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Enhancing Aotearoa New Zealand Clinical Trials

*Enhancing Aotearoa New Zealand Clinical Trials Project Team
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Mā te rongo, ka mōhio

Mā te mōhio, ka mārama

Mā te mārama, ka mātau

Mā te mātau, ka ora

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Executive summary

Background and approach

Clinical trials are a central element of a modern, high-functioning health system. Clinical trials can provide access to novel treatments for patients and deliver cutting-edge healthcare. Further, investment in clinical trials allows for efficient healthcare and provides health sector returns in excess of the dollars invested. The evidence generated by clinical trials is used to improve our health services, ranging from public health and prevention interventions through to specialised medicines and novel devices. Clinical trial research increases the efficacy and efficiency of care, thereby bettering the health of New Zealanders.

While there are examples of high-quality research, Aotearoa New Zealand does not invest as effectively as it could, and should, in clinical trial research. We do not realise the significant potential benefits of clinical trial research for the people of Aotearoa New Zealand and those benefits that are realised are distributed inequitably because of the current health system's fragmentation and rigidity, and because clinical research is not embedded within it as part of a learning healthcare system. To respect Te Tiriti o Waitangi and meet obligations as a treaty partner, it is critical that we have clinical evidence of the efficacy and safety of healthcare interventions for Aotearoa New Zealand's population, especially Māori. This project proposes a future direction for developing infrastructure that will support equitable clinical trial activity, ensure that trials (including commercial ones) benefiting from publicly funded infrastructure are responsive to the needs of New Zealanders and ultimately enable the equitable delivery of the best healthcare we can achieve to all New Zealanders.

This report is the outcome of independent research funded by the Health Research Council of New Zealand and Manatū Hauora | Ministry of Health.

This project was conducted by a diverse group of clinical researchers from a range of backgrounds and disciplines and involved a specific Māori Rōpū, a Pacific advisory group and a consumer group. It also consulted a group of international researchers. The project reported to an expert steering group appointed by the Ministry of Health (MOH) and the Health Research Council (HRC).

The project proceeded with a characterisation of the current state of clinical trial activity, both in Aotearoa New Zealand and in terms of international practice. We collected information from the Australian New Zealand Clinical Trials Registry (ANZCTR), conducted a survey of researchers, carried out 58 individual and group interviews, and met with the Māori Rōpū, Pacific advisory group and consumer group. This information was reviewed by iNZight Analytics through the Te Ao Māori lens.

Current-state findings were reviewed by many stakeholders in a workshop at which approaches for improving the clinical trial infrastructure in Aotearoa New Zealand were canvassed. These approaches formed the basis for a modified sector-wide Delphi process to find consensus on a variety of clinical trial infrastructure options. Options that were supported in the Delphi process formed the basis for the research team to propose a preferred model for the infrastructure needed to support clinical trials and achieve benefit

from them for the people of Aotearoa New Zealand.

Clinical trial research is a barometer for health research activity in general. High-quality clinical trial research gains will only be realised with a functioning and supported health research infrastructure. Thus, while this project is focused on clinical trial research, a number of the recommendations (for example, those targeting improving research leadership, knowledge translation or data governance) apply to health research activity more broadly. Therefore, actioning the recommendations contained within this report will achieve gains within a wider context of health system research, innovation, and improvement.

Current-state findings

The main findings of our current-state analysis were:

- The New Zealand health system does not generally have a strong research culture, notwithstanding individual examples of excellence. Health system decision-making often does not facilitate research activity and, in many cases, can be a barrier to the conduct of research.
- Prioritisation of clinical trials, in the sense of funders systematically considering what research will reduce inequities and bring benefits for New Zealanders, is rarely practised outside of the HRC.
- There is great diversity in existing clinical trial activity across different kinds of health intervention, different phases of intervention development, and different settings.
- Institutional settings for clinical trials vary significantly across philanthropic organisations, universities, district health boards and community health organisations. Within the window of our stakeholder and current-state analysis, few trials have been conducted in Māori health provider settings and none in Pacific provider settings.
- There is a gap in partnership with Māori, both in the design and conduct of individual trials, and in the wider infrastructure of trial activity, including in the management of data and tissue samples with appropriate tikanga.
- There is a need for clinical trial methodologies and conduct to be more responsive to Māori needs, and more sensitive to cultural requirements.
- Consumers have a rapidly growing role in clinical trials and in making sure research is relevant and meaningful. Through the consultation process we have heard there is a need to create more opportunities for consumers to be research partners.
- Clinical research workforces are fragile.
- The Māori clinical research workforce is particularly thinly stretched, with barriers to development and support for those wishing to pursue a research career.
- There are examples of good access to key infrastructure, such as statistical advice, or experienced research nurse support,

but that access is very patchy, making this an important barrier to undertaking research and to development of a sustainable research workforce.

- Existing clinical trial networks provide critical support for researchers, enabling high-quality success, but they are fragile and not resourced sustainably.
- Information needs are changing, data governance processes are diverse and often not systematic, and there is little guidance on data sovereignty.
- There is relatively little focus on translation of research results into practice. Translation is a particular issue for Māori given the extractive nature of research, the need to tailor results for Māori providers, and a need to show Māori reasons to become involved in trials.
- Accurately costing and adequately funding clinical trials and clinical trial development is difficult, and the ability to conduct a long-term clinical trial (>3 years) within existing funding caps is problematic.

Overall recommendations

The intended audience for the recommendations which follow is Manatū Hauora | Ministry of Health, Te Whatu Ora | Health New Zealand and Te Aka Whai Ora | Māori Health Authority.

There is a strong case for significant investment in a national clinical trials infrastructure in Aotearoa New Zealand. These general recommendations form the foundations for a proposed infrastructure to harness the potential of clinical trials within Aotearoa New Zealand's healthcare system.

- The national clinical trials infrastructure must be underpinned by principles of Te Tiriti and developed in co-governance with Māori.
- The responsibility for ensuring high-quality research activity must be woven into the job descriptions of all senior clinical leaders in Health NZ and the Māori Health Authority. There must also be targeted measures of accountability for these senior clinical leaders.
- There must be an adequately resourced National Research Office for Health NZ, co-governed with the Māori Health Authority, with research leadership at the executive level of the organisations. While this function exists within the context of health research policy leadership from the Ministry of Health, in order to envisage possible gains it is essential for Health New Zealand to have research leadership at the operational level.
- There should be a National Clinical Trial Infrastructure Centre with expertise from across the country, which will provide leadership, governance, expertise, and overall, high-level national support and coordination of trial activity, including the support of clinical trial networks in Aotearoa New Zealand, as outlined in section 5.3 of this report.
- There should be Regional Clinical Trial Coordinating Centres around the country that between them provide the necessary expertise to support clinical trials as outlined in section 5.3 of this report. Each of these centres will support trial development and conduct across regional nodes to ensure equity of access for both researchers and participants and will collaborate with other centres to support local,

regional, national, and international trials.

- There should be sustainable and systematic networks for Māori researchers and for Pacific researchers to support Māori and Pacific research communities in a regular and coordinated way in accordance with recommendations and priorities identified above.
- Active development and support for the Māori health research workforce to meet commitments to Te Tiriti and to reducing inequities in health.
- Partnership with Māori and local Māori communities at every level, including trial implementation and national infrastructure.
- Supporting Te Ao Māori methods/priorities and engagement with researchers and communities.
- Embedding Māori data sovereignty and tikanga about data in the clinical trials system.
- Ensure knowledge translation has a positive impact for Māori and reduces inequities in health outcomes.
- When funding mechanisms are developed, ensure they are responsive to Māori community needs and researcher obligations.
- Support and train tauwi workforce to engage with Te Ao Māori.
- Active development and support for the Pacific health research workforce.
- All publicly funded clinical trials should include consumer research partners.
- There should be a national federated health data system with Māori data governance at the core, that allows embedding of research in routine clinical care and provides culturally appropriate long-term curation of research data.
- A clear responsibility for research knowledge translation and implementation must be established within Aotearoa New Zealand's new healthcare system that is well integrated with change management, clinical governance functions, and the health system's role and responsibilities as an effective Te Tiriti partner for Māori.

These recommendations were developed from consistent needs and themes across the project and from all those consulted. In addition, specific recommendations from the Māori Rōpū and Pacific and consumer groups (see section 6.2) further identify priorities to ensure their needs are met by the preferred infrastructure model.

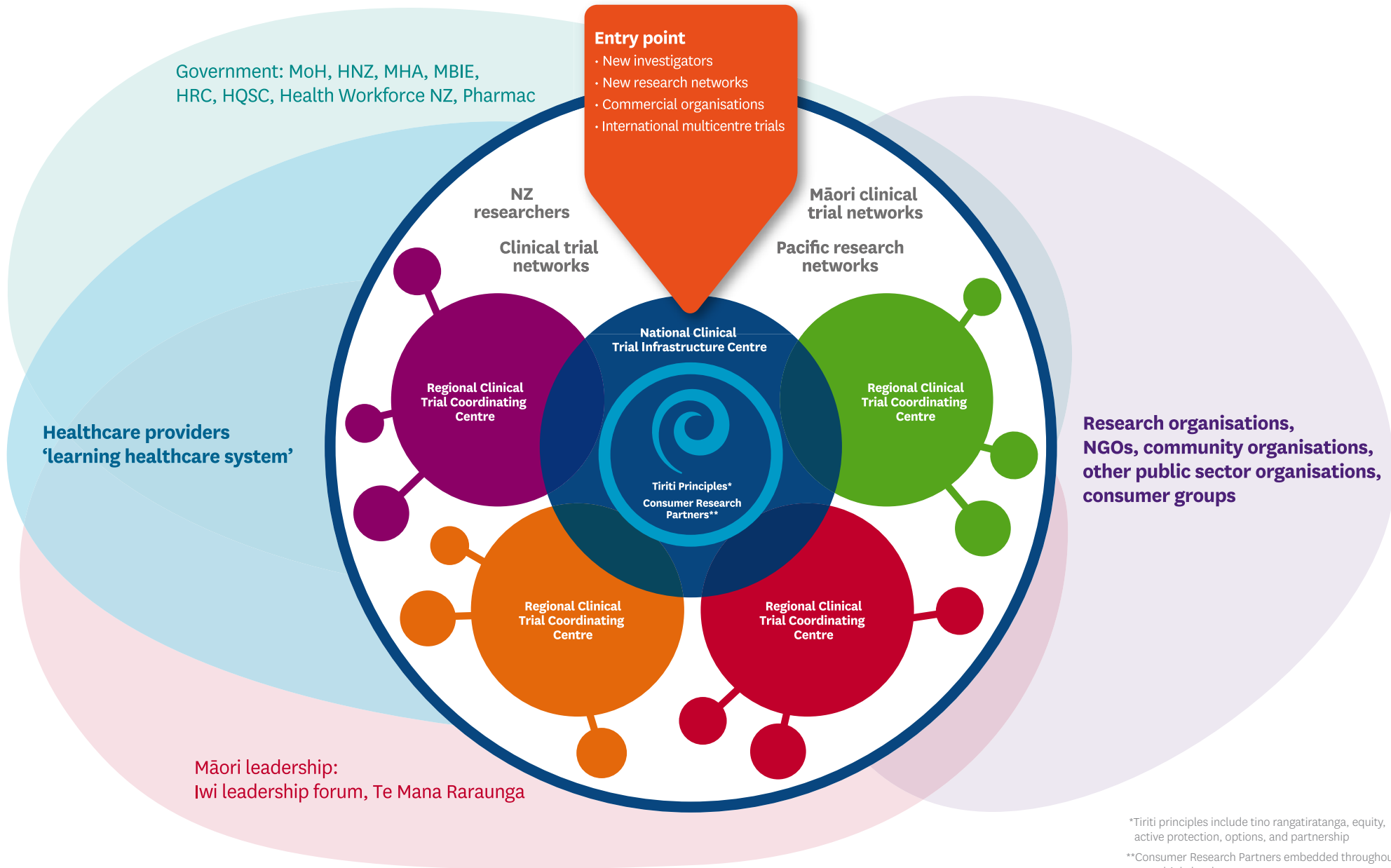
Preferred model

Our preferred infrastructure model will address the recommendations made by our extensive groups of stakeholders. Our proposal consists of two main components:

- A National Clinical Trial Infrastructure Centre that manages some of the functions and activities that have been agreed to be critical through the Delphi survey process.
- Multiple Regional Clinical Trial Coordinating Centres, procured by the National Clinical Trial Infrastructure Centre, that manage operational functions and activities at local level or across specific communities on behalf of the centre. Supporting organisations may be consortia or could contract other organisations as suppliers for necessary resources.

We have identified a detailed set of functions and activities to be provided across the National Clinical Trial Infrastructure Centre and the Regional Clinical Trial Coordinating Centres. We envisage that the National Clinical Trial Infrastructure Centre will be an integral part of the newly developing Health New Zealand and Māori Health Authority, with the capability and resources to influence their culture to develop a genuinely learning health system for the benefit of all people in Aotearoa New Zealand. The research leadership must be closely integrated with leadership in clinical governance and quality, innovation and change management, and the professions in order to achieve the promise of improved healthcare based upon high-quality evidence that is relevant for New Zealanders.

The diagram below illustrates the main components of the preferred model.



*Tiriti principles include tino rangatiratanga, equity, active protection, options, and partnership
 **Consumer Research Partners embedded throughout at multiple levels

1. Project overview



1.1 Project context

Clinical trials and health research are not seen as priorities within Aotearoa New Zealand's health and disability system. This is due to a lack of recognition of the significant value these activities can generate for individuals, society and the funders of the health system. As such, comprehensive infrastructure and support systems in Aotearoa New Zealand to enable clinical trials and health research activity do not exist or, where they do, are not well developed or appropriately resourced, making clinical trials and health research difficult to undertake. This has considerable impact for the health workforce, for patients, consumers and whānau, and for wider society.

First and foremost, there are requirements under Te Tiriti o Waitangi to ensure treaty principles are at the forefront of, and embedded in, clinical trials in the future and that Māori are partners in all governance structures. A Te Tiriti-based science structure should be at the foundation of any new infrastructure. This project provides the opportunity to systematically refresh the clinical trials systems of Aotearoa New Zealand, embedding Te Tiriti and Māori partnership from the beginning. Secondly, this project provides significant opportunity to enhance clinical trials research in the public health system within Aotearoa New Zealand. It will address critical infrastructure needs and inequity in access to (and participation in) clinical trials and enhance workforce and system capability throughout the country.

Realising the potential of clinical trials research in Aotearoa New Zealand is aligned with the *New Zealand Health Research Strategy 2017–2027* and the *New Zealand Health Research Prioritisation Framework*, which provide a mandate for:

- achieving a stepwise change in the role of research in clinical practice, including embedding clinical trials and clinical trial networks, as one element of a learning healthcare system generating timely evidence to support clinical practice, cost effectiveness of healthcare, and the development of new interventions;
- harnessing the power of multi-centre and multi-national clinical trials to improve the management of health conditions in a timely manner for New Zealanders;
- building a solid clinical trials research network with the support and systems (including ethics) to facilitate efficient multi-centre and multi-national trials;
- developing systems to reduce inequity; for example, through a national system of networks to ensure appropriate access to clinical trials according to need and want, and
- strengthening capacity in the clinical health research workforce to improve clinical services and care and to attract and retain top clinicians in Aotearoa New Zealand.

This project began in February 2021. In April 2021 the Minister of Health announced a restructuring of the health system, consolidating 20 district health boards into a single entity that will both operate hospital services and commission primary and community healthcare. This is a significant change to New Zealand's health system. Legislation has been introduced to implement the change and came into effect on 1 July 2022.

1.2 Goals and deliverables

The goals for this project have been defined by the Health Research Council (HRC) and Ministry of Health (MoH) as the joint funders of this work and as the bodies responsible for health research and health policy and service delivery, respectively. The goals of this project include:

- an overview of the strengths, gaps and areas of need for clinical trial systems and data infrastructure in the Aotearoa New Zealand public healthcare system;
- information on opportunities available for participation in clinical trials activity and how best to support and build upon existing clinical trial networks in the Aotearoa New Zealand context;
- an understanding of international best practice clinical trial systems and how Aotearoa New Zealand can use this to build its enterprise, and
- recommendations at a policy and system level to support the HRC and MoH in implementing policy that facilitates and develops a sustainable, nationally coordinated and equitable clinical trials enterprise in Aotearoa New Zealand.

The deliverables included an interim report detailing preliminary results and findings from stakeholder consultation, an analysis of data collected, and a final report that explores, in detail, the results from consultation and proposes key findings and evidence-based recommendations to inform the development of an infrastructure roadmap.

1.3 Scope

The HRC and MoH defined the scope of work for this project, as outlined in the Request for Proposals (RfP). The primary area of focus has been on the conduct and coordination of clinical trials occurring within the public healthcare system in Aotearoa New Zealand. Areas in scope cover all public-good trials, including the spectrum of trials from pragmatic to exploratory, all phases of trials, single and multi-site/national trials, the range of clinical disciplines and intervention types (prevention, diagnosis, and treatment), and the different settings within the healthcare system (including community, primary and secondary care in rural and urban settings). Commercial trials conducted within the public healthcare systems are also in scope. Ethics, regulatory, and funding systems are out of scope. Facilities are essential components of clinical trials infrastructure, but most aspects are excluded from the scope.

In defining "clinical trials" for this project, the World Health Organization (WHO) definition was used:

"Any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate effects on health outcomes. Interventions include but are not restricted to drugs, cells and other biological products, surgical procedures, radiologic procedures, devices, behavioural treatments, process-of-care changes and preventive care." (WHO, 2022).

The RfP defined two areas for focus: systems and data (see Table 1, following page). Within the focus areas, the research sought to provide a current-state assessment of clinical trial activity in Aotearoa New Zealand by scoping existing information and undertaking primary data collection. A synthesis of international best practice and

models for clinical trials infrastructure and a review of their strengths, gaps, and opportunities was undertaken. In consultation with key stakeholders, evidence-based recommendations were outlined to inform the infrastructure roadmap and an operating model for a sustainable, nationally coordinated, and equitable clinical trials enterprise in Aotearoa New Zealand.

Activity within the project was divided into five significant workstreams. This was done to ensure that work within the project aligned to the RfP focus areas.

1. Clinical trial activity, infrastructure, and networks
2. Data systems and curation
3. Equity and consumer engagement
4. Prioritisation, knowledge translation, and implementation
5. Workforce capability.

Table 1 below outlines the areas of focus.

1.4 Approach

Project work occurred in five phases:

1. Current-state analysis and international models review
2. Synthesis of data and information
3. Options development
4. Socialisation of proposed options
5. Outline recommendations.

The project team collected primary and secondary data from multiple sources during the current-state analysis phase. Data

gathered included clinical trial registry information from the Australian and New Zealand Clinical Trials Registry (ANZCTR) and the Standing Committee on Therapeutic Trials (SCOTT), a rolling-wave workforce survey, and interviews and focus group sessions with key stakeholders. A review of international models transpired at the same time. This included a targeted review of relevant literature around trial conduct and best practice within the Australian Clinical Trials Alliance (ACTA), the United Kingdom's National Institute for Health and Care Research (NIHR), the United States National Institute of Health (NIH) and indigenous healthcare research.

The project team summarised the findings from the current-state analysis and international models review during the synthesis phase. When reviewing the international models, factors influencing their implementation were reviewed in relation to the Aotearoa New Zealand context. Preliminary findings were discussed with the Named Investigators (NI) identified in the RfP, and, where interesting areas of the landscape were identified, the team undertook targeted case studies to uncover further information.

Two participatory processes were utilised to identify and prioritise critical elements of what is needed in clinical trial infrastructure. The first was a World Café-style workshop attended for all or some of a day by 72 people. The second was a Delphi survey process in which 347 stakeholders and researchers participated.

The project had specific processes to ensure responsiveness to Māori voices. It convened a Māori Rōpū to undertake scrutiny of the work as it progressed and to provide feedback on the processes and results. Material specific to Māori was analysed by Māori researchers

Table 1: Areas of focus of the project from the RfP

Area of focus
<p>Systems Community/organisational/regional/national and international systems and networks that improve coordination of, and collaboration for, New Zealand clinical trials, and subsequent knowledge transfer.</p>
<p>Description</p> <ol style="list-style-type: none"> a. Pathways/models for identifying research that reflects clinical priorities of the health sector and public/patients. b. The reach and capability of clinical trials networks, both New Zealand-only networks and New Zealand arms of multi-national networks, particularly with respect to reach across disciplines, geographical regions/units, levels of the health system, and current and potential future capabilities and sustainability. c. Clinical trial site and coordinating centre structures, functions, and facilities for public-good and commercial clinical trials (conducted in the public healthcare system). d. Workforce capabilities that are specific to the conduct of public-good and/or commercial clinical trials (conducted in the public healthcare system), above normal service delivery personnel, to include identifying roles or capabilities that would be better centralised or viewed as shared services. e. Systems for a national equitable approach to patient/participant recruitment for public-good and commercial trials (conducted in the public healthcare system). f. Culturally appropriate involvement of consumers (including Māori) in the trial process, including in trial design, monitoring, and as participants. g. Processes for knowledge translation, including audience-specific pathways for patients, service providers, and decision makers (managerial or policy), including implementation (as appropriate) of trial results (from New Zealand and international research).
<p>Data Clinical quality registries, electronic medical records, administrative datasets, research databases and research-supportive IT systems.</p>
<p>Description</p> <ol style="list-style-type: none"> a. Identify and address data silos and/or optimise interoperability in a clinical trial setting. b. Availability and adequacy of routinely collected data for public-good and commercial clinical trials throughout the trial lifecycle, and associated issues such as ethical aspects related to use of routine data. c. Types of and standards for clinical research databases, including Australasian and international. d. Management and availability of data outputs from public-good research for further use, with specific consideration of cultural and ethical aspects of data use. e. The use of clinical trial management systems to aid efficiency and effectiveness.

from iNZight Analytics, to ensure that an appropriate Te Ao Māori lens was applied. In the Delphi process, consensus scoring from Māori researchers was analysed separately, in order to ensure that disagreement from Māori researchers was not masked within the overall consensus statistics.

1.4.1 World Café

An all-day Zoom “World Café” workshop kicked off the Options Development and Socialisation phases on September 30, 2021. The workshop was facilitated and attended virtually due to COVID-19. The World Café process facilitated dialogue between a group of 72 stakeholders; ideas were synergised through multiple perspectives at a lower level and then translated at a higher level in discussions with the entire group. Attendees included consumer representatives, primary care (including rural GPs), community trialists, pharmaceutical and medical device companies, Māori, Pacific, and hospital-based clinical trial researchers, to name a few.

The workshop provided deep insight from a wide range of stakeholders on what the ideal clinical trials infrastructure for Aotearoa New Zealand looks like and, if implemented, what benefit should come from this unique opportunity in the health sector.

The findings from this World Café workshop, alongside previously gathered current-state material, were used to refine and develop options for a Delphi survey presented to key stakeholders. These options were then fed back to stakeholders through a Delphi survey process to test the criticality of them and whether stakeholders thought they were necessary for inclusion in any infrastructure this project proposed.

1.4.2 The Delphi survey

Based on previous phases and the World Café workshop findings, the project team identified various infrastructure options. The broader stakeholder group was invited to vote, using a modified three-round Delphi survey, on these options based on their criticality to a sustainable, nationally coordinated and equitable clinical trials enterprise in Aotearoa New Zealand. The idea of criticality was used to assess what the bare minimum requirements of the proposed infrastructure would be to still deliver the desired outcomes and successes. Infrastructure options not identified as critical for inclusion could still be valid additions to the proposal but not at the cost of any of the minimum requirements. It must be recognised that infrastructure options not identified as critical for inclusion are not necessarily any less important.

The Delphi method originated as a systematic, structured, and interactive way of dealing with uncertainty in forecasting or decision-making (particularly in financial markets) that relies on a panel of experts to form a judgement about some future state (K. C. Green et al., 2007). The key principle that underlies the Delphi method is that forecasts or decisions from a structured group of individuals are more accurate than those from unstructured groups (Rowe & Wright, 2001). The experts answer questionnaires in two or more rounds. After each round, a facilitator provides an anonymised summary of the experts’ forecasts or decisions from the previous rounds as well as the reasons they provided for their judgements. The experts are encouraged to revise their earlier answers based on the ideas and forecasts or decisions of other experts so that eventually the group will converge on the “correct”

answer (i.e. where there is some consensus). A key modification of the Delphi method for the purposes of this project was that investigators reserved their right to include infrastructure options even if not deemed critical by the stakeholders, which is particularly important for areas of the infrastructure that should be a “given” such as Māori data sovereignty mechanisms, embeddedness of Te Tiriti within the clinical trial system, and Māori co-governance and input into operational matters and priorities.

Conducting the Delphi survey helped capture the viewpoints of the diverse stakeholder groups. Being an iterative process, it assessed the level of agreement and provided a mechanism for resolving disagreement to build consensus around the proposed options. During the first round, participants were able to submit options that might have been missed; the group voted on the additional options in the two remaining rounds. In each round, stakeholders were given a list of potential infrastructure options and asked to rank them on a scale of 0 (not important) to 9 (critical) in terms of how critical the option was for inclusion in the proposed infrastructure (i.e. how necessary its inclusion was for the system to be successful). After each round the aggregate results were presented back to the stakeholders. There was the opportunity for stakeholders to provide feedback to refine the options within the next round as well as add new options.

At the end of the three rounds conducted between October 2021 and February 2022, it became clearer where there was consensus for critical inclusion of infrastructure options and where there was not.¹ A further consensus meeting was held with investigators post-survey as a final test of consensus for inclusion of critical infrastructure options and to discuss and finalise a decision on the options that did not reach a consensus.

The findings of the Delphi survey were categorised by respondent group (Māori, Consumer, and General, where General refers to all other stakeholders) to compare the perceptions of criticality between groups. This categorisation was of particular importance for understanding Māori respondents’ perceptions and whether they differed from the perceptions of the rest of the stakeholders, particularly given the relatively small proportion of Māori respondents.

Based on the Delphi survey results and data from the previous phases, the project team outlined a high-level roadmap of the steps required to transform the current state to the desired future state. Critical factors considered the needs to best support a sustainable and nationally coordinated clinical trials enterprise in New Zealand; and to contribute to improved and more equitable health outcomes for New Zealanders.

Many of the specifics of the new health system structure and how it operates remain to be determined, but several aspects of the changes are strongly aligned with our final recommendations for improving clinical trial infrastructure. These include a focus on addressing issues of equity on both a national and a local basis, implementing more consistent national processes in the management and delivery of healthcare, and achieving a more integrated and consistent health system for New Zealanders. We see this set of changes as an opportunity to address some of the existing barriers to running effective and equitable clinical trials, in much the same way as they are intended to remove barriers to delivering effective and equitable healthcare.

¹ There was consensus for inclusion when at least 70% of respondents had voted a score of 7 out of 9 or higher **and** fewer than or equal to 15% of respondents voted a score of 3 out of 9 or lower. For consensus for exclusion, the criteria were reversed.

2. Value of clinical trials and health research



Key points of value of clinical trials and health research

- Clinical trials and health research play a critical role in the review and development of all aspects of healthcare, leading to health, social and economic benefits (improved outcomes, efficacy, and appropriateness of care, including disinvestment in existing practices that are found not to improve outcomes or be cost-effective, as well as informing introduction of new approaches).
- Kaupapa Māori health research allows Māori to hold autonomy over the knowledge considered relevant and legitimate to Māori, creates meaningful engagement, treats the individual as the expert on their own health and wellbeing, leads to higher engagement of Māori with health research, and results in positive health outcomes.
- Individuals receive potential health gains from participation, access to new treatments not funded by the Government, a sense of hope, and the chance to contribute to the future health of their communities.
- Clinical trials and health research improve outcomes even for those not in the treatment arm by offering more systematic and consistent care.
- Hospitals that are more research-active achieve better overall patient outcomes than hospitals that are inactive in health research.
- Every 1 GBP of public investment in health research in the UK is shown to increase private investment in health research by at least 1 GBP (spill-over effects of public investment).²
- Estimates of benefit-cost ratio of Government investment in Australian health research range between 2.2-5.0:1.

It is first important to understand the value of clinical trials and health research, what this means for Aotearoa New Zealand, and why there should be a focus on developing a strong, sustainable, and equitable clinical trials system.

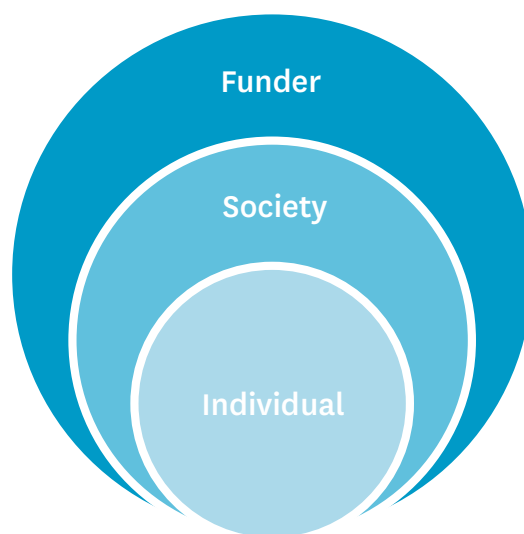
Clinical trials and health research more broadly play an integral role in the advancement of science and medicine and of health, social, and economic outcomes (Novitzke, 2008). Kaupapa Māori health research is a vital mechanism for Māori to gain tino rangatiratanga (self-determination) within research and maintain control and autonomy over the knowledge considered relevant and legitimate to Māori (Mikahere-Hall, 2017). Kaupapa Māori research in the broadest sense embeds the principles of being Māori and Te Ao Māori worldview within research by acknowledging the “Māori way of doing things” (Curtis, 2016; Hoskins et al., 2012).

There has been considerable recent work developing models and applications to correctly measure the social, health, and economic impacts of health research on people and health systems (Grant & Buxton, 2018; Raftery et al., 2016). The total value of clinical trials and health research to society is comprised of monetary and non-monetary, and quantifiable and non-quantifiable values. A useful exercise is to view the value from the perspective of an individual, of society (aggregate of all individuals), and of the funder (who is charged with resourcing health services, clinical trials and health research). In this exercise, “value” refers to the measurement of benefit of clinical trials and health research.

The value an individual sees in clinical trials and health research arises from individual gain from involvement both through personal health gains and gains to society from research activity (i.e. altruism and the “warm glow” effect). Society’s perspective on the value of clinical trials and health research is about aggregate health, social, economic, and system-level outcomes. The perspective of the funder focuses typically on the return on investment (both monetisable and non-monetisable returns) of enabling clinical trials and health research to be undertaken within society.

As shown in Figure 1 (below), the perspective of the individual can be nested within the perspective of society, which can be nested within the perspective of the funder.

Figure 1: Relationship of perspectives of value across the individual, society, and funder



2.1 Individual perspective on value

The individual’s perspective on the value of clinical trials and health research can be seen through their choice to participate. The choice to participate in a clinical trial or health research is complex and has many contributing factors such as increasing age and state of disease, social considerations such as family and work pressures, altruistic behaviour, and the individual’s opinions on their illness and on medical care and those providing the care in general (Lowton, 2005; Olsen et al., 2020; Verheggen et al., 1998). Main motivations for participation include:

- personal benefit and access to treatments otherwise not accessible;

² This suggests that developing the clinical trials research industry will create more highly skilled jobs in an innovative industry, which is aligned with Government policy for employment.



- contribution toward a “public good” activity and the advancement of medical care (altruistic behaviour), and
- the opportunity to give to whānau and/or community.

Gaining personal benefit is understood to be a primary motivation for participation in clinical trials and health research, with altruistic considerations largely secondary – although this can vary according to the condition and need for a trial (Locock & Smith, 2011). The key personal benefit for individuals is access to innovative, leading-edge treatments within a specialty area (Wendler et al., 2008). Part of the attraction might be getting treated by a doctor with specialist interests in the individual’s disease (and therefore the possibility their progress will be monitored closely), as well as access to medicines that are not funded in Aotearoa New Zealand (Slevin et al., 1995).

Another motivator for participation is satisfaction from contributing toward clinical trials and health research as a “public good” activity, knowing that an individual’s actions will be helpful for the advancement of medical care (Dixon-Woods & Tarrant, 2009; Wendler et al., 2008). This is also known as the “warm glow” effect, which is emotional gain when an individual does something altruistic (Andreoni, 1990).

For Māori, there is a sense of responsibility to whānau when making decisions that impact individual health and wellbeing (such as partaking in health research), and individual health and wellbeing are interwoven into the collective health of whānau (Carlson et al., 2016). A study of Aboriginal health research participants in Australia found that the primary motivation for taking part in health research was to give to their community, to feel good about their identity, to see research translated into the Aboriginal community, and for the purpose of helping the Aboriginal researcher get ahead (again, benefiting the community) (Guillemin et al., 2016).

Kaupapa Māori research by design treats individuals as experts on their own health, which is not typically found in Western healthcare

(Haitana et al., 2020). This has been shown to be particularly relevant and important in mental health because it allows individuals to share sensitive information and allows for personal critique of the influence and impacts systems around them have on their health and wellbeing (Haitana et al., 2020).

Kaupapa Māori health research has also been shown to provide successful health outcomes for individuals when measuring health outcomes against the stated aims of the research, as well as positive health experiences for individuals by providing meaningful engagement (Rolleston et al., 2020; Wilson, 2008).³

Clinical trials and health research may also provide a sense of hope when dealing with a disease, enabling individuals to deal better with uncertainty about their future health (Hallowell et al., 2016). One study found that expression of high expected therapeutic benefit in early-phase oncology trials had little to do with reporting knowledge of previous clinical outcomes and more to do with individuals expressing optimism (Sulmasy et al., 2010).⁴

2.2 Societal perspective on value

Clinical trials and health research form the scientific evidence base for new, revised, and long-established therapies, treatments, or delivery of care. Clinical trials and health research allow for healthcare to be as up-to-date as possible and therefore as effective, safe, and efficient as possible to provide the best outcomes for individuals and the health system. Publicly funded clinical trials are particularly important for head-to-head comparison of treatments or prevention measures and where there is no private or commercial motivation or desire to fund research (Neyt et al., 2016). They are also important for informing disinvestment from treatments that are shown to be of no benefit or are potentially harmful and can therefore create value through cost avoidance (to both patients receiving ineffective treatments, as well as society through costs of healthcare).

³ Refer to Rolleston et al. (2020) for more information on the health research projects studied.

⁴ This has led to some questioning of the validity of the informed consent process, and there is debate around whether participants of trials are making their decision to participate based on the assumption of high expected therapeutic benefit, or whether other benefits of involvement are more significant motivations. See Sulmasy et al. (2010) for more discussion.

Establishing what the social value is

The concept of social value of clinical trials and health research is, by nature, indeterminate and abstract. Clinical trials and health research are ethically acceptable only when the expected social and individual values exceed the exposure to risks for participants (Habets et al., 2014; Wendler & Rid, 2017). Humans should not be exposed to potential harm for the sole purpose of gaining knowledge (Habets et al., 2014).

There are multiple interpretations of the social value of clinical trials and health research. At the highest level, Habets et al. (2014) suggest the social value is the importance, relevance, humanitarian value, clinical value, or health value of the clinical trial or health research, and the nature and magnitude of the improvement the intervention is expected to have on the wellbeing of individuals and society as a whole.

Casarett et al. (2002) say the social value is the ultimate improvement in health as a result of a clinical trial or health research and the clinical trial or health research has instrumental value because it generates the knowledge that leads to the improvements in health. Others believe social value can be assigned to the clinical trial or health research itself, as well as the information human experiments produce (Kimmelman, 2010).

In sum, the act of conducting clinical trials and health research studies themselves (given the expected value generated from the research outweighs risks to participants) as well as the information generated can both be considered the value generated for society.

Examples of the value to society

We can observe the value generated for society from clinical trials and health research through the health, social, and economic outcomes of the activity.

It has been shown that targeted and relevant recruitment strategies that align with Māori principles and fit within a Kaupapa Māori framework have increased engagement of Māori in health research (Dyall et al., 2013; Kearns et al., 2021).

Clinical trials are more likely to have a positive rather than negative effect on health outcomes (Braunholtz et al., 2001). Numerous studies show that even those in the control arm (not receiving the studied treatment) of a clinical trial have better outcomes than those who were eligible but not part of the trial (Nijjar et al., 2017; Schmidt et al., 1999); this is due to the trial process itself, which demands a systematic (i.e. less “random”) approach to treatment with more intensive scrutiny and follow-up (Braunholtz et al., 2001; Karjalainen & Palva, 1989; McCarney et al., 2007).

A study of colorectal cancer outcomes demonstrated that high, sustained hospital-level participation in clinical trials improves the outcomes for *all* colorectal cancer patients managed in those research hospitals (i.e. not just those participating in the trial), which may be down to medical staff providing more systematic care (that is, consistent across patients) because it is what they have become familiar with (Downing et al., 2017).

At a higher level, there is evidence that health outcomes are better in hospitals that are more research-active, and that engagement in clinical research is associated with improved wider healthcare

performance at an organisational level (Hanney et al., 2013; Ozdemir et al., 2015). Analysis of acute coronary syndrome in US hospitals concluded that those hospitals that participated in trials provided better care and had lower mortality rates than those hospitals that did not participate (Majumdar et al., 2008). Studies in the UK showed a significant negative correlation between hospital academic output and mortality rates in NHS Trusts, as well as lower risk-adjusted mortality in research-active NHS Trusts for acute admissions, which was persistent even after adjusting for staffing and other systematic factors (Bennett et al., 2012; Jonker & Fisher, 2018; Ozdemir et al., 2015). A study of German ovarian cancer care similarly found that survival outcomes were worse at institutions not participating in studies (Du Bois et al., 2005).

Additionally, it was found that higher levels of clinical research activity were positively associated with better quality of information provision to patients, a higher degree of observed staff teamwork, more patient confidence in the doctors delivering treatment, and overall better inpatient experiences (Jonker et al., 2020).

2.3 Funder perspective on value

The funder’s perspective on value encapsulates both patient and society perspectives and considers the value (both monetisable and non-monetisable, and quantifiable and non-quantifiable) against the costs the funder will bear, looking to achieve a positive return on investment where the value outweighs the costs. The funder’s focus on return on investment comes from the scarce nature of resources and the necessary trade-off across objectives both within and outside of healthcare. Here the funder refers to the Government, which is the funder of much of the public-good clinical trials research that takes place in New Zealand.

Given the slow recognition and acceptance of the value of clinical trials and health research to both patient outcomes and healthcare cost, there is a critical need for ongoing and consistent measurement and recording of funding amounts as well as cost-effectiveness of interventions to be able to determine value for money and return on investment (Bentley et al., 2019; Grant & Buxton, 2018; UK Clinical Research Collaboration, 2020).

A scan of the literature helps to determine the potential value generated for the funder from clinical trials and health research.

A study of the spill-over effects of public investment in health research in the UK found that every additional 1 GBP of public spend was associated with an eventual additional 0.99 GBP of private research and development spend in the UK (Sussex et al., 2016). Combined with other estimates of rate of return on investment, the findings suggested investment into public medical research in the UK retrieves a return between 15 and 18 per cent per annum. This return was also thought to potentially be additive to other estimates, extending the estimated rate of return to a conservative 25 per cent per annum (Grant & Buxton, 2018; Health Economics Research Group, 2008).

Studies looking at the return on Australian health research and development investment produced benefit-cost ratio (BCR) estimates between 2.2:1 and 5:1 (Access Economics, 2003, 2008; Lateral Economics, 2010).⁵ A further study focusing only on the Australian National Health and Medical Research Council (NHMRC) expenditure

⁵ This means that, at the time, for every 1 AUD of costs, there were between 2.17 and 5 AUD of benefits.

estimated a BCR ratio of 3.2:1 from 10 billion AUD of R&D funding, highlighting benefits of (in AUD):

- \$7.7 billion reduction in burden of disease;
- \$1.3 billion direct health system expenditure savings;
- \$1.9 billion reduction in productivity loss;
- \$0.6 billion reduction in other financial costs;
- \$0.3 billion reduction in deadweight loss, and
- \$2.6 billion value of commercialisation (Deloitte Access Economics, 2014).⁶

A scoping review of 288 clinical trials concluded there are spill-over benefits for healthcare systems, including better health outcomes, enhanced research capacity, and drug cost avoidance (Bentley et al., 2019). A range of other literature assessed bundles of trials and health research to estimate the monetary value generated, shown in Table 2 below.

In sum, the value of investing in clinical trials is net positive for funders (although the scale of the net positive benefits is context-specific) through improved health outcomes, cost avoidance, and spill-over effects that encourage wider private spending. It is in health providers' / funders' best interests to ensure and support clinical trial activity.

The value of trials being integrated into healthcare

The recent RECOVERY clinical trial investigating interventions for COVID-19 has highlighted the value of integration of clinical trials in healthcare. In early 2020 treatments were being administered for COVID-19 without any reliable assessments of safety and efficacy, and therefore establishment of high-quality evidence was required extremely quickly (Pessoa-Amorim et al., 2021).

The RECOVERY trial is described as a streamlined, pragmatic, randomised controlled trial (RCT) set up to respond to this need, with over 39,000 patients enrolled from 178 hospital sites in the UK. Within 100 days of initiation the trial had shown dexamethasone improved survival for people with severe COVID-19. This advice was then speedily implemented in the UK and worldwide, significantly reducing mortality (Pessoa-Amorim et al., 2021). Additionally, the RECOVERY trial demonstrated the ineffectiveness of hydroxychloroquine, a drug put forward at the start of the pandemic to help treat COVID-19 and complications, rapidly removing the therapy from clinical practice (Singh et al., 2021; The RECOVERY Collaborative Group, 2020).

The trial was set up as part of routine NHS care in an adaptive platform trial,⁷ and any individual hospitalised with confirmed or suspected COVID-19 was potentially eligible. The collection of data was through web-based systems and linked to national healthcare datasets of other routinely collected data, which allowed for follow-up of individuals. The findings were then able to be implemented into guidance and policies for dealing with COVID-19 worldwide. If the trial had not been integrated into routine healthcare, the data collection would likely have been slower and the findings would likely have come much later, resulting in significantly higher mortality and persistence of use of ineffective therapies.

The value of a learning healthcare system

A learning health/healthcare system (LHS) is one that combines internal data and experiences with external evidence to inform practice. An LHS effectively has research and analysis functions at its core, allowing it to reflect upon and critically review practice to continuously improve and update care (i.e. in a cyclical process) in

Table 2: Summary of literature assessing value of a range of clinical trials

Source	Context	Findings
Johnston et al. (2006)	Assessment of 28 RCTs at a US institute with a total cost of 335m USD (2006). 21% of the trials resulted in measurable improvements in health, and 14% resulted in cost savings to society.	At 10 years, programme of trials (including additional healthcare and other expenditures) had estimated cost of 3.6b USD with a gain of 470,000 QALYs, or \$15.2b in benefits. Results led to increases in healthcare expenditures, but health gains were large and outweighed costs.
Shen et al. (2011)	Assessment of drug cost avoidance at medical centre because of sponsored clinical trials in Taiwan	Estimated drug cost avoidance of 11.2m USD at the centre in 2008 due to sponsored drug trials (i.e. Taiwanese healthcare system did not have to pay for the drugs, which came at the expense of pharma companies).
Wong et al. (2012)	Analysis of the RxPONDER breast cancer RCT to determine cost versus benefit. Cost estimated to be at least 27m USD.	Expected value of return of RxPONDER trial ranged from 450m to \$1b USD, or a return of from 17–39:1. Expected value increased by \$50–100m after stakeholder input on additional data collection.
Pham et al. (2017)	Comparison of 23 perinatal RCTs, of which 6 reported superior interventions. Total funding amount for the trials of 20.3m AUD.	Potential cost-savings over 5 years estimated to be 26.3m AUD if only 10% of the eligible populations received the superior interventions, and 262.8m AUD with 100% implementation. The potential cost-savings outweigh the cost of implementing the trials considerably.
Joint ACTA/ACSQHC Working Group (2021)	Assessment of 25 investigator-initiated RCTs across 3 clinical trial networks in Australia. Gross costs of trials estimated at 335m AUD.	Gross economic benefits estimated at \$2b AUD, with 70% of benefits coming from improvements in patient health outcomes, and 30% coming from health service cost avoidance. BCR of 5.8:1 given 65% of eligible Australian population implementation for one year.

⁶ The costs were measured in 2014 AUD, and the benefits are assumed to accrue with approximately a 40-year lag (between 2052/53 and 2062/63).

⁷ An adaptive trial platform is a relatively new type of RCT for the study of multiple interventions in a disease or condition in a perpetual manner with interventions entering and leaving the platform on the basis of a predefined decision algorithm (Angus et al., 2019). Adaptive trials do not have to study multiple interventions; they also can adapt randomisation proportions based on real-time results to obtain a final result more quickly. Effectively, using an adaptive trial platform meant the RECOVERY trial was able to determine interventions' safety and efficacy in the treatment of COVID-19 much more rapidly.

near real-time based on the latest evidence and experience (AHRQ, 2019). Figure 2 (below) shows the cyclical nature of an LHS, moving clockwise.

While the potential value generated from an LHS also relates to the individual and society, it is of particular importance for the funder who invests in the system and is therefore looking to maximise the benefits of investment while simultaneously minimising the costs of operating. An LHS provides the framework to continuously update practice to ensure best value for money invested.

The literature around LHS is still in early stages of development, with most contributions focusing on the theory and implementation of LHS. However, the policy settings required to achieve an LHS increasingly are being studied (Platt et al., 2020).

The value of an LHS is detailed primarily theoretically throughout the literature (Braithwaite, 2019; Friedman et al., 2015; Menear et al., 2019):

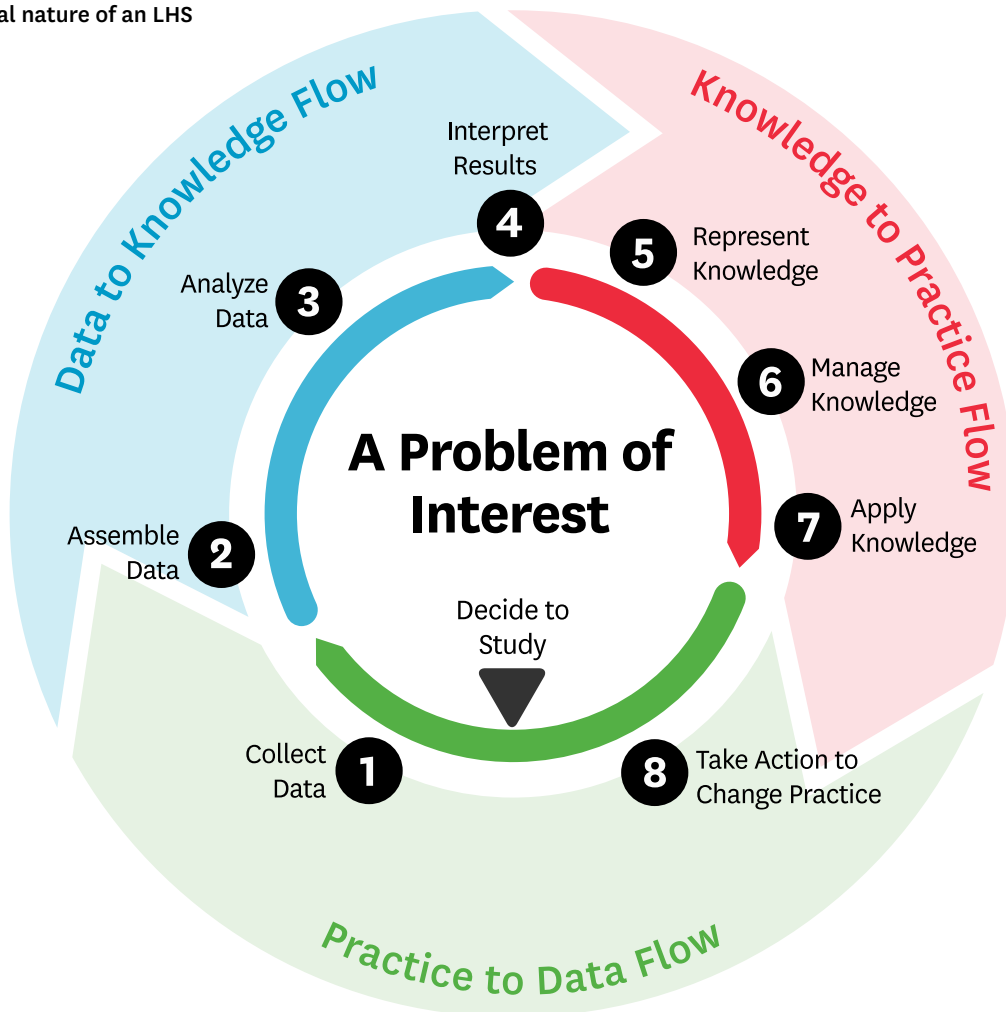
- improved patient outcomes through use of best-practice interventions and disinvestment of interventions shown to be ineffective, as well as reduced unjustified variation in interventions used and quality and type of care more generally;
- better value healthcare by using more cost-effective interventions and disinvestment in interventions shown to be less cost-effective;

- generation of generalisable knowledge that is applicable in other settings (i.e. spill-over benefits of generating knowledge);
- expanding the education, training, performance, and research culture of clinicians, and
- interoperability and reusability of datasets in different contexts throughout the LHS (e.g. with administrative datasets, for social study purposes, etc.) that can widen the use and value of collected data.

Enticott et al. (2021) conducted a systematic review of established LHS across a range of settings and places to understand the value generated. The value was shown as benefits in patient self-management, evidence-based clinician care, clinical organisation and/or system performance and in research activity.

This research began in February 2021. In April 2021 the Minister of Health announced a restructuring of the health system, consolidating 20 district health boards into a single entity that will both operate hospital services and commission primary and community healthcare. This is a significant change to New Zealand’s health system. Legislation has been introduced to implement the change and came into effect on 1 July 2022. The expectation is that the new health sector will do better than the old, and the relevance of being an LHS will be even greater than before.

Figure 2: Cyclical nature of an LHS



Source: (Flynn et al., 2018)

3. Current clinical trials environment



3.1 Main findings

Consultation with stakeholders has led us to believe the current clinical trials environment in Aotearoa New Zealand fails to provide consistent, sustainable, and equitable access and support to participate in and orchestrate clinical trials. There are some merits to the system and examples of excellence; however, they are not commonplace. Stakeholders engaging or wanting to engage in clinical trials revealed the system is fragmented and largely unsupported and, therefore, in need of significant change.

Stakeholder experiences, captured through interviews and surveys, form the basis of our understanding of the current clinical trials environment in Aotearoa New Zealand. Table 3 (below) shows the survey response we received. In total, 311 respondents completed the survey with 12 identifying as Māori researchers and four identifying as Pacific researchers. Snowball sampling, where initially enrolled respondents recruited more respondents through their networks, was used for this survey to increase the sample size. This led to a wide range of respondent types, including people who were not involved in clinical trials for a number of reasons but who may have wanted to be involved.

Table 3: Summary of survey respondents by group

Survey group	Entered survey	Identified as a Māori researcher	Identified as a Pacific researcher
Primary Investigator (PI) etc.	162	12	4
Research Nurse (RN) etc.	84		
Statistician	16		
Database or IT	6		
Health economist	3		
Not involved	40		
Total	311		

We conducted 58 interviews (with 132 individuals) encompassing organisations and individuals involved in all aspects of clinical trials, from policy, funding, delivery, participation, industry, and dissemination. Consultation with Māori stakeholders was assessed by iNZight Analytics to ensure the themes prioritised by Māori stakeholders were recognised.

Additionally, data from all interventional clinical trials listed on the ANZCTR between 2011 and 2020 were analysed to provide a snapshot of trial activity in Aotearoa New Zealand. This analysis may be an incomplete picture of the entirety of trial activity in Aotearoa New Zealand given some trials may be registered with other international clinical trial registries rather than on ANZCTR and because of data quirks;⁸ however, it can be used as a lower boundary.⁹

3.1.1 There is enormous diversity in trial activity

Interviewees reported conducting trials in a wide range of settings, with a wide range of goals, and in a variety of ways. These included trials at all three phases of medicine discovery (discovery and development of medicine, preclinical research, clinical research) as well as of public health interventions, functional foods, biotechnology development, devices, and trials to

improve standards of routine care. In some cases, clinical trials are undertaken principally to provide access to medication, rather than primarily for a research goal.

In terms of size, clinical trials being undertaken in Aotearoa range from small (≤ 50 participants) to very large ($>1,000$). The ANZCTR registry (Table 4, below) indicated the most prominent areas of study in smaller trials are mental health, diet and nutrition, cancer, metabolic and endocrine health, and public health. In large and very large trials, the focus is mostly on public health, respiratory health, mental health, infection, reproductive health, and cancer.

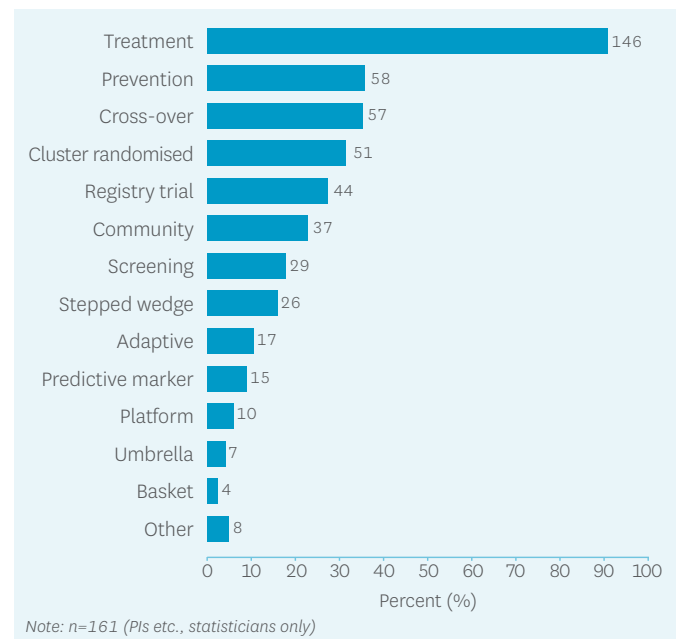
Table 4: Most prominent areas of study for each sample size

Sample size	Three most prominent areas of study (left to right)
Small (≤ 50)	Mental health, diet and nutrition, metabolic and endocrine health
Medium (51–500)	Mental health, cancer, public health
Large (501–1000)	Public health, respiratory health, mental health
Very large (> 1000)	Infection, reproductive health, cancer

Source: ANZCTR data, Sapere analysis

Survey respondents (PIs and statisticians only) said there was a wide range of clinical trial design types with which they have worked (Figure 3, below).

Figure 3: Responses to the survey question with which clinical trial designs stakeholders have worked



Many interviewees emphasised that New Zealand has a strong reputation for clinical research, and that New Zealand investigators are often respected partners for international projects. Several interviewees felt that New Zealand’s international reputation was enhanced by having relatively straightforward ethics processes compared to other jurisdictions and that the record of being able to establish trials quickly was a good one, a particularly important factor for industry partners. In saying that, however, stakeholders

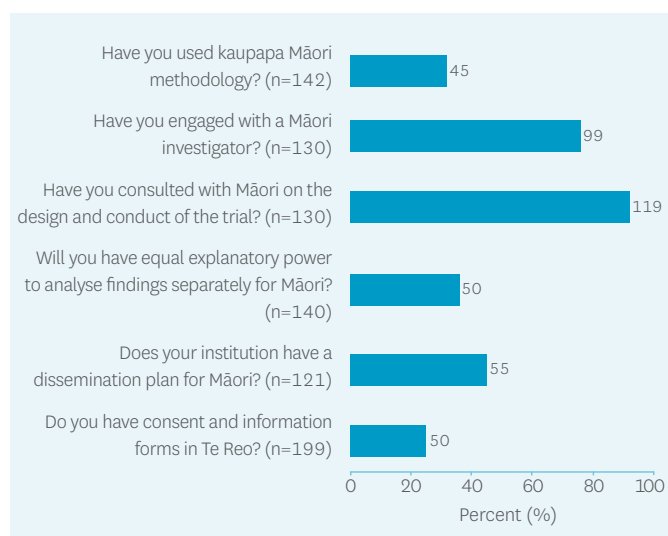
⁸ Footnotes within this section note where assumptions have been made about the nature of the data.

⁹ The trials analysed have been characterised by their target sample size instead of actual sample size since the data series was more complete. Henceforth, the term “sample size” refers to the target sample size.

expressed that having to go through multiple ethics and/or locality approval processes when running a trial across more than one locality is particularly burdensome and a barrier to running trials.

Participants in the survey responded variably when asked about Māori engagement within their research (Figure 4, below). Māori participant recruitment is not often accounted for and Māori are less likely to participate in clinical trials. Not many had used Kaupapa Māori methodologies before or had their consent and information forms in Te Reo Māori. Māori stakeholders recognised clinical trials may sometimes engage in culturally inappropriate practices for Māori (i.e. where the measures and tools are not accurate or appropriate for Māori), but also that there are some places where methods are developing (i.e. where there are specific needs for Māori samples). Additionally, racism is still a problem for Māori researchers, participants, and communities.

Figure 4: Responses to survey’s Māori engagement questions



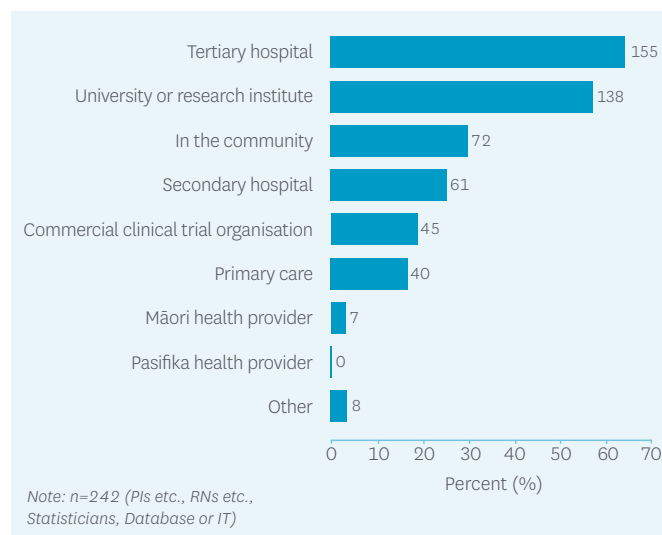
3.1.2 There are many different institutional settings in which trials are managed

Clinical trials are being managed in private or philanthropic organisations, universities, Health NZ hospitals, and private hospitals (Figure 5, right). While some trials are managed in primary and community settings, these are typically managed from a university or other entity, rather than by practising primary care clinicians.

Few respondents had conducted trials within Māori health provider settings and none had conducted a trial within a Pacific health provider setting. Māori stakeholders identified the need for more suitable, culturally safe physical locations for stakeholders to engage with trials.

Funding for clinical trials in Aotearoa New Zealand mainly comes from HRC or commercial sources, although some smaller trials are funded by charities. Commercial/industry-funded trials (registered on ANZCTR) make up the second largest number of trials in Aotearoa New Zealand for both small and medium sample sizes.¹⁰ However, funding and management of funds are typically separated. Funds are often managed by other institutions, such as universities, charities, or other research organisations.

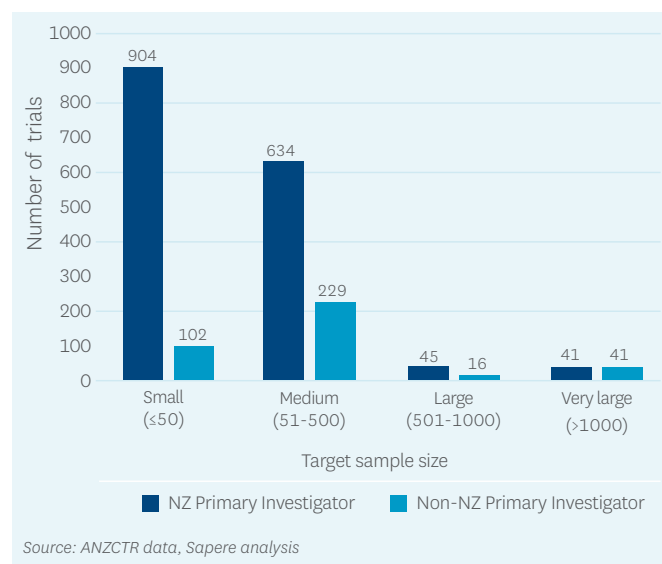
Figure 5: Responses to survey questions on the settings of trials with which respondents have been involved



There is reported to be broad interest in taking part in conducting trials among clinicians across several different settings, although some interviewees noted that the research component in standard clinical training was often minimal and that some clinicians may not be aware of the potential to participate in trial activity. Some hospital-based interviewees felt that a small number of enthusiastic clinicians were interested in trials, but that there was little wider interest.

Most small and medium sample size trials registered on ANZCTR have a New Zealand Primary Investigator (PI) as the key contact (i.e. NZ-led) (Figure 6, below). For very large sample size trials there is a greater proportion of non-New Zealand Primary Investigators listed as the key contact (i.e. not NZ-led).

Figure 6: Number of trials registered on ANZCTR that are NZ-led by sample size¹¹

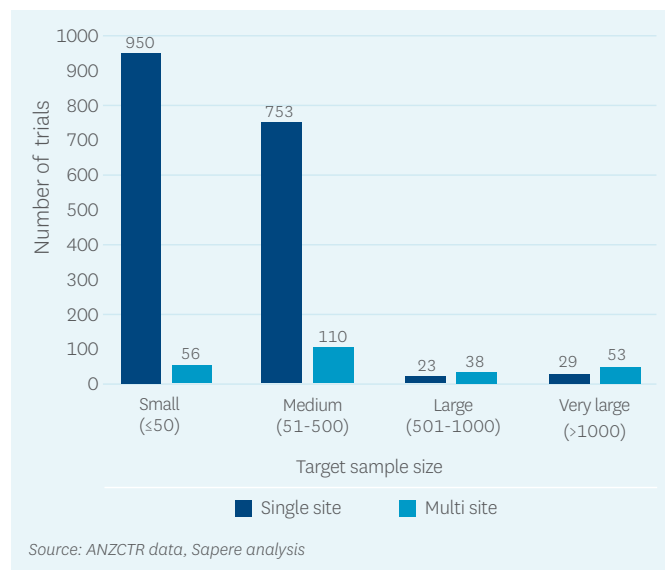


¹⁰ Commercially sponsored trials are often listed on international registries (such as clinicaltrials.gov) and therefore this metric is likely to underestimate the level of commercial clinical trial activity in Aotearoa New Zealand.

¹¹ It was assumed that if the listed primary contact (main investigator) was from New Zealand, the trial was NZ-led.

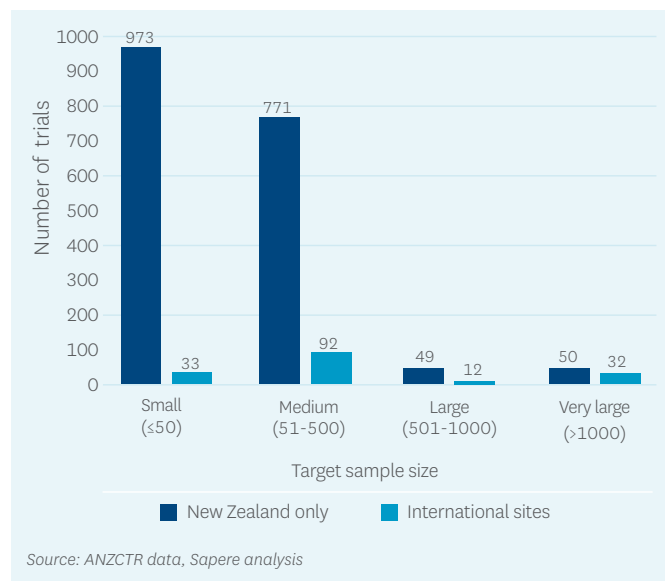
Most trials in Aotearoa New Zealand (registered on ANZCTR) are single-site for small and medium target sample sizes, and multi-site for large and very large target sample sizes (Figure 7, below).¹²

Figure 7: Aotearoa New Zealand single site versus multi-site trials registered on ANZCTR by sample size



Proportionately, most small and medium trials have sites in Aotearoa New Zealand only and do not have international sites. Conversely, for large and very large trials the proportion of trials that have international sites is higher (Figure 8, below).

Figure 8: Number of trials with international involvement registered on ANZCTR by sample size



3.1.3 Trial networks can provide significant support, but this is not widespread

Forty-seven per cent of Primary Investigator (PI) and Research Nurse (RN) respondents to the survey said they are a member of a national, trans-Tasman, or international clinical trial network (which are mostly organised by disease area or clinical specialty).

Trial networks play an important part in supporting researchers to conduct effective trials. Networks vary in the degree to which

they provide active support for their members, but in some cases can provide extensive support for prioritisation, recruitment and data management. Networks can range from relatively intangible relationships, to providing specific aspects of infrastructure and support.

Networks can also provide standards and specialist expertise within a given discipline or area of investigation, encouraging use of consistent outcome measures and reporting, providing quality control through peer review and network endorsement of trials, and sharing expertise and experience among the membership. In some cases, networks have been able to undertake effective prioritisation of research within a given field.

This, however, is not widespread and there is great variation across area and specialty. We heard from stakeholders that, while some networks try hard to provide support for their members, they are not well-resourced and rely mainly on the goodwill of the network coordinators to stay functional at a minimum level. As a result, some networks' activities are constrained (particularly by administrative support) and members do not receive the support they need.

3.1.4 Workforces are often fragile

Many interviewees felt that the workforce involved in delivering trials was fragile, in several different respects. Important factors include:

- Training and development. Many people, whether investigators, trial coordinators, data managers, or research nurses, enter clinical research without a clear career pathway, frequently learning on the job or from an informal mentor. This means that it can take time for individuals to become skilled in their roles, and that replacing people is challenging.
- Although they have specific professional knowledge, it is also often the case that statisticians and health economists enter the field of clinical research without clinical trials expertise and require further training and experience.
- In some cases, workers with valuable experience can be attracted away by private sector and international employers.
- Much of the workforce is employed on a soft money basis, with short-term grants and project funding, making continuity of employment uncertain and jobs unattractive. It is increasingly difficult to keep people employed between grants with small amounts of unallocated funding, particularly when there has been a significant centralisation of management and staffing decision-making in the institutions undertaking clinical trials.
- While there are a few early career awards for salary support for junior clinical trialists, there are few sources of salary support for mid-career researchers to the point of achieving more stable employment as a senior researcher.
- Potential investigators from a range of clinical disciplines may not be aware of the opportunities and benefits of clinical research. Training programmes often do not provide exposure to research. For example, General Practice Registrars are not required to complete a clinical research project.

The fragility is particularly evident in the Māori workforce and substantial development and investment are needed. Stakeholders

¹² Large and very large target sample size groups were cross-checked with other trial resources and publications to determine whether they were single- or multi-site trials. Numerous trials listed as single-site within the ANZCTR registry were recategorised as multi-site upon inspection.



identified that the Māori workforce is small in size (estimated by the Rōpū as 4 per cent of the total workforce), under-represented across research and support roles, not well funded, and stretched in its duties, with researchers taking on a wide range of roles within clinical trials ranging from ensuring mātauranga Māori is incorporated in the trial approach through to ethical review processes and governance. There are only a few highly skilled (in terms of general research skills *and* Te Ao Māori) and overcommitted Māori researchers. We heard some stakeholders had to take on responsibilities relating to Māori engagement and Kaupapa Māori methodology simply because they were Māori, regardless of whether they had been trained or resourced to do so. As such, people leave their roles due to the workload, as well as insufficient pay.

There is no systematic pathway for the development of the Māori workforce within clinical trials (including limited or no scholarship or research funding opportunities) and barriers exist for Māori students, postgraduate students and early career researchers, which further compounds issues with workload as well as succession planning. Māori researchers said that other Māori, supportive work arrangements, collaborations, and close Māori allies helped them to succeed.

Workforce development opportunities have also been identified for non-Māori researchers to become more culturally competent in their understanding and use of mātauranga Māori, Kaupapa Māori methodologies, and engagement with Māori. This development is critical to ensure Māori health advancement is at the forefront of clinical trials undertaken in Aotearoa New Zealand.

Similar issues were identified for the Pacific clinical research workforce, which is extremely small. There is no systematic approach to bringing together or strengthening its capability or capacity and no network for mutual support, posing similar issues for the ability of the Pacific clinical research workforce to be involved in clinical trials and also for succession planning. Often Pacific researchers-in-training are mentored by non-Pacific people and unable to lead their own Pacific research in areas that matter to Pacific people. Pacific researchers-in-training said they were sometimes used by non-Pacific mentors as a way to connect to the

Pacific community but not necessarily for exploration of issues that are important for the Pacific community.

3.1.5 Access to key infrastructure is patchy

There are a number of organisations that have achieved the scale necessary to maintain an effective infrastructure to support trial activity, including statistical expertise, trial development and coordination, health economics expertise, data management and consumer engagement. This includes both public-good institutions such as research trusts, and larger research organisations. In university settings there is usually some degree of access to statistical expertise and technical support, although in practice this can be variable.

Investigators who currently have access to research infrastructure are keen to maintain this and see the relationships they have with specific people and research teams as important to their future success. Developing a national infrastructure to support clinical trial research is supported by most of the interviewees who expressed a view on this issue. In some cases, there is a view that a small team with strong and close-knit relationships can be more productive than a larger centralised organisation.

Developing a national infrastructure, however, is not meant to replace or displace well-functioning teams / groups that already exist. The development of a national infrastructure is rather about creating opportunities for *all* researchers to further enhance Aotearoa New Zealand's research potential.

While current systems work well for some, and in some disciplines, for others any clinical trial infrastructure they can access is fragmented. Furthermore, it can be difficult for people entering the field to pick up key skills and knowledge about how to manage trials. Of the PIs who responded to the survey, 44 per cent said a potential site for a clinical trial had been unable to participate due to a lack of infrastructure and/or clinical research staff at the site. Resourcing issues likely impact the Māori workforce more.

Statisticians and health economists should have a role in both designing and implementing a trial, but the design process is typically unfunded. This can mean that timely access to statistical and health economic expertise is difficult and that integrating these

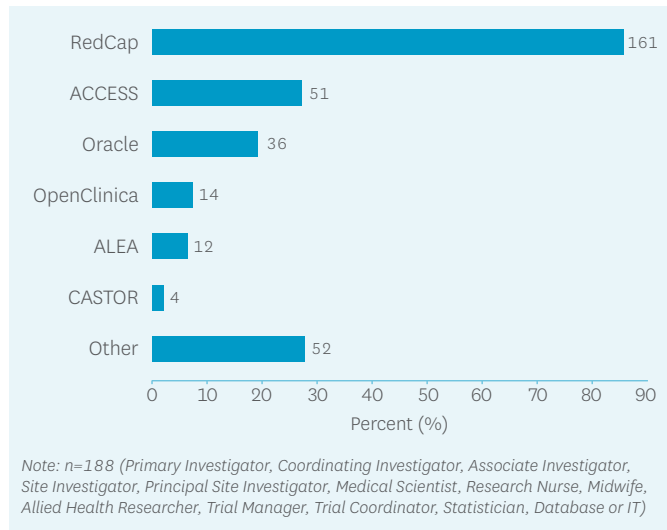
roles into the research team at an early stage is problematic. It is particularly difficult where aspects of the trial design are complex or novel and simulations or methodological research are required as part of the design.

What is clear is that any new infrastructure established must provide an opportunity for partnership with Māori, embed Te Tiriti o Waitangi, and allow for Māori to have greater leadership and governance to ensure Māori responsiveness.

3.1.6 Information needs are changing

Information management in general has developed in the past decade – a number of interviewees reported that there is far less reliance upon ad hoc individual spreadsheets or MS Access databases than in the past, and web-based applications which incorporate electronic data entry and database systems are more commonly used. Various systems are used internationally, but many reported using REDCap (Research Electronic Data Capture; open-source software developed by international health researchers, with data stored locally) as it is available at no charge to non-profit organisations (Figure 9, below). Effective use of REDCap to meet international standards requires it to be embedded in an appropriate environment, requiring IT support and coding skills. Other database systems, which ensure compliance with international standards (such as ORACLE and ALEA), are supported by some institutions or organisations. There is little in the way of systematic support or collegial networks among data managers to develop and standardise approaches.

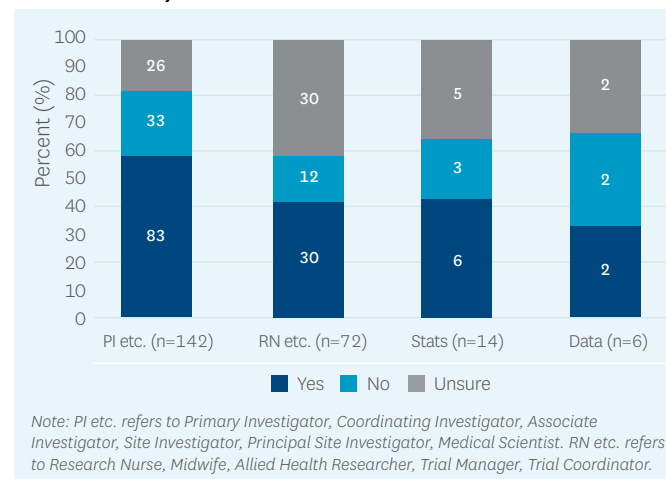
Figure 9: Database software used by survey respondents



More broadly, clinical trial research increasingly is dependent upon wider health information systems. Access to such information across the New Zealand health system is fragmented and, in some areas (particularly primary healthcare), almost impossible. Research organisations are seeing an emerging need to invest in information infrastructure that can safely and securely manage information from a range of sources and that can provide analytical access in a secure and well-governed manner. The standard level of functionality that is expected to be covered by research overheads (i.e. the portion of funding allocated to cover overhead expenses and fixed costs) is expanding rapidly and there is a need for institutions to recognise this.

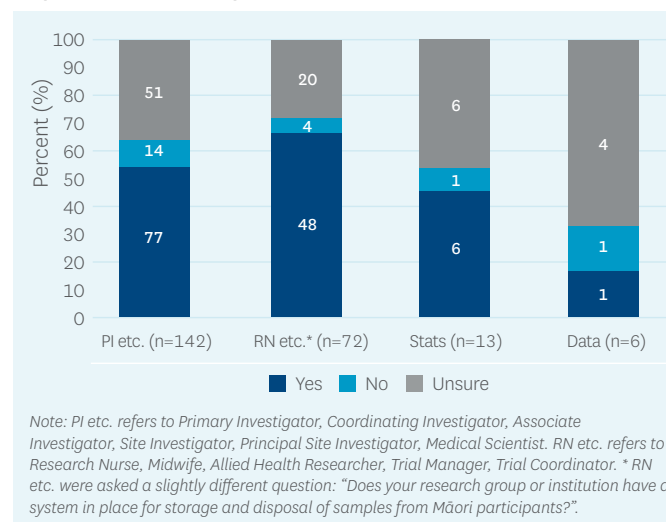
The tikanga for storing Māori samples and data is different to tauiwai norms and needs to be recognised as such. Data governance processes are currently highly diverse and a number of interviewees expressed concerns about lack of policy in their organisations on matters such as retaining / destroying data, data security, and reuse of data for subsequent research. It was felt by many that there is inadequate guidance on rapidly changing expectations and standards for data security and governance. Survey findings confirmed that data curation is not well developed amongst institutions (Figure 10, below).

Figure 10: Proportion of survey respondents' institutions that have systems in place for data curation (storage and sharing for future research)



Issues of data sovereignty were not high on the radar of many interviewees, although a number indicated that they were aware of sovereignty issues at some level (Figure 11, below). Again, there is an appetite for guidance on best practice. A few interviewees expressed awareness of issues of Māori data sovereignty. The survey further confirmed that not all people are aware of how to navigate Māori data sovereignty, or whether it is being appropriately considered. Māori stakeholders raised concerns about open-access data, data being stored overseas, and other areas where there may be data sovereignty issues. What is clear is that Māori partnership needs to be central to research questions and methodology.

Figure 11: Awareness of survey respondents' institutional systems for dealing with Māori data sovereignty and storage and disposal of Māori samples





3.1.7 Prioritisation is rarely practised systematically

Prioritisation of research, in the sense of systematically considering what research will reduce inequities and bring benefits for New Zealanders, is not widely practised. A number of clinical trial networks practise prioritisation to some degree and there were a few examples of comprehensive, well thought out prioritisation processes (e.g. the ON TRACK network; see Groom et al., 2022). Funders other than the Health Research Council seemed to have little formal prioritisation within the scope of their activity.

For Māori, there are tensions in the framing and scoping of any work. Is it a case of how Māori fit within clinical trials, or about how clinical trials best meet the needs of Māori?

When questioned about prioritisation, many interviewees said that funding availability determined which trials were done and that there was relatively little scope for prioritisation beyond that. Unsurprisingly, the more commercial and funding-dominated settings for trials tended to emphasise that priorities were driven by commercial potential (and often by commercial potential in countries other than New Zealand) and by the availability of funding for specific interventions.

3.1.8 There is relatively little focus on translation

Interviewees raised numerous issues with the translation of knowledge from clinical trials. This includes issues with interaction – translating knowledge, data insights and research findings from researcher to researcher – as well as translating knowledge from trials into clinical care and practice.

The translation of findings and knowledge from clinical trials (and in wider healthcare and research) can be very challenging and is very variable in its effectiveness across Aotearoa New Zealand. There are some good examples of interdisciplinary groups that translate knowledge from researcher to researcher, but not necessarily into healthcare practice. However, New Zealand is not alone in this regard, with an estimate of an average of 17 years for evidence to be incorporated into clinical practice (L. Green, 2014; Institute of Medicine, 2001; Morris et al., 2011;

National Foundation for Medical Research and Innovation, 2020). As with most aspects of clinical trial research, effective translation begins by designing the clinical trial with consideration of the implementability of the findings (Cumpston et al., 2021). Expertise such as statistics and health economics are often critical to the consideration of implementability, as is wide stakeholder engagement but, as noted above, these aspects essential to trial design are rarely, if ever, funded nor readily available or accessible to many clinical trials researchers.

Māori stakeholders said there is insufficient researcher and funder engagement in knowledge translation, a particular issue for Māori given the extractive nature of research, the need to tailor results for Māori providers, and a need to show participants reasons to participate in research.

Other interviewees expressed the view that there is not enough focus on trials with pragmatic end points and applications to society, and that there is typically a greater focus on novel small-sample trials that are not likely to translate into everyday healthcare.¹³ This may come back to the drivers and prioritisation processes of funding bodies.

Academic settings in particular can struggle with translation – there is not a strong tradition in Aotearoa New Zealand of academic roles for facilitating translational science and strategic links with factors that may influence practice in the health system are weak. Many interviewees identified that it can be hard to bridge the gap between clinicians in clinical practice and academics at universities, often with a mismatch of needs and ideas. This issue to some extent comes back to prioritisation and identifying research that has strong translational potential, as well as the underlying issue of the divide between the health services and research.

Overall, translational research is expensive and therefore any research institution that is resource-constrained (i.e. most) likely struggles.

¹³ In general, small-sample trials may provide useful contributions to the development of pathways for treatments but need to be translated into larger-sample and more extensive trials to become clinically relevant (i.e. to ensure findings are not isolated to small samples only and can be generalised to large populations). There may be circumstances where a small trial is appropriate.

3.1.9 Funding and costing are problematic in many ways

Funding is, unsurprisingly, cited as a constraint by many interviewees. This can play out in several ways, including:

- Funding bodies' caps for the size and duration of clinical trial grants are insufficient to conduct adequately powered clinical trials of sufficient duration. Furthermore, these caps have remained constant for some time, while costs have increased, meaning that the ability to conduct optimum trial design within the available funding is increasingly constrained. Funders often resist co-funding arrangements, compounding the issue of fixed caps from any one source.
- Much funding is short-term and project-based, meaning that it is difficult to support infrastructure and that key roles in research teams can be subject to uncertainty of tenure, reducing their attractiveness and making it difficult to retain expertise.
- The consequence of this project-based funding is that, upon receipt of new funding (already of inadequate duration to conduct a clinical trial of scale), significant time is spent recruiting and training project personnel.
- It is possible in some cases to cross-subsidise investigator-initiated research from commercial research activity, although there is a wide range of attitudes on the propriety of working in this manner.

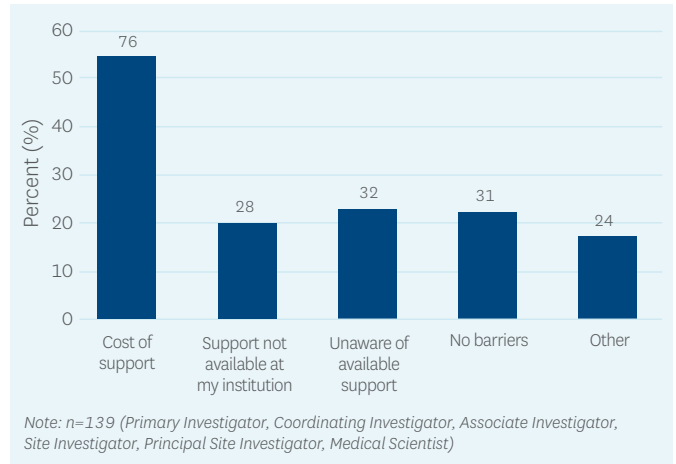
A key issue, emphasised by many interviewees, is that clinical trial investigators often do not have their time funded (or adequately funded) and that much research occurs in spare time over and above usual clinical commitments. Even where clinical time is nominally bought out, the reality tends to be that the clinical load does not decrease and the research activity has to be shoehorned in. This story was repeated frequently.

The issues of project-based and short-term funding also have consequences for the Māori workforce and for appropriate partnership with Māori in trial design and conduct. This contributes to the lack of sustainable development of the Māori health research workforce due to lack of job security. It also leads to issues with sustained engagement with Māori communities, meaning the needs of communities are not met because of lack of Māori engagement and community awareness of participation. A focus on funding for longer time periods and appropriate resourcing is needed to engage Māori communities.

Costing research is often complex – one funder explained that different projects cost their applications in different ways, making it hard to assess them in comparable ways. Several interviewees noted that researchers may not be aware of the true costs their project imposes on key services. For example, specific testing requirements mean that tests may need to be done on dedicated laboratory equipment with different setup from standard health service settings and separate from the usual production pipeline. Institutional research offices, which process grant applications, work to standardise costs, and ensure that they are fully accounted for, but there is widespread suspicion that the actual costs of trial activity, especially in public hospital settings, are opaque, and not necessarily fairly accounted for, with a great deal of regional variation in, for instance, radiology and laboratory costs.

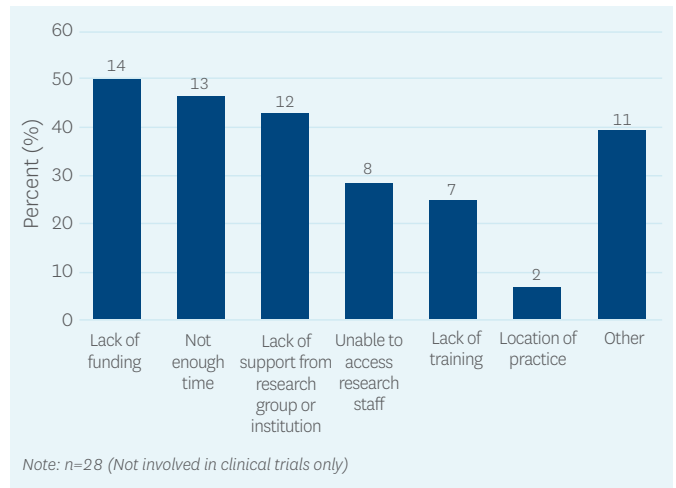
Figure 12 below shows that over half of those who are involved in trials (who responded to the survey) are unable to get the desired level of support for trials because of the cost associated with it.

Figure 12: Percentage of respondents that have identified barrier to receiving desired level of support



Those who responded to the survey and were not involved in trials highlighted lack of funding as the primary barrier to involvement (Figure 13, below).

Figure 13: Barriers to involvement in clinical trials



3.1.10 Health system culture

Interviewees frequently commented that New Zealand's health system does not have a research culture beyond that exemplified by hardworking and respected individuals. Health NZ hospitals do not currently have any incentive or mandate to conduct or encourage research and in some cases are actively antagonistic.

As a system, there is little provision for research to be conducted as an inherent part of health services and there is no dedicated resource for undertaking research as part of service delivery or service improvement. These comments applied across a range of health services, although were frequently made in the context of Health NZ hospitals. In primary care, where a number of services are provided by small private entities (whether in pharmacy, physiotherapy or general practice), there is even less ability to take part in research activity.

The commercial imperatives of delivering care in a financially sustainable manner are often paramount and there is no readily available resource to counter this, other than seeking academic positions.



3.2 Findings from literature

A review of the literature and international best practice examples was conducted to provide a reference point for the current state of Aotearoa New Zealand, as well as insight into the potential future state we would like to see. Across the international examples of best practice that we have identified, comparisons are made between:

- trials conduct, frameworks, and infrastructure;
- data systems and data management;
- workforce capability;
- research prioritisation and knowledge translation, and
- inclusion and focus on indigenous peoples and minority groups.

The literature identifies that clinical trials systems are generally complex and multi-dimensional. Some of the most well-recognised trial systems are the National Institute of Health Research in the United Kingdom, the Australian Clinical Trials Alliance in Australia, and the National Institutes of Health in the United States. Although some of these trials systems share common traits, no two systems are the same, and what works in one jurisdiction may not work (and has not worked) in others.

From the literature and other international examples, we have identified a series of high-level messages:

- no system is perfect, and even those that are best practice have things to improve;
- the systems in place are often complex with feedback loops and are a product of many moving parts;
- before anything, there needs to be a strong research culture to enable funding and investment in research infrastructure;
- there must be more effective avenues for development of capability of trials and dissemination of results;
- networking among all trial operators is an essential mechanism for sharing workloads, developing research ideas, and encouraging higher capability;
- research prioritisation must be a transparent process that especially involves patients, consumers, and communities;
- uniformity and ease of access to data are key to successful sharing and collaboration, and
- research must work with indigenous populations, culture, and identity to be successful. Non-indigenous research methods cannot be applied to indigenous populations with the expectation of the same results.

The full review is included in Appendix D.

4. Desired clinical trials infrastructure



Two participatory processes were used to develop the preferred infrastructure options. The purpose was to identify clinical trial infrastructure that would meet the following overarching principles:

- reducing inequity;
- increasing access to, and participation in, clinical trials, and
- implementing options relevant to Aotearoa New Zealand.

4.1 Results

Two sets of results emerged from the World Café and Delphi processes: criteria for a preferred option, and elements of future clinical trials infrastructure that were deemed critical.

4.1.1 Criteria used to assess the preferred option

Table 5 (right) sets out criteria for a preferred approach to addressing the challenges that were derived from these participatory processes.

Other important considerations for a preferred approach are:

- Cost effectiveness – is this approach providing value-for-money outcomes? Are there options that provide the same level of benefit at a lower cost?
- Implementation – how does this approach compare to others when thinking about the ease of implementation? Are there potential complications (such as national investment capacity) that will limit the ability to meet desired outcomes?

4.1.2 Critical elements

The infrastructure options voted as critical for inclusion in the final consensus meeting are shown in Table 6 below. Alongside analysis from other parts of the project, these form the basis of the proposed infrastructure and help to shape the implementation roadmap (i.e. the order of implementation of proposed infrastructure components). They have been grouped by relevant theme (loosely following the workstreams of the project).

Table 5: Criteria for preferred option

Criteria for preferred option	Workstream(s) retrieved from
Embodies Te Tiriti o Waitangi principles	All Workstreams
Strategic alignment of option with health priorities	Prioritisation, Knowledge Translation, and Implementation Workforce Capability Equity and Consumer Engagement
Strengthens networks between researchers and relationships with research funders (including community and primary research, connecting with hospital system), and builds bridges between research and healthcare providers	Workforce Capability Data Systems and Curation Prioritisation, Knowledge Translation, and Implementation
Builds capability for clinical trials in both infrastructure and workforce	Workforce Capability Clinical Trial Activity, Infrastructure, and Networks
Enhances knowledge translation to day-to-day clinical care and health delivery, promotion, prevention	Prioritisation, Knowledge Translation, and Implementation Clinical Trial Activity, Infrastructure, and Networks
Feasibility and sustainability	All Workstreams

Table 6: Infrastructure options voted critical for inclusion in the consensus meeting

At a national level	
	Governance ¹⁴ and advice on strategies to support Māori health advancement through clinical trials
	Governance and advice on Māori data sovereignty
	Governance and advice on developing relationships with iwi, Pacific, and consumers for co-design and partnership
	Governance and advice on funding availability, e.g. registry of all clinical trial funding available
	A coordinated information resource on trial activity, e.g. consumer-facing registry of all clinical trial activity
	Governance and advice on data governance, systems, curation and sharing
	Advice on adverse event recording and reporting
	Advice regarding handling, storage, and disposal of human specimens
	Accountability on education of the public about the benefits of clinical trials to Aotearoa and to individuals and their whānau who participate in clinical trials
	Transparent national guidelines for determining which trials are supported by the clinical trials hubs
	Advice on research methods for working with Pacific communities
	Data Safety Monitoring Committee (DSMC) set-up and advice
	Advice on trial methodology, including design of complex or innovative trials, and statistical expertise
	Advice on health economics
	Governance and advice on national approach to locality assessment
	Advice on trial pharmacy services
	Clinical trials infrastructure being available to industry through an appropriately funded model
	Monitoring and audit activity advice

¹⁴ Consensus discussion clarified that the original Delphi question did not refer to governance of individual clinical trials. The organisation of the national infrastructure will require some elements of governance and accountability, which will be developed in accordance with principles of co-governance and Te Tiriti.

Table 6 (continued): Infrastructure options voted critical for inclusion in the consensus meeting

At a regional level	Consumer engagement, including recognised patient groups
	Support for Māori community engagement and Māori health advancement
	Development of protocols, data management plans and other trial documentation
	Statistical input into the design, conduct and analysis of trials
	Ethics and regulatory approval
	Site locality approval
	Health economics input into the design and analysis of trials, where Health Economics needs to be considered
	Finance and budgeting
	Database design, provision, and maintenance
	Innovative data capture, including text messaging, data from wearable devices and innovative data entry
	24-hour randomisation service, including randomisation, unblinding and drug delivery
	Access to accredited pharmacy services
Clinical trials management system (software to manage all aspects of clinical trials, including progress and reporting)	
Data governance and long-term curation	A national, coordinated approach to data governance, which recognises Māori data sovereignty
	Aotearoa New Zealand to have its own national federated repository for long-term storage of data collected in clinical trials
	Once a trial is finished, data collected from publicly funded New Zealand-led trials should be available to other researchers in New Zealand for approved purposes
Collaboration	National resource of people and information to support clinical trial activity
	Resource is underpinned by a set of values that promotes a culture of collaboration
	Resource has a publicly accessible register of actively recruiting clinical trials
	Resource provides opportunities for meetings between consumers, Māori, Pacific, and researchers
	Resource provides a database of trial expertise for potential collaboration
	National governance body to develop and implement funding models that promote/support collaboration
	Resource provides a database of key stakeholders for collaboration
Resource provides 'collaboration' opportunities such as virtual meetings or workshops	
Prioritisation	Clinical trial activity should occur at a regional/local level to identify areas of specific importance for local communities, including Māori
	Prioritisation should consider potential health gain (impact) of the research
	Prioritisation should consider feasibility of the research
	Prioritisation should consider feasibility of the implementation of the intervention
	Prioritisation should consider the ability to achieve health equity across all Aotearoa New Zealand and its peoples, including Māori, Pacific and rural
	Prioritisation should include consumer engagement
	Prioritisation should consider wider societal gain (impact) of the research
	Prioritisation should be undertaken by discipline-based clinical trial networks
	Prioritisation should include community engagement
	Prioritisation should consider whether the population to be researched is an under-researched population
Consumers	Aotearoa New Zealand should have a national system for identifying a diverse range of consumer research partners (Māori, Pacific, rural, disabled, youth, collectives)
	Aotearoa New Zealand should have a national system for supporting and empowering consumer research partners
	Aotearoa New Zealand should have a national system for supporting and educating researchers in engaging with consumer research partners
	Aotearoa New Zealand should support consumer research partner networks
	All publicly funded clinical trials should include consumer research partners
	Consumer research partners should be offered remuneration for their roles in clinical trials (this is not remuneration for participating in a clinical trial)
Networks	A national clinical trials alliance that provides a forum for the networks to share ideas, best practice, resource
	Access to administrative support for networks
	A transparent process for reviewing, at appropriate intervals, which networks should receive support from a national clinical trials infrastructure

Table 6 (continued): Infrastructure options voted critical for inclusion in the consensus meeting

Knowledge translation	Health New Zealand/Māori Health Authority/Ministry of Health, supported by the Health and Quality Safety Commission, should be responsible for ensuring effective knowledge translation and implementation to achieve equity across Aotearoa New Zealand's health system
	A lay summary of the results from clinical trials should be posted on the Aotearoa New Zealand national clinical trial centre site
	The proposed clinical trial infrastructure should provide support to disseminate clinical trial results to Māori, Pacific, rural and other key stakeholders
	A dedicated national infrastructure to fund systematic review and Aotearoa New Zealand-specific guideline development
	Individual researchers or networks should be responsible for ensuring effective knowledge translation and implementation to achieve equity across Aotearoa New Zealand's health system
Workforce development, being provided nationally	Training and accreditation in Good Clinical Practice (GCP)
	A GCP programme that is tailored for Aotearoa New Zealand
	GCP training and accreditation that is free for all
	A modular training programme that upskills users in clinical trials methods
	Job security and career pathways for people in the clinical trials workforce
	Training programmes, other than GCP, should be accessible to all, although some may come at a cost
Workforce sustainability	Established clinical trials research career pathways for investigators
	For HNZ staff, clinical research activity should be recognised as an integral part of the job
	Research roles should be embedded within hospitals to support clinical trial activity
	Research roles should be embedded in the community to support clinical trial activity across the healthcare system, including iwi and Māori health providers
	Costs of embedded research roles should be underwritten by Health New Zealand

4.2 Comment on important themes

Several themes emerged and were debated at both the World Café-style workshop and the consensus workshop.

4.2.1 Collaboration, visibility, and mentoring

Stakeholders made it clear that they wanted greater visibility of the clinical trials happening in Aotearoa New Zealand to lower the barriers to collaboration and involvement of patients, clinicians, and researchers. This may be possible through a repository or open register that tracks and reports frequently on the clinical trials activity in Aotearoa New Zealand. Greater visibility of the types of trials being undertaken, and in what specialty areas, may bring people with similar interests closer together and encourage them to collaborate more. Development of a strategy / plan that outlines the health objectives and goals of research, as well as a strong leadership, may help to increase the visibility of activity and incentivise collaboration.

There must also be some form of channel that facilitates collaboration between those who do not have confidence and/or clinical trials experience and those who do. Some suggested the development of well-resourced mentor programmes to upskill those without the confidence and/or experience. Building and sustaining (i.e. funding adequately) more networks may make it easier for those without confidence and/or experience to be involved and collaborate by bringing people together as a starting point for engagement. This should also extend more widely than just investigators / researchers – allowing consumers, nurses, pharmacists, and people from participating sites to collaborate and be involved if they wish. Greater engagement will ensure more meaningful research.

4.2.2 Being clear to consumers about the value of clinical trials

An explicit, mandated requirement or mechanism for greater consumer representation in strategy, funding, and priority setting, as well as trial design and focus, is required. Stakeholders suggested the establishment of some form of consumer council or centralised group that can act on behalf of consumers, defend their interests, and integrate consumers into all stages of clinical trial activity.

Stakeholders want clear, palatable, and easy-to-understand information about the nature of clinical trials and treatments, the importance of clinical trials as a means of improving health outcomes. This will enable consumers to see how they fit into the landscape and engage with research activity to contribute and gain the most value. Creation of a website was suggested (in addition to, or as part of, a national trial repository) to act as a port-of-call for consumers to find information about active trials as well as collate useful resources for consumers.

There should be training and guidance for researchers to be able to communicate effectively, comfortably, and safely with consumers in the design stage as well as conduct of a trial. Part of this might include further research and development of guidelines for effective engagement with consumers in ways that are meaningful, appropriate, and convenient for the consumer. This is particularly important given the sacrifices consumers make to be involved with clinical trials are often not recognised.

Consumers need to be engaged at the trial design stage and not just as trial participants.

4.2.3 Data systems, data governance, use of data, and information technology

There should be an information technology and data governance strategy developed around the gathering of data, how data are used, and how data can and should be integrated across clinical trials and the wider health system. The strategy should develop national standards for culturally appropriate use, sharing, and storage of data throughout the trial process, including data security. Development of these standards and strategy should be led by iwi and Māori data governance and sovereignty experts. The standards need to be actionable and hold some sort of power (perhaps legislative) to ensure that researchers are accountable for their actions when using, sharing, and storing data and that they follow Māori data sovereignty principles.

The impact of the information technology and data governance strategy should be to create national consistency in data capture and storage so that all regions have access to the same level of data and data infrastructure while embedding and following Māori data sovereignty principles. Funding will be required to ensure that any guidance reflects best practice, is reviewed regularly and updated if necessary, and can be met easily and effectively by those using, sharing, or storing data.

Similarly, stakeholders wanted to see a mandate for consistency in the clinical trials data systems used across the country so that researchers have access to similar capability and a standardised form of data management that can be taught and streamlined. This would also allow for easier data sharing and integration across different areas of the country, and again should be developed with iwi and Māori data governance and sovereignty experts to ensure the interaction of the systems with Māori data is appropriate.

Some suggested a central data storage system to ensure appropriate access and maximisation of the value drawn from data collected (and re-use of data). However, this may have its drawbacks when considering risk management and data breaches and would have to respect issues of Māori data sovereignty and Māori control of data. Further discussion about this is necessary.

Training and education are needed alongside this development to make sure those involved in clinical trials are competent, educated, and aware of the responsibilities around the culturally safe use, sharing, and storage of data, as well as the opportunities and ways to make the best use of data.

4.2.4 Equity, and rural and primary care

Te Tiriti o Waitangi must be at the forefront of any clinical trials strategy. After that, equity must be the next highest priority, across ethnicity as well as geographical location. Māori and Pacific must be represented at the governance level of the system to ensure:

- Māori and Pacific interests, priorities, and perspectives are present in the determination of national strategy;
- Vision Mātauranga is embedded within the system, and
- the value of Kaupapa Māori and Pacific research methodologies are recognised, understood, and promoted in the Aotearoa New Zealand healthcare system.

A Te Tiriti o Waitangi-based science structure should be the foundation of any new infrastructure and the accompanying strategy must describe what effective participation looks like at all levels, from governance down through the whole system. It will be important to get the tone and language right, to balance an overarching prioritisation view with the priorities driven by Māori, Pacific, and other high-need communities, and to enable a more distributed and inclusive research structure through the healthcare system. The funding systems for clinical trials must also recognise the importance of relationship building and co-design of research with communities (including whānau) to ensure equitable participation.

Achieving this Te Tiriti-based science structure will require extensive relationship building with, and input from, communities and iwi across multiple levels (governance, policy, institutions and networks, researcher) to establish the needs and wants of communities and provide a holistic approach when determining what is important and how best to engage and enable participation.

Stakeholders agreed that incentives should be in place for primary care to become involved in research, particularly to involve participation (from all people, not just researchers) in rural areas to improve equity. The research system should be less centred around tertiary and secondary care. This will require a funding mechanism to allow all of primary care, including rural primary care, to be involved (i.e. researchers resourced to be able to do research, and others resourced to be able to contribute). Additionally, increasing the use of technology such as telehealth and teletrials could be useful in supporting the rural workforce and increasing participation of those residing in rural areas.

A centralised resource was suggested by stakeholders to act as a knowledge pool for people to access, including the establishment of cultural coordinator roles to manage and improve effective engagement in clinical trials.

When considering equity in the workforce, stakeholders said there is a role for schools as well as universities and communities to promote and enable research as a career option. To encourage Māori and Pacific students to undertake a research-focused career path, stakeholders suggested:

- increase school capability to teach science in Te Reo Māori;
- include research opportunities within school and then university across all health fields (e.g. medicine, nursing, allied health, statistics, health economics, etc.) and specifically Kaupapa Māori and Pacific research methods – people seeing themselves in research will encourage participation;
- listen to Māori and Pacific students to find out what will help to bring them into a research career;
- make research a career rather than an add-on;
- include aspirational objectives in universities' five-year plans to build research capacity and opportunities, particularly for Māori and Pacific students;
- formally recognise the role of education by Māori, and
- partner with Māori research groups to develop the clinical trial workforce.

4.2.5 Knowledge translation and implementation

Stakeholders recognise that knowledge translation and implementation are vital activities for clinical trials to have meaningful impact on healthcare and healthcare delivery. There is, therefore, a need for a dedicated funding stream within the healthcare system (not necessarily just within clinical trials infrastructure) to ensure that knowledge translation and implementation are not *ad hoc* arrangements and are able to be done routinely. Policy changes and mandates for knowledge translation and implementation activities may improve the level of activity.

Attendees of the World Café generally agreed there should be a body or network within the public health system tasked with enabling knowledge translation and implementation of findings in Aotearoa New Zealand. It should take what has worked well in different contexts and adapt it to our national environment where appropriate, in collaboration with Māori. The body or network needs enough power to be able to mandate knowledge translation and implementation activities in the design and undertaking of research. The National Institute for Health and Care Excellence (NICE) in the UK was referenced as a good concept, but the system in its current state would not be suitable for Aotearoa's healthcare environment. The former New Zealand Guidelines Group (NZGG) was also referenced in discussion.

Stakeholders referenced the Australian Department of Health translational funding system as an example of what successfully supports translational research and the implementation of findings. Other stakeholders said existing funding streams for clinical trials and contract arrangements should include contingencies that allow for funding allocations for knowledge translation once a trial has been successfully completed.

Well-defined workforce and career development opportunities, as well as permanent roles in knowledge translation and implementation, may help to make it more systematic and successful by disseminating ideas, findings, and best practice. This should be across the system to be able to input the findings into strategies as well as point of care.

4.2.6 Prioritisation

Stakeholders gave a range of suggestions regarding prioritisation activity for clinical trials:

- It is critical that prioritisation processes be transparent, regardless of the level at which they occur.
- Any new system should build upon the role of networks that are already prioritising within their individual fields; however, they need additional resources to do this effectively.
- Consumers need to be more systematically involved in prioritisation. This requires additional resources and having consumers embedded at the level at which prioritisation occurs.
- Front-line clinicians and consumers, particularly in rural areas, need to be involved in prioritisation at a local level. Having end users involved helps to understand where the priorities are, particularly at the local level. If priorities are not reasonably aligned to researchers' interests or specialty areas, then prioritisation might not work.

- Prioritisation of research needs to balance pragmatism and blue-skies research – do not squeeze out innovation.
- Combining prioritisation with trial development can help in producing good research proposals and protocols that have community support.

Prioritisation was an area where there was a difference of view between Māori respondents and other respondents. Māori respondents believed clinical trial prioritisation activity should occur at a national level to identify areas of specific importance to Aotearoa New Zealand, whereas most other respondents did not. In the consensus meeting it was voted critical for inclusion that trial prioritisation activity should occur at a regional level to identify areas of specific importance to Aotearoa New Zealand.

The choice of the prioritisation activity occurring at a regional level was suggested to ensure research happening within a specific region is most relevant and meaningful to the local population. Prioritisation activity occurring at a regional level does not necessarily preclude prioritisation also happening at a national level. Some degree of prioritisation, particularly of health issues or topics relevant to Māori, must happen at a national level within the wider health and research strategy-setting processes.

4.2.7 Infrastructure and activity

Stakeholders made suggestions about the proposed infrastructure and activity. First, there is a need to embed research at a high level in the health system, with research leadership and ownership from the top level of MoH, MHA, and HNZ. This will ensure that research is well-recognised as a priority and an important area of added value for the healthcare system. Recognition of research as a valid and important part of the healthcare system is necessary to provide options and opportunities for the development of the workforce and clinical trial activity within Aotearoa New Zealand. It is also necessary that there be sustainable, non-project-specific support available to allow people to advance through research-related careers in the healthcare system.

Any new research system will have to have strong governance that is tied to those responsible for the health system. The research system will have to be accessible and connected to all, with a representative governance structure that connects with a wide range of stakeholders, particularly consumers, Māori, Pacific, and rural communities. The system should provide resources in terms of best practice across the different areas of clinical trials and be a place for people to go for advice and guidance. This requires infrastructure (both human and physical) with core central activities and dispersed site activities to make sure that it is well connected but also substantial enough to be directive.

5. Recommendations and proposed model



Collation and synthesis of the information-gathering steps of the project (through the survey, interviews, International Advisory Board, and World Café workshop), as well as the results from the Delphi survey and consensus meeting, unveiled the main problems of the current system and the benefits stakeholders wanted to see arising from improvements to clinical trials infrastructure in Aotearoa New Zealand.

The Investment Logic Mapping (ILM) framework used within New Zealand Treasury business case guidance has been adapted and used here to present the identified main problems and benefits. The map (Figure 14, below) provides a clearer picture of the current and desired states of the system and therefore allows a model to be proposed that bridges the gap.

5.1 Investment logic

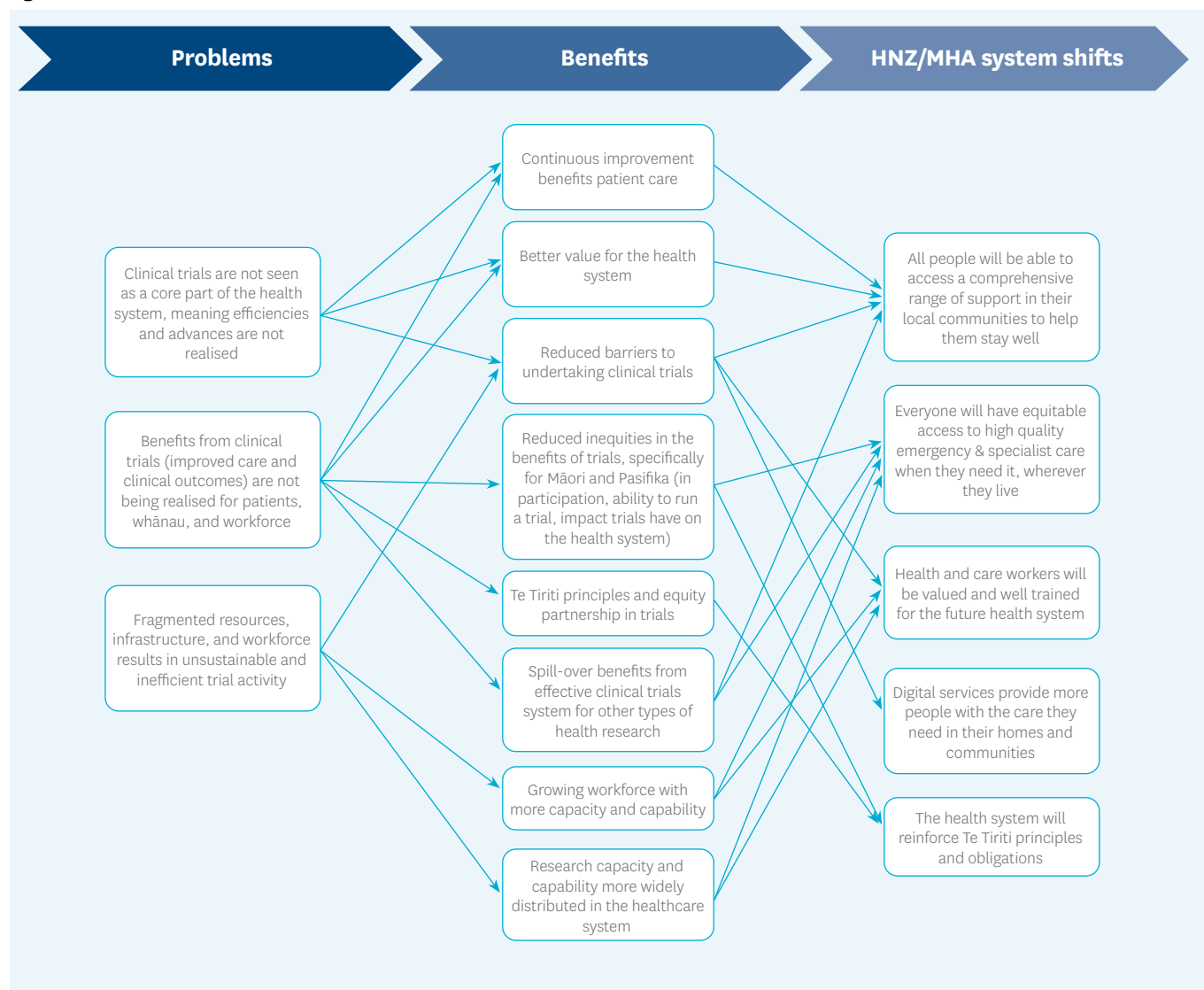
Our understanding of the current state based on information from stakeholders and international best practice literature allows us to define the problem at hand as well as the desired outcomes of

a future system: what we want the system to be able to do for its stakeholders. Once the problem is defined and benefits identified, the necessary steps to get there inform our proposed model and recommendations.

The benefits identified reflect the fact that clinical trials can make a big contribution to the overall healthcare system and therefore to the system shifts that Health New Zealand and the Māori Health Authority have set as goals. It is important to note it will take a wider research and innovation strategy, complementing the specific focus on clinical trials, to fully realise the benefits identified.

The other element that will be key to achieving benefits from improved clinical trial infrastructure is an effective system for knowledge synthesis, meta-analysis, guidelines, and knowledge translation. This function will be critically important for embedding the knowledge generated from clinical trials and other sources of evidence into the Aotearoa New Zealand healthcare system and achieving better and more equitable health outcomes for New Zealanders.

Figure 14: Problem definition and identification of benefits





It is worth exploring the foundations for each of the three higher-level problems defined throughout the process. Below provides a summary of key issues that aggregate into the higher-level problems.

Clinical trials are not seen as a core part of the healthcare system, meaning efficiencies and advances are not realised

The health system, at best, does not recognise or prioritise the benefits of clinical trials and health research and therefore does not provide adequate support for research. Yet clinical trials, and health research in general, are fundamental to how the system improves and efficiencies are gained. The system does not allocate time for researchers to partake in clinical trials and health research more broadly. Participation comes at the expense of other commitments.

Where activity does occur, it is clear Te Tiriti o Waitangi principles are not embedded within the clinical trials system. Additionally, the current clinical trials system does not always address health priorities or inequities, there is a lack of systematic prioritisation of which trials to undertake, and there are too few trials being undertaken with too few participants enrolled.

Benefits from clinical trials (improved care and clinical outcomes) are not being realised for individuals, whānau, and the workforce

There are gaps and inequities in access to clinical trials based on a range of factors, including an individual's geographical location. As such, individuals are missing out on the benefits of participating in trials and access to novel interventions, and the findings from clinical trials cannot be generalised to all. There are also opportunities missed for the workforce to participate in trials, training, and professional development for similar reasons. This has an impact on workforce recruitment and retention.

For trials that do happen there is a failure to translate the findings systematically and rapidly into practice, where appropriate, and therefore the potential benefits are not realised.

There are fragmented resources, infrastructure, and workforce, which results in unsustainable and inefficient trial activity

The current system for clinical trials is fragmented, and the resources, infrastructure, and workforce that do exist are piecemeal and not organised in any systematic way across the country,

which has implications for the sustainability and efficiency of trial activity. A lack of clear direction means current best practice in clinical trials development and implementation is not being met, particularly regarding Māori responsiveness, co-design, consumer engagement, and cultural safety of researchers. Further, there are no data governance or sovereignty structures and there is a lack of consistency in data system use.

In many places poor infrastructure limits the settings in which trials can take place and therefore who can conduct or participate in the trials. This fragmentation also means there are inequities in the clinical trial workforce by ethnicity, location, site, and expertise. Areas that are less research-active likely have less defined research career pathways, as well as limited training and development opportunities.

Lastly, commercial and investigator-led trials are not integrated within the system and therefore benefits are being lost with respect to system efficiency.

5.2 Recommendations and priorities

We set out a number of broad recommendations for the overall approach to developing clinical trials support infrastructure, recognising there is a strong case for significant investment in national clinical trials infrastructure in Aotearoa New Zealand. These broad recommendations are complemented by a number of detailed recommendations developed by this project's Māori Rōpū, and priorities identified by our Pacific and Consumer Focus Groups. These general recommendations are in addition to the Māori Rōpū recommendations and Pacific and consumer priorities and form the foundations for the proposed infrastructure.

- The national clinical trials infrastructure must be underpinned by principles of Te Tiriti o Waitangi and developed in co-governance with Māori.
- The responsibility for ensuring high-quality research activity must be woven into the job descriptions of all senior clinical leaders in Health NZ and the Māori Health Authority. There must also be targeted measures of accountability for these senior clinical leaders.

- There must be an adequately resourced National Research Office for Health NZ, co-governed with the Māori Health Authority, with research leadership at the executive level of the organisations. While this function exists within the context of health research policy leadership from the Ministry of Health, in order to envisage possible gains it is essential for Health New Zealand to have research leadership at the operational level.
- There should be a National Clinical Trial Infrastructure Centre with expertise from across the country, which will provide leadership, governance, expertise and overall, high-level national support and coordination of trial activity as outlined in section 5.3 of this report.
- There should be Regional Clinical Trial Coordinating Centres around the country that between them provide the necessary expertise to support clinical trials as outlined in section 5.3 of this report. Each of these centres will support trial development and conduct across regional nodes to ensure equity of access for both researchers and participants and will collaborate with other centres to support national and international trials.
- There should be sustainable and systematic networks for Māori researchers and for Pacific researchers to support Māori and Pacific research communities in a regular and coordinated way in accordance with recommendations and priorities identified above.
- Active development and support for the Māori health research workforce.
- Partnership with Māori and local Māori communities at every level, including trial implementation and national infrastructure.
- Supporting Te Ao Māori methods/priorities and engagement with researchers and communities.
- Embedding Māori data sovereignty and tikanga about data in the clinical trials system.
- Ensure knowledge translation has a positive impact for Māori and reduces inequities in health outcomes.
- When funding mechanisms are developed, ensure they are responsive to Māori community needs and researcher obligations.
- Support and train tauīwi workforce to engage with Te Ao Māori.
- Active development and support for the Pacific health research workforce.
- All publicly funded clinical trials should include consumer research partners.
- There should be a national federated health data system with Māori data governance at the core, that allows embedding of research in routine clinical care and provides culturally appropriate long-term curation of research data.
- A clear responsibility for research knowledge translation and implementation must be established within Aotearoa New Zealand's new healthcare system that is well integrated with change management, clinical governance functions, and the health system's role and responsibilities as an effective Te Tiriti partner for Māori.

5.2.1 Māori Rōpū recommendations

The recommendations below have been developed by the project's Māori Rōpū and informed by iNZight Analytics' analysis in consultation with Māori stakeholders of the project. Given the potential impact of clinical trial activity on aspects of equity, specific recommendations are needed to give effect to the aspirations of Māori as Treaty Partners, both in the conduct of research and relationship with Māori communities and priorities, and in supporting the Māori research workforce to realise its potential.

Active development and support for Māori health research workforce

- Proper, sustained funding for Māori early career researchers (that has competitive-enough pay rates).
- Māori cultural advisor roles, paid and resourced, to help current researchers resist the "cultural double-shift".¹⁵
- Mentoring programmes are needed, but there is a need to balance this with the time constraints for busy researchers.
- Consider pathways at all stages from secondary education onwards through to research.
- Māori researchers need cultural development; workforce development needs to recognise Māori are diverse.
- A Māori-specific trials network to support the Māori research workforce, with proper resourcing (not another responsibility for those currently overworked).

Partnership with Māori and Māori local communities at every level, including trial implementation and national infrastructure

- There is a need for Māori roles within governance structures, or for Māori governance structures.
- Attend to workforce issues, mentioned above, to ensure there are sufficient Māori kaimahi and leaders.
- Consider Māori rights and needs (partnership) at every step of project formation.
- More resources (financial, people) are needed to ensure sufficient recruitment for reasonable numbers of Māori participants in clinical trials. There may often be a need to oversample Māori.
- Researchers are engaging in measures at a level that could seem tokenistic, e.g. translating cover letters, offering karakia, but these are good steps and appreciated by some. More of this is encouraged.
- Researchers need to plan for sufficient statistical explanatory power for Māori participants.

Supporting Te Ao Māori methods/priorities and engagement with researchers and communities

- More Māori-led research work on making clinical trials (and research generally) responsive to Māori.
- Need to design work that Māori want to participate in (seek Māori input, design, and feedback).
- Develop resources across areas of need and make them standard, and a standard requirement across the workforce.

¹⁵ "Cultural double-shift" refers to the Māori workforce effectively having to work two jobs: managing their commitments to their science role as well as ever-growing expectations of leading and teaching others about Te Ao Māori.



- Co-locate researchers in communities; develop spaces where Māori participants and whānau are comfortable.

Embedding Māori data sovereignty and tikanga about data in the clinical trials system

- In building infrastructure, there is a need to embed Māori data sovereignty; systems and processes need to be developed.
- Create a national code for data sovereignty and guidelines around tikanga.
- Researchers need training on Māori data sovereignty, with consistent, standardised resources, case studies, and examples in clinical trials research.

Ensuring knowledge translation has a positive impact for Māori and reduces inequities in health outcomes

- Include knowledge-translation-specific roles in the infrastructure; but these roles need to be Māori-specific too.
- Incentivise. Build in the need for researchers to have to consider the implications of their results for Māori communities (and base this at the output level, rather than just the grant/initial level).
- Knowledge translation needs to be planned with end-users at the start of the research.

When funding mechanisms are developed, ensure they are responsive to Māori community needs and researcher obligations

- Longer-term funding is needed to ensure timelines align with Māori community needs/rights/researcher obligations to people.
- Researchers within institutions (e.g., universities) need to be trusted with their own budgets and timelines.
- Practically, there needs to be a budget for miscellaneous expenses that does not cause administrative barriers for Māori researchers (e.g., koha, bringing kai easily).

Support and train tauwi workforce to engage with Te Ao Māori

- The system needs to incentivise being a good treaty partner, and help to develop good allies.
- The two highest-rated areas, where (all) survey participants wanted more support, was in Kaupapa Māori methodologies and in Māori data sovereignty: training is needed.

- Consider how to operationalise cultural safety; there was a suggestion of micro-credentials or certifying people as safe to work with Māori (and Pacific).

5.2.2 Priorities of Pacific advisory group

The main priorities of the Pacific advisory group are below. The Pacific advisory group met on three occasions, reviewed current-state findings, and identified key priorities for Pacific researchers.

- Pacific leadership role within the health and research system, with a strategy for Pacific clinical trials to facilitate activity and uplift capability. This should include an advocatory role for trials of relevance to Pacific peoples (gout, diabetes, etc.).
- Provision of resources that are targeted for Pacific peoples to encourage involvement in trials (e.g. translated documents, using understandable and relatable language and concepts, explaining benefits for individual, family, and community).
- More support and resources available for the small and stretched workforce, including (but not limited to) ring-fenced workforce development funding for Pacific peoples (scholarships etc.) to be able to train in clinical research and support roles, and mentorship roles plus the appropriate infrastructure to guide students through to clinical research careers.
- Making research activity visible to students by including research in training across all health fields to encourage research as a career path. Further consultation with Pacific students is necessary to discover what will help them undertake a career in research.
- Sustainable culturally-safe spaces (physical or virtual) for collaboration, discussion, and community among Pacific researchers, students, and patients.
- Inclusion of Pacific research methods and frameworks within research and training opportunities.
- Training in cultural capability for the workforce (both Pacific and non-Pacific) to be able to work effectively with Pacific researchers and communities.

5.2.3 Priorities of consumer focus group

The consumer focus group met twice and participated in the World Café, Delphi survey and consensus meeting. This group identified key requirements to establish a consumer voice in the proposed infrastructure.

- Appropriately resourced consumers should participate in an integrated manner across all dimensions of the clinical trials infrastructure (i.e. not at arm's length) both horizontally and vertically to ensure the consumer perspective is present in the right place at the right time. Consumer engagement must be required, but also convenient and readily available.
- The consumer voice must be a combination of functions at multiple levels so that it has a hand in policy and priority setting (strategic oversight), mandating and self-regulating of consumer engagement, promoting and connecting trials and researchers to consumers, training consumers and researchers for effective partnerships, and interlinking different patient groups to form a network and database.
- The Health Quality and Safety Commission (HQSC) has recently undertaken work to establish a consumer health forum that brings all consumers to one point. This should be a key partner for drawing upon the consumer voice.
- Consumer groups will need to involve people who have expertise in system-level arrangements, processes, and governance, as well as those who are experienced at the trial-level and within certain condition areas that are being investigated. The people at both levels are necessary as the experiences at the trial-level inform the actions at the system-level and the system-level influences the actions at the trial-level.

5.3 Proposed model

It is important Te Tiriti o Waitangi and Māori partnership are embedded within the ownership, accountability, and operation of any model of infrastructure. The following proposal sets out the main elements and functions that it is important for the clinical trials infrastructure to include. The specifics of the model should be developed in partnership with Māori and in accordance with Te Tiriti, in a spirit of Te Tiriti partnership.

To give effect to our recommendations, we have considered in further detail what a proposed model for trials support infrastructure should look like. Our proposal consists of two main components:

- A National Clinical Trial Infrastructure Centre with expertise from across the country, which will provide leadership, governance, expertise, and overall, higher level national support and coordination of trial activity and of clinical trials networks.
- Multiple Regional Clinical Trial Coordinating Centres around the country that between them provide the necessary expertise to support investigator-led trials. These Regional Clinical Trial Coordinating Centres will play an integral role in supporting trial development and conduct across regional nodes (i.e. regional organisations that are actually conducting the trials) to ensure equity of access for both researchers and participants. These

will collaborate with other centres to deliver national and international trials.

These two main components of the infrastructure will be responsible for a range of functions and activities. Some of the functions and activities will be distinct to one or the other component, whereas others will be shared across both. For this system to work it requires strong, consistent, resourced national leadership. The key principles for deciding the functions and activities of each of the components are defined below.

The National Clinical Trial Infrastructure Centre should manage functions and activities where there are likely:

- economies of scale from having the functions and activities managed at a central, national level;
- avoided transaction costs from having the functions and activities managed at a central, national level;
- benefits realisable from being able to implement standardised and cohesive management frameworks, and
- strong links of accountability required, particularly relating to functions and activities around governance, standards setting, system ownership, and review of best practice.

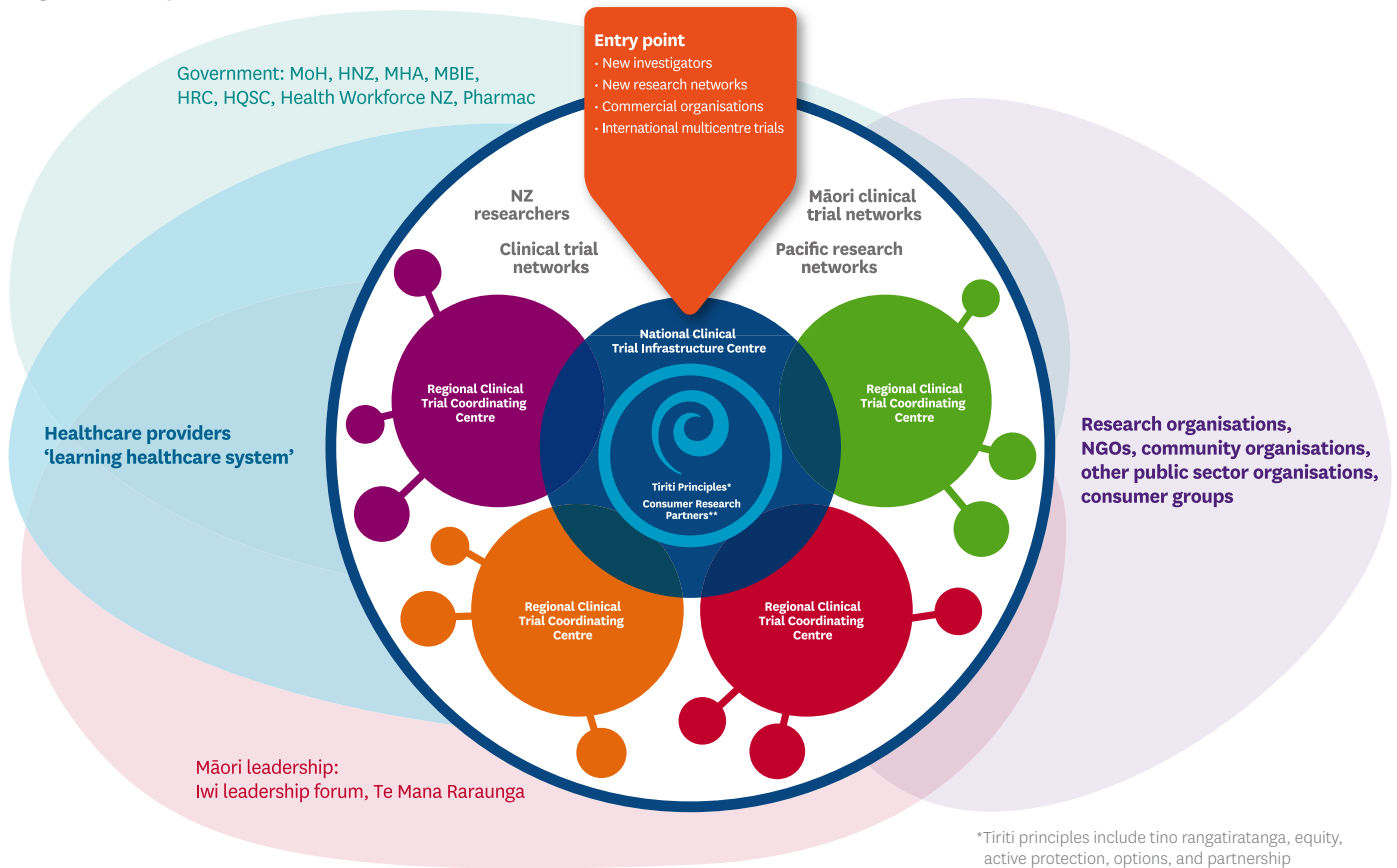
The Regional Clinical Trial Coordinating Centres should manage functions and activities where:

- the functions and activities are not able to be (or should not be) completed remotely, and/or are not automated/automatable, so local delivery is important;
- functions and activities could vary based on geography, researchers, and target population, their needs, their communities and systems, as well as infrastructure. For example, one of the Regional Clinical Trial Coordinating Centres could be focused on supporting rural research, while another might have a special expertise in trial design;
- there are benefits arising from direct local relationships with communities and researchers, and
- in-person and local links are necessary for reaching the communities the system is trying to serve, such as iwi partnerships.

The National Clinical Trial Infrastructure Centre will represent the central point of access to the Regional Clinical Trial Coordinating Centres, directing researchers towards Centres with the skills and capacity best suited to support them. Researchers and networks seeking funded access to the resources of the Regional Clinical Trial Coordinating Centres will need to go through the National Clinical Trial Infrastructure Centre. Both the National Clinical Trial Infrastructure Centre and the Regional Clinical Trial Coordinating Centres could also provide their services on a commercial basis directly to industry or other customers conducting non-public-good trials. A transparent set of criteria for researchers and networks to receive funded support versus commercially procured support from these organisations will be very important.

The following diagram (Figure 15) shows the proposed interactions and activities/functions of the various organisations.

Figure 15: Proposed model






*Tiriti principles include tino rangatiratanga, equity, active protection, options, and partnership

**Consumer Research Partners embedded throughout at multiple levels

The Legend below (Table 7) explains the components of the diagram of the proposed model.

Table 7: Legend for the diagram of the proposed model

Legend	Description of component
	<p>National Clinical Trial Infrastructure Centre (section 6.3.1)</p> <p><i>Collaboration of expertise and key stakeholders from across the country to provide leadership and national support for clinical trial activity:</i></p> <p>Governance and advice, including Māori and consumer partnerships; Administration and data systems; Signpost, information collation, connections and marketing; Education and methodology.</p>
	<p>Regional Clinical Trial Coordinating Centre(s) (section 6.3.2)</p> <p><i>Region-specific collaborations between academia, healthcare providers, Kaupapa Māori services, Iwi, Māori Partnership Boards, and other research organisations to support the development and conduct of investigator-led trials using a system of regional nodes:</i></p> <p>Partnership and engagement at the local level, including with Māori and with consumers; Prioritisation of local research need and resource use; Expertise and support.</p>
	<p>Entry point</p> <p><i>New researchers, new research networks, commercial organisations and international trials will access the infrastructure through the National Clinical Trials Organisation.</i></p>
Government	<p><i>The stakeholders in the national clinical trials infrastructure should include representation from Government departments and agencies to ensure research is embedded and resourced: the Ministry of Health; Health New Zealand; the Māori Health Authority; the Ministry of Business, Innovation and Employment; the Health Research Council; Health Quality and Safety Commission, and Health Workforce NZ.</i></p>
Healthcare providers 'learning healthcare system'	<p><i>Functional relationships between the clinical trials infrastructure and healthcare providers are essential for embedding research in healthcare, and moving towards a learning healthcare system.</i></p>
Māori leadership	<p><i>Māori leadership would be embedded within the national clinical trials infrastructure; functional relationships with national Māori organisations, including the Iwi Leadership Forum and Te Mana Raraunga, are also critical.</i></p>
Allied organisations	<p><i>The stakeholders for the national clinical trials infrastructure should include representation from research organisations (including universities), NGOs, community organisations such as consumer groups, and other relevant public sector organisations.</i></p>

5.3.1 Activities / functions managed by the National Clinical Trial Infrastructure Centre

There are some activities / functions we believe should be managed by the National Clinical Trial Infrastructure Centre based on the key principles established (Appendix G), options voted as “critical” for inclusion in the Delphi survey and consensus meeting, and general discussion between co-investigators and stakeholders. National management of some activities/functions does not necessarily imply these activities/functions should sit nationally in a physical sense.

These activities/functions reflect what we heard from Māori and Pacific stakeholders, who wanted to see explicit Māori-specific and Pacific-specific networks that allow for Māori and Pacific people and expertise to be organised and brought together in a sustainable, systematic, and culturally safe way and allow for ideas, knowledge, and resources to be shared.

Some of the activities / functions cross over between the high-level groupings, as well as between the National Clinical Trial Infrastructure Centre and the Regional Clinical Trial Coordinating Centres.

Table 8 (right) summarises the main activities / functions which should be managed by the National Clinical Trial Infrastructure Centre. The activities / functions have been grouped into four higher-level categories (governance and advice, signpost and service, people and information collation, and education and knowledge base).

There may be additional activities / functions not covered in this assessment that become more well-defined over time as the infrastructure is developed.

5.3.2 Activities / functions managed by Regional Clinical Trial Coordinating Centres

There are other functions we believe are better suited to be managed by the Regional Clinical Trial Coordinating Centres at a sub-national level. These have again been determined through the establishment of key principles (Appendix G), Delphi survey results, and discussion amongst co-investigators and stakeholders. Table 9 (following page) illustrates the activities and functions and groups them into two higher-level categories: prioritisation and support.

We envisage all Regional Clinical Trial Coordinating Centres will have a number of core capabilities. These are likely to include:

- biostatistical expertise;
- data management expertise;
- health economics expertise;
- research nurse capability;
- trial coordination capability, and
- site locality approval processes.

Other functions, such as specialised database design skills or a randomisation / unblinding service, could be performed by one of the Regional Clinical Trial Coordinating Centres on a national basis. The Regional Clinical Trial Coordinating Centres with a specific focus on Māori and on Pacific research would also have national geographic scope. Networks will be able to keep their current team structure, with expertise in specific areas, within the regional centres (possibly with team members across all regional centres to ensure equity of access to trials).

Table 8: Activities / functions to be managed by the National Clinical Trial Infrastructure Centre

High-level grouping	Activities / functions
Governance and advice	Identifying strategies for Māori health and advancement through clinical trials; Standards and advice on Māori data sovereignty; A national federated repository for long-term trial data storage; Developing national-level relationships with Iwi, Pacific, and consumers, for co-design and partnership; Advice on funding availability; Data governance, systems, curation, and sharing; Adverse event recording and reporting; Practice for handling, storage, and disposal of human specimens; Guidelines for determining which trials are supported by infrastructure; Research methods (and resources) for working with Pacific communities; Data Safety Monitoring Committee (DSMC) establishment; Trial methodology (including design of complex or innovative trials) and statistical expertise; Health economics; Locality assessment; Trial pharmacy services; Monitoring and auditing, plus systematic review of infrastructure
Signpost and service	Front door for clinicians and industry to use resource (industry access through appropriately-funded model); Administrative support; Other expert input (further than advice on) such as statistics, health economics, trial design
Network support	NZ and trans-Tasman networks (and those leading some of those networks and their aspects, funding etc.); Establishment of systematic and sustainable networks for Māori and Pacific
People and information collation	Database of people and information able to help run a trial; Publicly-accessible register of actively recruiting trials; databases of trial expertise and key stakeholders for potential collaboration; collaboration and meeting opportunities such as virtual workshops, especially for Māori, Pacific, consumers; system for identification of diverse range of consumer research partners (Māori, Pacific, rural, disabled, youth, collectives); coordinated information resource on trial activity; national clinical trials alliance that provides forum for networks to share ideas, best practice, resource (this will be a key source of support for networks); Opportunity for Māori and Pacific to participate in networks for Māori and Pacific
Education and knowledge base	Education of public about benefits of trials; supporting and empowering consumer research partners and their networks; supporting and educating researchers in engaging with consumer research partners; lay summaries of trial findings on national website; targeted dissemination of trial results to Māori, Pacific, rural, and other key stakeholders; free Good Clinical Practice (GCP) training and accreditation; development of GCP tailored for Aotearoa; modular training programme for upskilling in trial methods, including Māori and Pacific methods and for working with Māori and Pacific communities; other training programmes made available (user-pays basis); roles and career pathways for investigators to do trials, particularly for Māori and Pacific research methods and investigators.



Table 9: Activities / functions to be managed by Regional Clinical Trial Coordinating Centres

High-level grouping	Activities / functions
Prioritisation	Working with communities and researchers to identify areas of importance specific to populations being served, especially for capturing local communities' and Māori needs and wants; consideration of feasibility of research and intervention, potential health gain, ability to achieve equity, wider social gain, whether it is an under-researched population.
Support	Consumer engagement, including recognised patient groups; Māori consumer engagement and Māori health advancement; development of protocols, data management plans, and other trial documentation; statistical input into design, conduct, and analysis; ethics and regulatory approval; site locality approval; health economics input into design, conduct, and analysis in trials where it needs to be considered; finance and budgeting; database design, provision, and maintenance; innovative data capture; 24-hour randomisation service, including randomisation, unblinding, and drug delivery; access to accredited pharmacy services; access to system for managing aspects of trials, including progress and reporting; dissemination of trial findings; embedded research roles within hospitals and the community to support trial activity, including within iwi and Māori health providers.

5.3.3 Approach to implementation of proposed infrastructure

This project has focused upon infrastructure for clinical trials specifically. However, the proposed infrastructure and the activities / functions will have to sit within the wider context of health research. Aotearoa New Zealand is too small to have parallel infrastructure systems in place for clinical trials and other forms of health research where there are common needs. There are some policy issues that will have to be worked through when considering the extent to which parts of the proposed infrastructure are specific to clinical trials or for health research more broadly. As non-exhaustive examples, consumer engagement functions, guidance and support for Māori data sovereignty, and co-governance and

priority setting are likely best shared across the entire system, since they should be grounded in all health research activity.

We recognise there are some necessary commitments on behalf of the funders and owners of the system (HNZ, MHA) to ensure that the proposed infrastructure is successful and provides the desired outcomes.

- Success of the proposed infrastructure is reliant upon strong leadership and governance at the executive leadership level within Health New Zealand and the Māori Health Authority. It is necessary that there be a strong directorate for health research and clinical trials, which must have effective partnership with Māori, consumer and Pacific stakeholders, that can provide the leadership needed to develop this infrastructure and ensure that it provides maximum value.
- At a minimum, we would propose a 10-year time commitment to the new infrastructure. Implementation of the infrastructure is expected to take between two and three years, and an individual clinical trial can take between three and five years, or longer, to complete. Any commitment of less than 10 years would limit the ability to assess the value of the system, since the full benefits would not be captured. It is also important to note the ethical requirement of a commitment to complete a given programme of research once participants have been recruited.
- The approach to developing supporting organisations for the proposed infrastructure should involve a collaborative procurement process to encourage current and potential infrastructure providers to work together. This is likely to require an expression-of-interest process, followed by a transparent negotiation between the central hub and consortia of potential providers of clinical trial support services in order to develop coherent groupings of support services.
- It will also be important for the research leadership to be well embedded within the health system. We identified a widespread lack of research culture to be a key barrier to realising the potential of trial research in Aotearoa New Zealand's health system. Research leadership must therefore be in a position to influence the overall culture of our newly emerging health system structures, working in an integrated manner with those

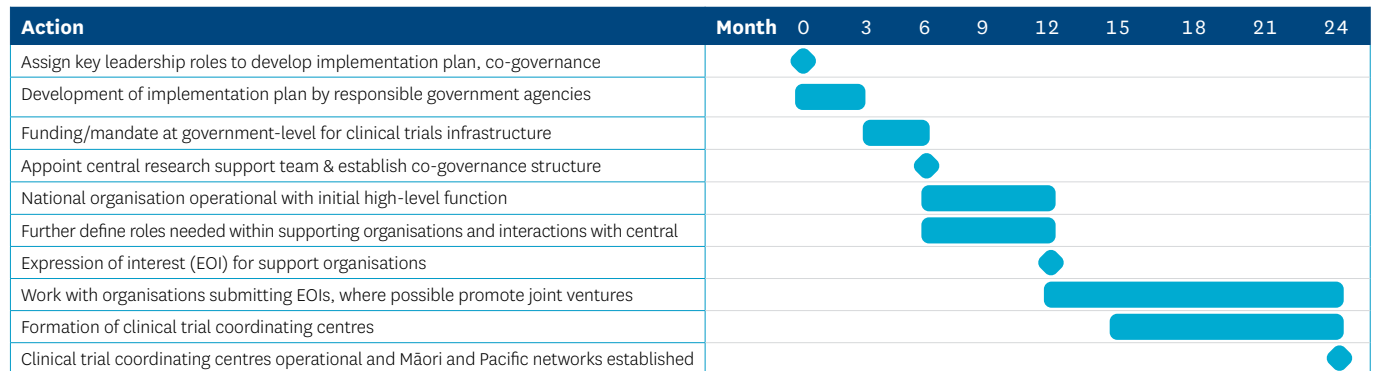
in charge of clinical governance and best practice, and those with responsibility for innovation and change management, and supporting clinical leadership to inculcate a culture of learning and research as a core element of healthcare delivery.

It is our strong view, therefore, that appropriately resourced research leadership should be embedded into our new health system structures at the highest level, and should have the opportunity to integrate research and development into everything that our health system does. We therefore have made specific recommendations.

We have not formally costed the infrastructure that we have proposed. This will require a detailed planning exercise and careful costing analysis. Informally, we anticipate that an effective implementation of the proposed infrastructure requirements is likely to require an investment of the order of \$20 million annually.

We have proposed an indicative timeline (Figure 16, below) for establishment of the infrastructure, anticipating a two-year timeframe for full implementation. This is a challenging horizon, but we believe it is achievable with sufficient ambition.

Figure 16: Indicative timeline for the establishment of infrastructure



6. Conclusion





This project charged our team with identifying an infrastructure that could improve the benefit to Aotearoa New Zealand from effective clinical trial activity. We have undertaken an extensive analysis of information from a large number of sources and have worked with a variety of stakeholders to identify our proposed infrastructure, and we believe that our proposal will significantly improve the value that Aotearoa New Zealand can derive from clinical trials.

We have worked with a Māori Rōpū and a team of Māori analysts to identify specific recommendations that will improve the benefits of trial activity for Māori, support Māori researchers, and reduce inequities. We have worked with a Pacific group to identify particular priorities that will make trials more responsive to Pacific needs and will support Pacific researchers. We have worked with consumers to consider how to integrate consumer voices effectively into a new clinical trial infrastructure, and we have consulted with international experts from Australia, Canada, and the United Kingdom. We drew upon the extensive information we collected from these sources and from reaching out to clinical trial researchers across New Zealand, and we synthesised aspects of a preferred approach. We ran a Delphi process to achieve agreement on aspects of the proposed infrastructure. Throughout this project we have been met with

enormous enthusiasm and support from stakeholders, who saw the potential to achieve improved health and equity for New Zealanders by improving and extending clinical trial research activity and who gave generously of their time.

This project has developed a set of recommendations founded in extensive discussion with a wide range of stakeholders. It will be important to build upon the enthusiasm that has been generated and to ensure that expectations are responded to in a meaningful manner.

The newly emerging structure for the New Zealand health system as a whole represents an opportunity to embed research into the heart of our health services, developing a learning health system that works to the highest level for the benefit of people in Aotearoa. With the right investment there is the potential to realise the unique contributions of Māori and Pacific culture and mātauranga to clinical research, while also further developing our existing international reputation for excellence in clinical trials. These are immensely valuable benefits and we hope that this project will make a constructive contribution to realising them for the people of Aotearoa.

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