start up timelines or giving predictability. Critics highlight that these national initiatives do not streamline ethics approval for clinical trials conducted in a mix of public and private trial centres and are still not nationally accepted by all States and Territories. Streamlining these initiatives into a true 'one-stop-shop' will enable the faster start-up of clinical trials in Australia.

1. https://www.pharmoutsourcing.com/Featured-Articles/568352-Decentralization-A-Direct-Approach-to-Clinical-Trials/
2. Ibid.
3. The effectiveness of telehealth and teletrials has been demonstrated through the three year Regional Trials Network led by Dr Craig Underhill, which provides access to clinical trials to rural and regional patients.
4. https://www.cosa.org.au/media/332325/cosa-teletrial-model-final-19sep16.pdf
5. https://www.health.gov.au/sites/default/files/documents/2021/03/national-standard-operating-procedures-for-clinical-trials-national-standard-operating-procedures-for-clinical-trials-including-teletrials-in-australia.pdf

3. Helping sponsors correctly fund clinical trials

Trial funders and sponsors[6] struggle to compare 'like for like' trials, because existing costing tools are outdated. Properly costing clinical trials is essential to avoiding underfunding by trial sponsors. Underfunding can result in delayed trial start, slow recruitment and even trial discontinuation. Currently, clinical trials conducted in Australia use a range of methods to assist with clinical trial costings, including:

- the Independent Hospital Pricing Authority (IHPA) list of standard costs associated with conducting clinical trials[7]
- the Medical Benefits Scheme 2017 and
- the Australian Medical Association (AMA) List of Medical Services and Fees 2016.[8]

The IHPA is a good starting point for a standardised national costing tool, but it has not been updated since 2015, resulting in outdated pricing structures.[9] The recent 2021 IHPA Work Program does not include any plans at this stage to update their standardised costing tool for clinical trials. Updating the IHPA costing tool would enable budgeting of clinical trials which is efficient, transparent and fair across all stakeholders.

4. Demonstrating Australia's high-quality clinical trials capacity to the world

A comprehensive picture of high-performing trial sites and those sites with specialist skill in particular disease areas, is key to being able to attract international clinical trials to Australia. A nationally agreed framework for the documentation and reporting of clinical trials is necessary to enable a national repository of data that provides granular level visibility on: participant recruitment and retention rates; start-up times; and skills base and experience of clinical trial staff and investigators.

Currently, there are multiple reporting mechanisms which differ between states. To access this kind of information, a sponsor would need to navigate multiple data sources and registries. A nationally agreed approach is required if Australia is to demonstrate its capabilities and promote international investment. Given that industry sponsored trials are conducted in both public and private health settings, this approach must include key performance data that is contributed from existing data systems used in private facilities to ensure that data systems capture all clinical trial activity across Australia.

In addition, compulsory reporting of trial activity in the ANZCTR is necessary. Registries in other international regions (including the US and EU) have adopted compulsory reporting of results as a core requirement of approvals and registration processes – this is yet to occur in Australia for the ANZCTR. Without comprehensive trial registration it is not feasible to accurately monitor the level of clinical trial activity in

6. In Australia, a sponsor can be an individual, company, institution or organisation that takes responsibility for the initiation, management, provision of insurance and indemnity and/or financing of a clinical trial. From https://www.australianclinicaltrials.gov.au/industry-and-sponsors/sponsorship.
7. The IHPA has acknowledged that in making this Determination they have utilised the best cost data available at the time, however the data has limitations. As such the standard cost should be regarded as a starting point for discussing the unique features of each proposed trial and the associated costs.
8. https://www.swslhd.health.nsw.gov.au/Ethics/content/pdf/1_0%20Clinical%20Trial%20Budgeting%20Manual%20July%202018.pdf
9. https://www.ihpa.gov.au/sites/default/files/publications/determination_of_standard_costs_associated_with_clinical_trials_in_australia.pdf



Australia. The 2018 independent review of the ANZCTR highlighted that requiring the reporting of clinical trials has the potential to improve research transparency, avoid duplication of research, improve patient recruitment, improved sector efficiency and value for money, and improve accountability of the registry.[10]

5. Incorporating health data into Australia's clinical trial system

With a technological shift in clinical trials, and an imperative to increase participation rates, access to a national, readily accessible and secure electronic medical record system, e.g. My Health Record, and public health data e.g. Medicare data[11], would be a significant enabler to clinical trial activity in Australia. There are two important uses and purposes for strengthening Australia's connectivity between health data and clinical trials:

- Identifying potential participants of clinical trials through Medicare Benefits Schedule (MBS) data, Pharmaceutical Benefits Scheme (PBS) data or My Health Record. These potential participants would need to be identified and contacted to seek their involvement in a clinical trial, or potentially their clinician or general practitioners could be the point of contact.
- Assisting in the initial decision about the feasibility of conducting a particular clinical trial in Australia through identified data routinely collected in our health system about the prevalence of certain conditions, or the use of particular medications.

In addition to these distinct purposes for health data in clinical trials, it is important to link this data into a centralised repository to both reduce the workload for clinical trial staff and streamline the many system that have been individually developed by various stakeholders across jurisdictions.

Research Australia recognises the broader questions and issues to be address within Australia's health data system. Australia has the resources, capabilities and a health care system infrastructure that is poised to rapidly adopt and enhance our capacity to utilise electronic medical and health records and data. Supporting a pathway for data routinely collected in our health system into Australia's clinical trial system would position Australia as a valuable location for international clinical trials.

6. The world's most highly-skilled clinical trials workforce

Strengthening Australia's high-quality clinical trial workforce is critical to attracting global clinical trials. There is a significant lack of nationally accredited education and training courses aimed at those overseeing the clinical trial design, conduct and approval processes.[12] Australian nurses, who are the backbone of clinical trial activity in Australia, are facing increased responsibility that is not recognised in their award wages and there is not appropriate standards being set within the system to ensure clinical trial staff have the right skill set.

Emerging initiatives to strengthen the collaboration between nurses and the clinical trial network are underway. Groups including Australian Clinical Trials Alliance (ACTA), PRAXIS Australia and University of South Australia are working to try to improve visibility and career progression of clinical trial nurses in Australia to help meet the skills gaps as reported in recent sector reports, including the Industry Growth Centre, MTP Connect Skills Gap reports. These initiatives are welcomed and must be adequately supported to be fully established as an avenue to build the knowledge and skills of the clinical trial workforce. This is important, as Australia faces an urgent shortfall in the clinical trials workforce that if unmet will impact our ability to compete globally.

7. Working with consumers to build better clinical trials

Many clinical trial funders now mandate evidence of health consumer involvement into the design and conduct of the research they fund, and often will invite consumers to be involved in the funding decision-making process.[13] Australia's Clinical Trial Governance Framework now sets 'partnering with consumers' as a standard for clinical trial services.[14]

More widespread use of PREMs[15] and PROMs[16] throughout Australia's health and medical research and the inclusion of these measures into Australia's clinical trial reporting is key to demonstrating our commitment to patient centric outcomes. These measures capture patient feedback to drive improvement in clinical trials and healthcare.[17] Other jurisdictions more routinely incorporate the participation of consumers in clinical trial design and delivery including the UK's National Institute for Health Research Clinical Research Network.[18] Directly involving consumers in the design of clinical trials has the potential to both increase clinical trial participation and deliver more effective, patient-centric clinical trials.

National awareness and education about the role and importance of clinical trials is also needed to ensure improved awareness, access and involvement in clinical trials. These campaigns must be aimed at both clinicians and patients/consumers. Although some work has been undertaken to raise the profile of clinical trials in Australia, including the work of *australianclinicaltrials.gov.au* and the NHMRC with the 'Helping our Health' campaign, more efforts are urgently needed.

10. Aspex Consulting Review of the Australian New Zealand Clinical Trials Registry. August 2018. Commissioned by the Department of Health.
11. Public sector data is data collected, created or held by or on behalf of a Commonwealth body.
12. Clinical Trials Industry Capability Report. January 2018. Commonwealth of Australia.
13. https://healthvoices.org.au/issues/april-2018/consumer-involvement-health-medical-research-whats-driving-change-can-health-consumers-contribute/
14. Australian Commission on Safety and Quality in Health Care. Sydney: ACSQHC; National Clinical Trials Governance Framework – Guide for implementation
15. Patient reported experience measures
16. Patient reported outcome measures
17. https://www.aci.health.nsw.gov.au/__data/assets/pdf_file/0003/253164/Overview-What_are_PROMs_and_PREMs.pdf
18. https://www.nihr.ac.uk/explore-nihr/support/clinical-research-network.htm

Stages of a clinical trial

To unlock Australia's potential as a beacon for global clinical trials, Research Australia has developed the diagram below which identifies key barriers and solutions at each stage of the clinical trial process, acknowledging that many more barriers and solutions exist. Research Australia also acknowledges that there is significant research conducted before a new intervention is tested as part of a clinical trial.

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Key: ⛔ Barriers or issues ✔ Solutions and recommendations

01 Funding

⛔ Clinical trials, relative to the research required to get to this stage, are expensive.

⛔ The research activities – key to securing commercial funding – to progress a trial from Phase 1 to Phase 2 commercial clinical trial are generally underfunded. This reduces the commercial viability of trials.

⛔ Lack of funding to upscale and implement successful non-commercial trials.

✔ Update the IHPA standard costing for clinical trials to be current and relevant.

✔ Projects that secure funding for a clinical trial need to be supported to develop a **commercialisation strategy from the outset.**

02 Trial Design and Approval

⛔ A single HREC is often not used when there is a mix of public, private and university sites on a study. The work-around, National Mutual Acceptance needs improvements as it is not universal and often still requires multiple HREC applications.

⛔ Research Governance processes are complex as a result of inconsistency within and across states. Due to lack of training, time frames for research governance are both variable and unpredictable.

⛔ Restricted access to available Federal and State administrative datasets.

✔ Approval granted by a **nationally NHMRC accredited ethics committee**[19] to be mutually accepted at all public hospitals, private hospitals, trial centres, and universities.

✔ Develop nationally agreed and implemented **Clinical Trial Management Systems (CTMS)** that capture and coordinate clinical trial information and knowledge systems.

03 Recruitment

⛔ Most Australians generally understand what clinical trials are. However clinical trials are still not universally understood as an effective pathway of care.

⛔ Inefficiencies in the recruitment for clinical trials, including the need to improve the reach into rural and regional Australia.

⛔ Lack of primary health care sector involvement and engagement in clinical trials.

✔ **National awareness campaign on the importance of clinical trials** aimed at clinicians and consumers.

✔ Encourage and build the infrastructure to make Australia the leader in decentralised clinical trials.

✔ **Reimbursement for GPs and allied health** that support trial recruitment via referrals and contributing data.

04 Trial Conduct

⛔ Australia's reliance on face to face clinical trial activities and lack of infrastructure for trials to be conducted remotely.

⛔ Lack of infrastructure and policy to support direct to patient trial drug delivery.

✔ To support decentralised trials, **invest in teletrials** which enable remote engagement for patients and clinicians. This would enable more people, particularly in rural and remote Australia, to participate in clinical trials.

✔ Better harmonisation of systems and improvements in interoperability with the adoption of common technology platforms, processes and reporting requirements by all parties, including state regulators.

05 Results Analysis

⛔ COVID accelerated the access to electronic hospital records but there is no national consistency on how this is enabled.

⛔ The National Health Data and Information Standards Committee (NHDISC) does not include representation from the TGA or consider data collected and reported for clinical trials.

✔ **Enable access to electronic health records** to better incorporate the collection and reporting of data for clinical trials with other health information routinely collected in our health system.

✔ **Expand the remit of the NHDISC** to include clinical trials data and inclusion of the TGA in its membership.

06 Outputs and Outcomes

⛔ Selective reporting of trial results – gaps in evidence base for future studies.

⛔ Low uptake of the patient reported outcome tools that support the integration of real-world evidence into trial outcomes.

✔ **Mandatory clinical trial registration and reporting** of all trial outcomes through the ANZCTR to bridge the gaps in Australia's evidence base and avoid research duplication.

✔ Increase the **interoperability of clinical trial datasets** to provide capacity for registry randomised clinical trials.



19. https://www.medicinesaustralia.com.au/wp-content/uploads/2020/11/20201103-sub-Medicines-Australia-Submission-to-HOR-Inquiry-into-approval-processes-for-new-drugs-and-novel-medical-technologies-.pdf

Building on existing reform in Clinical Trials

The reform of the Australian clinical trials environment has been ongoing for over a decade. The health and medical research sector welcomes measures including the $614 million MRFF 10-year clinical trial program, and $125 million for rural and remote clinical trials across Australia. Research Australia proposes building upon these research initiatives and the work underway by Commonwealth and State and Territory governments to unlock Australia's potential as a beacon for global clinical trials.

Initiative	What it does
COAG Health Council *Revitalised Clinical Trials Agenda* under the Encouraging More Clinical Trials in Australia initiative.	In April 2016 Health Ministers agreed to develop models and options to organise sites to better support and streamline clinical trials processes in Australia.[20] The Government provided $7 million to assist State and Territory governments to implement the system redesign outlined through the COAG Clinical Trials Agenda.
Clinical Trials Project Reference Group (CTPRG)	The CTPRG is an expert advisory sub-group within the Clinical Principal Committee under the Australian Health Ministers' Advisory Council (AHMAC).[21] Representing all states and territories and the Commonwealth, the reference group seeks to enable a streamlined and consistent national approach to clinical trials within Australia.[22]
National Mutual Acceptance (NMA) Scheme.	All states and territories, with the exception of the Northern Territory and Tasmania, are a part of a NMA scheme, which supports the acceptance of a single scientific and ethical review for multi-centre research conducted in publicly-funded health services.[23] In 2016, the NHMRC released the *Review and Evaluation of the National Certification Scheme for Institutional Ethical Review processes.*[24]
Australian Commission on Safety and Quality in Health Care, *National Clinical Trial Governance Framework* (2019).	The Governance Framework aims to improve the clinical trial environment, acknowledging the issues of inefficiency and fragmentation dominating Australia's clinical trial system. In November 2019, the Commission undertook a pilot on the Governance Framework in health service organisations currently accredited to the National Safety and Quality Health Service Standards that conduct clinical trials.[25]

20. https://www1.health.gov.au/internet/main/publishing.nsf/Content/EE207D978A44E4B8CA257FA90081B212/$File/Key%20Principles%20and%20Priority%20Action%20Areas%20%20Nov%202018.pdf
21. https://www.transparency.gov.au/annual-reports/australian-commission-safety-and-quality-health-care/reporting-year/2018-2019-34
22. https://www1.health.gov.au/internet/main/publishing.nsf/Content/Clinical-Trials
23. https://www.nhmrc.gov.au/research-policy/ethics/national-certification-scheme-ethics-review-multi-centre-research
24. https://www.nhmrc.gov.au/sites/default/files/documents/reports/ncs-evaluation.pdf
25. https://www.safetyandquality.gov.au/standards/clinical-trials#background

Initiative *(cont.)*	What it does *(cont.)*
	The pilot of the Framework commenced on 1 September 2020 where selected 'sites' (health services and hospitals) are to provide feedback on the Framework.
RDTI Scheme	The RDTI scheme provides an incentive for further commercial investment, and can support the significant investment required for Phase 2 and Phase 3 clinical trials to be undertaken on a commercial base in Australia.[26]
Participant recruitment and patient registry platforms	There are multiple investigator led recruitment platforms underway in Australia. For example, the Join Us registry, HealthMatch and ClinTrialRefer. Electronic Consent, currently being led by CT:IQ
Reports and investigations into clinical trials	Inquiry into approval processes for new drugs and novel medical technologies in Australia. Review of the Australian New Zealand Clinical Trials Registry. *Determination of standard costs associated with conducting clinical trials in Australia.*[27] *Analysis of Recently Conducted Clinical Trials by the Australian Department of Health.*[28] *CTPRG's Scoping and analysis of recruitment and retention in Australian clinical trials.*[29] *Clinical Trials in Australian Public Health Institutions 2016-2017 (NAS 3 Report).*[30]

26. https://researchaustralia.org/wp-content/uploads/2020/11/Research-Australia-Sub-Approval-for-new-drugs-and-novel-med-tech-FINAL-Oct-2020.pdf
27. ibid
28. https://www1.health.gov.au/internet/main/publishing.nsf/Content/EE207D978A44E4B8CA257FA90081B212/$File/Analysis%20of%20Recently%20Conducted%20Clinical%20Trials%20Report.pdf
29. https://www1.health.gov.au/internet/main/publishing.nsf/Content/EE207D978A44E4B8CA257FA90081B212/$File/EY%20Final%20Report%20-%20Recruitment%20and%20retention%20in%20Australian%20clinical%20trials%2030%20June%202016.pdf
30. https://www1.health.gov.au/internet/main/publishing.nsf/Content/EE207D978A44E4B8CA257FA90081B212/$File/NAS-3-Report-formatted.pdf



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