

Scoping and analysis of
recruitment and retention in
Australian clinical trials

Final report

June 2016

Table of contents

Executive Summary	2
1. Introduction	7
1.1 Scoping and analysis of issues in recruitment and retention in Australian clinical trials	7
1.2 Objectives and project scope	7
1.3 Approach	7
1.3.1 Research	7
1.3.2 Consultation.....	9
1.4 Opportunities for further research and consultation	10
1.5 Reporting.....	10
2. Recruitment and retention in Australian clinical trials	11
2.1 Background to scoping and analysis of issues in recruitment and retention in Australian clinical trials	11
2.2 Recruitment and retention data for Australian clinical trials	12
2.3 Barriers and enablers to recruitment and retention in Australian clinical trials	14
2.3.1 Leadership and coordination	14
2.3.2 Support for clinical trials	14
2.3.3 Leading practice and performance	25
2.3.4 Awareness of clinical trials	27
2.3.5 Regulation and safety	29
3. Key findings	31
4. Recommendations	35
5. Conclusion	40
Appendix A. Glossary	41
Appendix B. Initiatives that present opportunities for the CTJWG	43
Appendix C. Enablers and barriers to clinical trial recruitment and retention (findings from participants and general public consultations)	45
Appendix D. Opportunities for improvements to recruitment and retention (findings from the participants and general public consultations)	47

Executive Summary

Background

In 2015, the Australian Government Department of Health (the Department), commissioned EY on behalf of the Clinical Trials Jurisdictional Working Group (CTJWG) to undertake systematic scoping and analysis of issues in recruitment and retention in Australian clinical trials.

A key focus for the CTJWG is to better understand issues with recruitment and retention of participants in clinical trials, understand the barriers and provide recommendations to the Australian Health Ministers' Advisory Council (AHMAC), via the Hospitals Principal Committee (HPC), on how these can be best mitigated in order to support and progress the clinical trial industry in Australia.

Throughout this engagement, EY was required to undertake a national and international scan, including a literature review, to identify current initiatives underway in Australia; undertake a review of barriers and enablers through consultation with stakeholders, participants and the general public; and provide advice on where the CTJWG could most effectively direct effort to enhance clinical trial recruitment and accruals. This report is the culmination of that program of work as required in the agreed scope of services.

Approach

EY's approach to the engagement was a multifaceted program of work, designed to ensure input from a variety of relevant sources. Running a clinical trial is a complex process, reliant on interactions between sponsors, regulatory agencies, suitably qualified investigational sites and most importantly, participants. EY sought input from each of these stakeholder groups in an effort to understand the barriers and identify potential solutions to recruitment and retention in Australian clinical trials.

In conducting research and analysis, EY provided the following work products and services:

1. Detailed project plan, outlining the key activities and deliverables.
2. Consultation plan, detailing EY's stakeholder engagement approach.
3. International and national scan of clinical trials markets and innovative approaches to recruitment and retention.
4. Literature review, to identify emerging issues and themes in relation to recruitment and retention in clinical trials.
5. Stakeholder consultation report, noting the key themes and findings from the consultations.
6. Patient and public consultation report, detailing key findings from interviews with patients who had participated, withdrawn or refused clinical trials, as well as the general public.
7. Draft and final report, providing a detailed synthesis and analysis of the findings from research, consultation and analysis as above.

Recruitment and retention in Australian clinical trials

Clinical trials form an important component of the Australian health care system. The Australian Government invests heavily into medical research¹ with a further AUD\$1b annually invested by pharmaceutical companies into research and development.²

Australia has a good track record in relation to the safety and quality of clinical trials, both commercially-sponsored and investigator-led. Successive governments at the national, state and territory levels have joined with industry and stakeholders to improve the clinical trials environment and attract clinical trials from both a public health and an economic perspective. There is a need to promote the value of clinical trials, to consumers, clinicians and Local Hospital Networks (LHNs), focused on quality health outcomes and economic value gained from clinical trials.

Limited research and data is available on clinical trial participation nationally, with the exception of oncology trials, and there is currently no central coordination point for the collection of clinical trials data, including recruitment and retention rates. In 2011, the Clinical Trials Action Group (CTAG) reported that 18,600 people were enrolled in 1,265 trials conducted in 2009. A 2014 survey conducted by Clinical Trials Connect (CTC) assessed the recruitment success for a range of clinical trials in Australia. The survey identified that 20% of trials met their recruitment deadline and the majority of respondents met their targets 50-79% of the time. Research and consultation also revealed limitations on data in relation to retention, with exact rates generally unpredictable. Additionally, Medicines Australia reported an overall decline in the number of newly initiated pharmaceutical industry-sponsored clinical trials from 885 in 2007 to 681 in 2013.

These trends in trial numbers present challenges to Australia's clinical trials sector, with deeper understanding required in relation to the barriers and enablers to recruitment and retention in clinical trials. Further, there is limited research available into the success of specific recruitment and retention measures in clinical trials, which was frequently noted as a research gap within the current literature.

Key findings and recommendations

Research and consultation identified key themes relating to issues in recruitment and retention in clinical trials including:

- Leadership and coordination;
- Networks, registries and digital health;
- Leading practice and performance;
- Awareness; and
- Regulation and safety

¹ Australian Trade Commission (Austrade) May 2015, *Clinical Trials Capability Report*, Australian Trade Commission.

² Medicines Australia 2011, *Keeping clinical trials in Australia - why action is needed now*, Occasional Paper Series 3.

The terms of engagement for this project required EY to provide its opinion regarding possible solutions to clinical trials recruitment and retention issues in Australia. Accordingly, the recommendations below reflect EY's advice on a proposed way forward, and present possible solutions and feasible opportunities to be considered by the CTJWG, in addressing barriers and enablers to clinical trial recruitment and retention in Australia.

Recommendations

Leadership and coordination

Recommendation 1: The CTJWG/AHMAC to clarify leadership roles at the national, state and territory level to provide oversight and coordination of clinical trials initiatives to maximise the realisation of benefits of participation in clinical trials for health consumers and clinicians. This should involve the enhancement of existing national clinical trials roles and/or the establishment of dedicated structures at national and individual state and territory levels to improve clinical trial coordination across Australia.

Recommendation 2: The CTJWG, on behalf of the nine jurisdictions, to recommend to the Independent Hospital Pricing Authority (IHPA) to introduce activity based funding to hospitals for public hospital clinical trial activity utilising trial completion as an output measure. This would further encourage and embed research KPIs within the hospital setting and link specific funding to research activity.

Support for clinical trials

Recommendation 3: Over the short term, the CTJWG, the Australian Government Department of Health, the NHMRC, and Australian Clinical Trials Alliance, to formalise the structure, roles and support for clinical trials research networks, ensuring that they reflect national, consumer and community priorities for research. This will include promotion and encouragement of:

- Health consumer involvement in networks, via the Consumers Health Forum (CHF) and other patient advocacy groups, in the development of national research questions and involvement in appropriate clinical research networks;
- Access to Medical Research Future Fund (MRFF) or other sources of funding for support for clinical trials networks including resources for secretariat, data management and trial coordination;
- Research networks to utilise existing and future patient registries to encourage clinical trial participation, leveraging the opportunity to improve recruitment and retention through coordinated use of clinical quality registries to identify potential participants; and
- Involvement of primary care focused networks in design and conduct of research, recognising that recruitment of participants from primary care settings will need to involve primary care research networks.

Recommendation 4: The CTJWG to provide input regarding required enhancements to the Australian New Zealand Clinical Trials Registry (ANZCTR) to improve its

relevance for participants and researchers and ensure it is regularly updated, noting the current limitations in ANZCTR's scope and functional capabilities. This could include advice on consolidation of ANZCTR and AustralianClinicalTrials.gov.au and a strategic framework on how these registries continue to work simultaneously.

Recommendation 5: Over the short term, the Australian Government Department of Health and the Australian Digital Health Agency to build the capability of the My Health Record to facilitate clinical trial recruitment and retention. Furthermore, the state and territory health departments, and governing bodies of private sector health organisations, should ensure that Electronic Medical Records implemented in the public and private hospital and health service systems to facilitate the recruitment and retention of participants in clinical trials.

Recommendation 6: Over the medium term, jurisdictions to address sensitivities of secondary use of data and work with industry and sponsors to pursue opportunities to utilise existing data linkage regimes, through a central agency/ies, to identify prospective trial participants.

Recommendation 7: The CTJWG to work with jurisdictions to progress ongoing and long-term roles for research nurses, support the inclusion of clinical research into job descriptions for clinicians, and embed the need for ongoing site training and mentorship in running clinical trials.

Recommendation 8: The CTJWG to consider opportunities to build on existing innovations and initiatives as outlined in Appendix B. Initiatives that present opportunities for the CTJWG.

Recommendation 9: The CTJWG, the NHMRC and research entities to focus on clinical trial recruitment and retention strategies in special groups such as culturally and linguistically diverse (CALD) communities, youth, Indigenous Australians, rural and remote communities, and people with a mental illness. Focused strategies to also be developed for cognitively impaired potential trial participants, supported by advice to jurisdictions on guardianship legislation as an enabler of recruitment.

Leading practice and performance

Recommendation 10: Over the short term, the CTJWG to work with the NHMRC and the Australian Government Department of Health to devise an online leading practice guide to the successful design, management, administration and conduct of clinical trials starting with the creation of a culture that embeds clinical trials within leading practice clinical care and reflecting the primary consideration of safety for clinical trial participants. This resource should be continuously reviewed and updated, and could include a set of tools for practical implementation.

Recommendation 11: The NHMRC to devise guidelines for the consistent use of financial incentives for trial participants, to appropriately recognise the time commitment, rather than solely expenses incurred, of participants in clinical trials.

Recommendation 12: The CTJWG, in consultation with clinical trial sponsors, to continue to expand on national clinical trials metrics to support continuous improvement in clinical trial recruitment efforts, and consider the merit of future annual publication at LHN and individual research entity level.

Awareness

Recommendation 13: The CTJWG to work with the NHMRC and other relevant stakeholders and advocacy groups to define the value proposition for clinical trials, and design and implement strategies to raise awareness of the role and value of clinical trials amongst the general public, health care practitioners (including primary care clinicians), Local Hospital Networks (LHNs), and the philanthropic community, including promotion of a more distinct profile for the AustralianClinicalTrials.gov.au website.

Regulation and safety

Recommendation 14: The CTJWG to;

- reaffirm the primacy of safety in clinical trials across the sector; and
- consult organisations that conduct commercially-initiated and investigator-initiated clinical trials over impediments to recruitment that are derived from Food and Drug Administration (FDA), European Medicines Agency (EMA) or other requirements and to seek resolution with the relevant foreign authority through the Therapeutic Goods Administration (TGA).

Conclusion

This report provides synthesis of findings, proposed solutions and future approaches for the CTJWG based on extensive research and consultation undertaken throughout this project.

Improving recruitment and retention will require leadership and coordination of clinical trials across jurisdictions, supported by inclusive clinical trials networks, committed research staff and adequate systems, including registries and EHRs. Further, leading practice design, conduct and management of clinical trials, including recruitment and retention, should be driven by community priorities and underpinned by transparent performance reporting.

Research and consultation has identified that there is no single strategy that will improve recruitment and retention in Australian clinical trials. Rather, recruitment and retention must be considered together with the systemic, structural and cultural factors shaping the Australian clinical trials environment at the national, jurisdictional and institutional level.

1. Introduction

1.1 Scoping and analysis of issues in recruitment and retention in Australian clinical trials

In November 2015, EY was engaged by the Australian Government Department of Health (the Department), on behalf of the Clinical Trials Jurisdictional Working Group (CTJWG), to undertake scoping and analysis of issues and solutions in recruitment and retention in Australian clinical trials. The purpose of the engagement was to identify feasible opportunities and strategies for the CTJWG to enhance clinical trial recruitment and accruals, or retention, in Australia.

Within this report, EY has outlined key findings from research and consultation, and opportunities for the CTJWG to enhance clinical trial recruitment and retention in Australia, within the scope of the *Official Work Order* and the *CTJWG Terms of Reference*.

1.2 Objectives and project scope

The objective of this engagement was for EY to identify feasible opportunities and strategies for the CTJWG to enhance clinical trial recruitment and accruals in Australia. Consideration of practical approaches for the CTJWG were to include, but not be limited to, consideration of the following topics:

- Enhancing understanding of benefits of clinical trials amongst clinicians and consumers in order to increase clinical trial recruitment and participation;
- Better use of information technology platforms and innovative approaches for improving recruitment and accruals;
- Strategies for management of slow-recruiting trials;
- The status of development and utility of My Health Record, digital health and other electronic health record systems to link to recruitment initiatives; and
- Implementation of strategies regarding new approaches for consent and privacy to promote a culture of trust and improve clinical trial recruitment and participation.

1.3 Approach

EY's scoping and analysis of issues in recruitment and retention in Australian clinical trials comprised an extensive research and consultation process, including a national and international scan, literature review, stakeholder workshops, and participant and public interviews.

1.3.1 Research

EY undertook extensive research to understand the barriers and enablers of recruitment and retention in Australian clinical trials and to gather an evidence base for recommendations to the CTJWG. The national and international scan, and literature review, identified a number of key themes that were then tested throughout stakeholder consultation.

National and international scan

EY engaged internally with global subject matter resources (SMRs), from the USA, UK, Europe and Singapore, and undertook a desktop scan of national and international initiatives focused on recruitment and retention in clinical trials. The scan identified a number of solutions to recruitment and retention in clinical trials, related to study design and patient selection, engagement with consumers and clinicians, networks and partnerships, and use of technology and social media.

Literature review

EY undertook a broad search of current and relevant literature on recruitment and retention in clinical trials, including barriers to participation and strategies to increase participation. The literature search included Australian and international peer-reviewed literature, government reports, web based information and information provided by EY's global SMRs.

The literature demonstrates a number of issues for trial participation at the individual level including perceived inconvenience, concern over receiving a placebo or not receiving the best treatment, and the lack of awareness of clinical trials within the community. The review found that relationships between participants and health care professionals, including general practitioners (GPs), was a key factor in clinical trial participation.

A number of barriers to recruitment and retention were identified in relation to the design and conduct of clinical trials, including a lack of trial-dedicated site staff, and the inability to predict and identify suitable participants through effective measures such as registries or electronic health records (EHRs). The literature found that poor communication by the recruiting clinician, and a lack of awareness or willingness to refer participants to clinical trials, also impacted the success of recruitment to and retention in clinical trials.

The literature review found that there was no one strategy for successful recruitment and retention, rather numerous activities and solutions were identified that focused on the barriers that impact an individual's willingness to participate, and barriers that restrict the site's ability to recruit and retain participants effectively, including:

- Employing dedicated research staff at the sites able to focus on trials and recruitment;
- Improving training for researchers in communication and consent processes and building trust with participants;
- Raising awareness of clinical research with health care professionals and patients prior to trials commencing, emphasising that research is the norm rather than the exception, and promoting the benefits to consumers and clinical trial participants;
- Engaging early with consumer advocates to help design trials and reduce potential barriers for participants;
- Using networks to link researchers with each other and participants;
- Using registries to identify potential participants with particular diseases;

- Supporting researchers in better trial design to limit unnecessary impacts on participants' time and convenience;
- Planning early for the trial including assisting sites in understanding their true potential population, development of recruitment plans and contingency plans;
- Continually improving the consent form and information giving process to meet the needs of participants - consider approaches such as Question Prompt Lists (QPLs);
- Increasing use of social media platforms for recruitment and retention; and
- Increasing use of digital infrastructure to allow staff to focus on recruitment and retention of participants.

1.3.2 Consultation

Stakeholder consultation

Over 150 stakeholders were consulted in workshops and consultations including government, investigators, ethics committees, contract research organisations (CROs), clinicians, consumer groups and pharmaceutical companies, to provide insight to the clinical trials environment, issues in recruitment and retention in Australian clinical trials and potential solutions and innovative approaches for consideration by the CTJWG.

Workshops were held across four jurisdictions: WA, Vic, NSW, and QLD, with an additional teleconference held with delegates in SA. Stakeholders were identified by EY, the Department and representatives from the CTJWG. Invited stakeholders unable to attend a scheduled workshop were provided with the opportunity contribute via teleconference. EY undertook additional consultation with identified stakeholders following the workshops.

Workshops were delivered as structured conversations based on the initial findings from the literature and international scan. Attendees were encouraged to provide their insights into the key success factors in trials, the barriers they face and examples of leading practice that they were aware of or had participated in.

Patient and public consultation

Consultations with participants and the general public were conducted by EY Sweeney to understand the drivers and barriers of participation in clinical trials through an exploration of perceptions of, and experiences with, clinical trials.

EY Sweeney used a qualitative research approach to the collection of primary data for this research. Although the original target was to complete 30 interviews, a total of 33 in-depth interviews were conducted with the following two audiences:

- Patients, or clinical trial participants, defined as people who are currently or have completed a trial within the last 12 months (including those who have withdrawn from participating) and those who declined to take part in a trial (n=16); and
- Members of the public, or community members, defined as people who have not previously participated in a clinical trial (n=17). Two additional

community members were recruited to replace two interviewees who had participated in a clinical trial.

Ethics approval was required to interview clinical trial participants, and an application to the Alfred Hospital Research Ethics Committee was approved, with the generous support of research staff from the Alfred Hospital's Medical Oncology Unit. EY wishes to acknowledge the significant contributions of Dr Andrew Haydon and Ms Nikki Cross from the Alfred Hospital in recruitment of subjects for interview.

1.4 Opportunities for further research and consultation

A number of key opportunities were identified from the literature for additional research to further understand issues in recruitment and retention in Australian clinical trials. Specific participation and retention rates remain unclear for the majority of trials, notwithstanding data found specific to oncology trials. Confirming this data is not only important as a benchmark, it will assist stakeholders, including government and sponsor companies, identify how initiatives are progressing. Literature also indicates that few research projects focused on testing specific measures to recruitment and retention. This was frequently noted as a research gap within the current literature.

EY notes that further consultation could be undertaken to consider the role of the Medical Technologies and Pharmaceuticals Growth Centre, the Department of Industry, Innovation and Science (DIIS) and Therapeutic Innovations Australia, to engage with the CTJWG to implement the proposed solutions and align future approaches for recruitment and retention outlined in this report.

1.5 Reporting

Following research and consultation, the following reports were provided to the Department:

- Literature review;
- National and international scan;
- Stakeholder consultation report; and
- Patient and public consultation report, including a number of case studies highlighting the issues and experiences recalled by participants and community members.

These reports form the evidence base from which the key findings and opportunities for the CTJWG have been identified and tested within this final report.

2. Recruitment and retention in Australian clinical trials

Research and consultation highlighted that recruitment and retention could not be considered in isolation of the systemic, structural and cultural factors shaping the Australian clinical trials environment at the national, jurisdictional and institutional level. This section provides background to the clinical trials environment in Australia, and outlines the barriers and enablers to recruitment and retention in clinical trials.

2.1 Background to scoping and analysis of issues in recruitment and retention in Australian clinical trials

Australian governments and health institutions have been actively improving the environment and infrastructure required for conducting high quality clinical trials. The Australian Government invests heavily into medical research³ with a further AUD\$1b annually invested by pharmaceutical companies into research and development.⁴ Australia is widely considered to have world-class medical research and health care infrastructure.⁵

Australia has a good track record in relation to the safety and quality of clinical trials, both commercially-sponsored and investigator-led. Successive governments at the national, state and territory level have joined with industry and stakeholders to improve the clinical trials environment and attract clinical trials from both a public health and economic perspective. This includes National Mutual Acceptance (NMA), a national system for mutual acceptance of scientific and ethical review for multi-centre trials conducted in public health services.

In 2009, the Clinical Trials Advisory Group (CTAG) was formed to identify and progress necessary reforms to secure Australia's competitiveness in the clinical trials sector. The 2011 CTAG report, *Clinically Competitive: Boosting the Business of Clinical Trials in Australia*, made 11 recommendations to reform clinical trials, which were endorsed by the Australian Government. Notable progress was made on these recommendations, with the McKeon Review building on this work.

Significant investments have been made in clinical trial reform. To further recommendations from the CTAG report, AUD\$9.9m was invested over five years (2012-2017) through the *Expediting Clinical Trial Reform in Australia* initiative which aims to reduce the complexity and cost of running clinical trials in Australia and support investment in the pharmaceutical industry. Activities under this measure included developing a comprehensive and searchable clinical trials

³ Australian Trade Commission (Austrade) May 2015, *Clinical Trials Capability Report*, Australian Trade Commission.

⁴ Medicines Australia 2011, *Keeping clinical trials in Australia - why action is needed now*, Occasional Paper Series 3.

⁵ Medicines Australia 2011, *Keeping clinical trials in Australia - why action is needed now*, Occasional Paper Series 3.

interactive portal (AustralianClinicalTrials.gov.au), providing education and training to improve clinical trial conduct and timeliness, costing a list of standard clinical trial items and facilitating development of a nationally consistent approach to clinical trials via the NHMRC. Activities also included incorporating clinical research needs into the eHealth system however this was subsequently ceased and the activity did not progress. A further \$1.9m was then provided to the NHMRC over five years through the *Simplified and Consistent Health & Medical Research Budget Measure* to develop a nationally consistent approach to the ethical review of clinical trials.

The Clinical Trials Advisory Committee (CTAC) was established in 2014 to oversee and provide advice on implementation of Australian Government initiatives. CTAC is co-chaired by DIIS and the Department. Membership includes senior representatives from Australian Government and state and territory governments, industry, consumer organisations, and the clinical trial research community.

In recognition of the important role of jurisdictions and hospitals in progressing and implementing change, the time-limited CTJWG was established under the auspices of the Hospitals Principal Committee (HPC) in 2014. The purpose of the CTJWG is to identify and implement actions that will enable a consistent national approach to multi-jurisdictional clinical trials within Australia, with the intention of enhancing Australia's ability to attract national and international clinical trials. This work is being conducted in consultation with the NHMRC and CTAC to ensure effective coordination of activity and to minimise potential duplication.

The *CTJWG Implementation Plan* includes the following priority areas:

- Improving efficiency of recruitment and accruals (retention);
- Enhancing national consistency for ethics and governance ;
- Establishing a metrics system and promoting ICT interoperability; and
- Developing a strategy to position Australia as a preferred location to conduct clinical trials.

To improve efficiency of recruitment and retention, the CTJWG seeks to enhance its understanding of barriers and enablers to recruitment and retention in Australian clinical trials to explore innovative approaches and solutions.

2.2 Recruitment and retention data for Australian clinical trials

Limited research and data is available on clinical trial participation nationally, with the exception of oncology trials. Further, there is currently no central coordination point for the collection of clinical trials data, including recruitment and retention rates.

The ANZCTR statistics to the end of April 2016 report that there are 12,018 currently registered trials, with 8,506 of those listed as currently recruiting from Australia, although registering trials to ANZCTR is not currently mandatory with researchers and sponsors registering trials internationally. In 2015, Austrade reported that approximately 3,700 (1,000 new per year) clinical trials are conducted annually in Australia.

While widespread online research was unable to identify a reliable number for clinical trial participation in Australia, CTAG reported in 2011 that 18,600 people enrolled in 1,265 trials conducted in 2009, referencing an industry-sponsored benchmark survey by the Pharmaceutical Industry Council (PIC). The report referenced the PIC finding that 90% of industry-sponsored trials failed to meet recruitment targets and that Australia is less competitive at recruiting for Phase III studies which typically account for a larger volume of studies and participants.

A 2014 survey conducted by Clinical Trials Connect (CTC) assessed the recruitment success for a range of clinical trials in Australia. The survey identified that 20% of trials met their recruitment deadline and the majority of respondents met their targets 50-79% of the time. Consultation with Medicines Australia indicated that more than 50% of sites did not meet their recruitment requirements, pointing to fragmentation of the sector and the need for better coordination of effort at the national, state and territory level.

With respect to the number of ongoing trials in Australia, Medicines Australia reported an overall decline in the number of newly initiated industry-sponsored clinical trials from 885 in 2007 to 681 in 2013. Despite a noticeable increase in Phase I trials, from 100 to 200 between 2009 and 2013, and a steady state for Phase II trials, there was a noticeable decline in Phase III trials (that typically aim to recruit larger numbers of participants) from 250 to 200 in the same timeframe.^{6,7} While this increase in Phase I studies is encouraging, research suggests they are typically smaller oncology trials recruiting only a few participants very slowly, or trials involving healthy volunteers evaluating safety and dosage parameters.

Research and consultation also revealed limitations on retention data, with exact rates generally unpredictable. While conservative trial designers may factor in an attrition rate of 30%, rates are noted to appear higher in longer term trials.⁸

These trends in trial numbers present challenges to Australia's clinical trials sector and require deeper understanding of the barriers and enablers to clinical trial recruitment and retention.

⁶ Medicines Australia 2011, *Keeping clinical trials in Australia - why action is needed now*, Occasional Paper Series 3.

⁷ Australian Trade Commission (Austrade) May 2015, *Clinical Trials Capability Report*, Australian Trade Commission.

⁸ Evangelista E 2013, *Patient recruitment: the most recognised silent driver of clinical development costs*, International Pharmaceutical Industry. 5(1): 64-66.

2.3 Barriers and enablers to recruitment and retention in Australian clinical trials

This section presents a discussion of findings consolidated from activities, analysis and information undertaken or considered as part of the project.

2.3.1 Leadership and coordination

Leadership and coordination are key enablers of recruitment and retention in Australian clinical trials. Stakeholders identified a lack of initiatives and streamlined infrastructure as key barriers to recruitment and retention in Australian clinical trials. This indicates that in order for trials to be successful, appropriate coordination of priorities for investment and coordination of efforts at the national, jurisdictional and site level is required. This includes working with TGA on the safety of participants in clinical trials and IHPA to determine activity based funding for trials that could potentially be based on clinical trial completion or participant recruitment.

The COAG Health Council (COAG-HC) Communique (8 April 2016) called for improvements to the clinical trial environment and tasked AHMAC to develop options for models of best practice for national coordination of sites to overcome fragmentation and inefficiencies, better engage sponsors and improve trial start up times and outcomes.⁹

2.3.2 Support for clinical trials

a. Infrastructure

Stakeholders identified a lack of streamlined infrastructure as a key barrier to recruitment and retention in Australian clinical trials. Workshop participants identified that in order for clinical trials to be successful, appropriate investment in infrastructure, and coordination of efforts, at the national, jurisdictional and site level is required.

For the purposes of this report, infrastructure encompasses clinical trials networks, registries, clinical trials units and EHRs, as well as clinical trials staff including research coordinators. Streamlined tools and resources for protocol design, information and consent, and feasibility assessments were also considered as part of this infrastructure.

Clinical trials networks

Clinical trials networks form a significant component of clinical trials infrastructure, bringing together clinicians and research professionals to design and conduct clinical trials. In Australia, these networks are voluntarily aggregated by like-minded researchers within a specific disease group, though may also be organised by

⁹ COAG Health Council 8 April 2016, Communique, 'Advancing the Clinical Trials Environment in Australia', accessed 3 June 2016, <http://www.coaghealthcouncil.gov.au/Announcements/ArtMID/527/ArticleID/92/CHC-Communique-8-April-2016>.

geography. Networks undertake a number of functions relating to clinical trials. In a survey conducted by the Australian Clinical Trials Alliance (ACTA), the common core functions undertaken by networks were 'supporting the collaborative development of research proposals and process of internal peer review of study proposals and protocols to ensure scientific merit and rigour.'¹⁰ Other functions undertaken by networks include identification of potential trial participants, fundraising, data management and project management for clinical trials. ACTA provides support to clinical trials networks, as well as trial coordinating support centres and clinical quality registries, and advocates for sustained infrastructure and investment for networks to support the design and conduct of trials.

There is a significant role for networks in the recruitment and retention of participants to clinical trials, for both investigator-led and commercially-sponsored trials. Research and consultation confirmed that the role of networks needs to be more clearly defined and communicated to investigators, sponsors and clinicians. The literature on clinical trials networks, and international examples from the UK, suggest that networks are most successful when they include consumer representatives, GPs and private health services as necessary, and leverage existing infrastructure such as clinical quality registries and EHRs, to design research questions, connect investigators with potential participants for recruitment and conduct trials focused on quality health outcomes. Research and consultation demonstrated a high need to establish networks to align research with national priorities. Currently in Australia research is generated largely through sponsor-initiated action, rather than designed to focus on consumer and community priorities.

Research and consultation identified a high need for networks to engage with primary care clinicians including GPs and primary care researchers. This represents a missed opportunity to encourage patients in primary care to participate in trials. Additionally, site staff reported that finding participants who fit complex eligibility criteria is a major barrier to recruitment. Issues with protocol criteria, and the design of research questions, could be overcome through coordination of clinical trials networks and other infrastructure, including clinical quality registries and EHRs. In relation to investigator-led trials, networks can assist the researcher to design the trial based on population needs and an understanding of successful measures for the conduct of trials, that is, leveraging lessons learned.

Research and consultation highlighted that while networks are functioning well in some areas, for example ICU, haematology, cancer and paediatrics, there are disciplines where networks are fragmented and geographical presence is variable. There is a high need to formalise the approach to networks, clearly define their role and what they are expected to achieve with consideration for geographical coverage. In particular, areas of research that would benefit from networks where there are none operating currently, need to be identified. There are a number of

¹⁰ Australian Clinical Trials Alliance (ACTA) November 2015, *Report on the Activities and Achievements of Clinical Trials Networks in Australia 2004-2014*, National Health and Medical Research Council.

opportunities for networks across disease-specific groups to interact and engage with one another with the view to improving quality of care and clinical trial participation. For example, paediatric research networks working with others, such as cancer research networks. Stakeholder consultations also raised the issue of the visibility of clinical trials networks, and noted that networks should have the capability to disseminate leading practice information quickly and build a community of practice that extended further than the network itself.

Clinical trial networks require improved digital infrastructure and data storage to have significant gains for identification of participants and recruitment to clinical trials.¹¹ Infrastructure to manage and maintain databases to the appropriate standard is required to enable large scale data sharing and employing effective recruitment methods and technology (e.g. EHRs, registries, referral programs), highlighting the interdependent nature of each of these factors in recruitment and retention of trial participants.

In the UK, 15 Local Clinical Research Networks (LCRNs), supported by the National Institute for Health Research (NIHR), support clinical research and ensure the successful establishment and delivery of research projects, access to a local network of skilled research support staff and service departments, and dedicated research time for clinicians. These networks also take on responsibility for recruiting patients and involving consumers at a national level in the design, conduct and management of clinical trials. LCRNs have more than doubled the number of recruiting studies from 1,681 in 2008-2009 to 4,107 in 2013-2014. The UK has leveraged data on health, lifestyle and health habits (collected since the 1940s) towards enabling a needs-led approach to clinical trials that is embedded within the health system and has supported an infrastructure network. While consideration must be given to the differences in health systems between Australia and the UK, this model seeks to demonstrate the impact of embedding research into health care, supporting clinical trials through a dedicated structure, and setting expectations clearly when it comes to defining a clinician's role in clinical research.¹²

Research and consultation identified a number of leading practice examples of networks in Australia and overseas:

- Australian and New Zealand Intensive Care Society, noted as a good practice example by stakeholders due to its focus on infrastructure, leadership and coordination;
- Critical Care Trials Network, characterised by strong, consistent communication, leadership, strategy and coordination, working together to develop questions, coordinate studies and distribute workload across sites;
- Trans-Tasman Radiation Oncology Group, funded by competitive grants and provided infrastructure for networks; and

¹¹ Australian Clinical Trials Alliance (ACTA) November 2015, *Report on the Activities and Achievements of Clinical Trials Networks in Australia 2004-2014*, National Health and Medical Research Council.

¹² Walley, T 2015, *Integrating research into the health care system - why and how. The NIHR model in practice*, ACTA 2015 International Clinical Trials Symposium, Sydney, 7 - 10 October.

- European Clinical Research Infrastructure Network supports the conduct of multinational clinical trials in Europe, connects networks, develops and implements policy and advances integration of European clinical research within the health system.

Research and consultation also identified a high need to engage with primary care clinicians including GPs and primary care researchers, through primary care research networks. Stakeholders indicated that this represented a missed opportunity to include patients in primary care in trials.

Clinical trial registries¹³

Infrastructure limitations¹³ have created a significant gap in data relating to conduct of trials in Australia.¹⁴ Stakeholders noted the difference between clinical quality registries, which monitor the quality of healthcare to benchmark outcomes and inform improvements to clinical care¹⁵, and clinical trial registries, i.e. lists of clinical trials being conducted or registers of interest in clinical trials from patients or other interested individuals¹⁶. There is strong support for the use of web-based, searchable clinical trial registries of recognised clinical trials sites that provide information on site facilities, track record, collaboration, outcomes and real time metrics. Use of these registries enhance the possibility of a future recognition scheme to increase willingness for site participation in clinical trials and increasing the network of available sites.¹⁷ This may assist to embed clinical trials within the health system leveraged through trials networks to allow the design of, and investment in, high priority research.

The literature review found that in Australia the trial registries have provided a clear picture of the clinical trials landscape relative to the burden of specific diseases,¹⁸ helping to inform recruitment initiatives and understand which specific diseases are under-represented in research. Stakeholder consultations suggested that while clinical trials registries were an enabler of participant and site recruitment, and provided potential opportunity to move away from reliance on time-intensive recruitment initiatives, there were clear limitations in relation to keeping registries up to date and accurate, and promoting registries to patients and the general public. Anecdotal evidence from stakeholder consultations indicated that registries, including the ANZCTR, were mostly out of date and not relied on to provide accurate

¹³ NHMRC (n.d), *Clinical Trials Registries*, accessed 21 April 2016, <https://www.australianclinicaltrials.gov.au/clinical-trial-registries>.

¹⁴ Australian Clinical Trials Alliance (ACTA) November 2015, *Report on the Activities and Achievements of Clinical Trials Networks in Australia 2004-2014*, National Health and Medical Research Council.

¹⁵ Australian Commission on Safety and Quality in Health Care 2014, *Framework for Australian clinical quality registries*, ACSQHC, accessed 30 June 2016, <http://www.safetyandquality.gov.au/wp-content/uploads/2014/09/Framework-for-Australian-Clinical-Quality-Registries.pdf>

¹⁶ Australian Clinical Trials, accessed 30 June 2016, <https://www.australianclinicaltrials.gov.au/clinical-trials-registries>

¹⁷ NHMRC 2015, *Development of the Clinical Trials Ready Initiative*, accessed 12 April 2016, <https://www.nhmrc.gov.au/research/clinical-trials/nhmrc-clinical-trials-initiatives/development-clinical-trials-ready-initiat>.

¹⁸ Dear RF, Barratt AL, McGeechan K, Askie L, Simes J, Tattersall MHN 2011, *Landscape of cancer clinical trials in Australia: using trial registries to guide future research*, *Medical Journal of Australia*. 194(8): 387-391.

information in relation to clinical trials, or national priorities for trials. Consultations with clinical trials participants and the general public did not identify registries as an information source when considering participating in a trial.

Dedicated clinical trial units and staff

Research and consultation demonstrated that a lack of dedicated resources at the site level, particularly in relation to the conduct of trials, was a barrier for recruitment and retention to clinical trials in Australia and elsewhere. Workshop participants also noted the lack of dedicated clinical trials units, including a lack of dedicated space to conduct trials, and issues relating to the short-term contract-based nature of the clinical trials workforce, were a barrier.

Stakeholders agreed that the role of research coordinators and nursing staff in clinical trials is an enabler of recruitment and retention, though these positions are not adequately resourced and are often not visible on site. In workshop consultations, EY heard one example of a research coordinator employed on three month rolling contracts over 26 years. Trial staff experience a high rate of attrition and a lack of training and professional development opportunities.

Research highlighted the need for dedicated research staff at the site level to focus on clinical trials and, importantly, recruitment and retention for successful completion of trials. Consultation indicated that clinical trials are complex in nature and that many sites underestimate the level of skill and experience required to run a trial effectively. The impact of losing this capability within a site or health service is detrimental to the ability of research staff to conduct clinical trials, and to recruit and retain participants. A lack of continuity and consistency at the site level can potentially impact participant safety and the quality conduct of research as a direct impact of inexperienced research teams. In the workshops, research directors from two separate hospitals noted that they were uncertain of the number of research coordinators currently operating on their sites. Sites with experienced, well trained and dedicated staff were seen to be more successful in the conduct of clinical trials, including recruitment and retention of trial participants. Limitations in resourcing of staff may be restricting the overall output of trials and time for staff to interact with participants.¹⁹ Research noted that dedicated trial recruitment staff are more successful at achieving recruitment targets than those only involved in trials sporadically. Participant and public consultations also revealed that people were most willing to take part in a trial when they felt that the medical and nursing team were accessible should they have any questions or encounter any problems. The relationships that participants developed with these staff also aided retention in trials.

Higher participation rates in oncology trials in the UK were attributed to the national Cancer Research Network (CRN) which made significant investment in strategies designed to successfully boost participation rates, including providing additional

¹⁹ Australian Clinical Trials Alliance (ACTA) November 2015, *Report on the Activities and Achievements of Clinical Trials Networks in Australia 2004-2014*, Australian Government -National Health and Medical Research Council.

funding to recruit and retain specialised staff (such as research nurses and data managers) to support the screening, consent and enrolment processes, and data management requirements for supervisors. The dedicated staff were able to streamline recruitment by taking the time to explain trial details to participants, manage the informed consent process, and collect follow-up data.²⁰ The CRN reached a record of 600,000 (14%) participants recruited in 2013-2014. This surpassed the original goal of 7% of oncology patients enrolled after implementation of these measures.²¹

In Australia, the Sunshine Coast Hospital and Health Service has successfully improved visibility of clinical trials and research across the Local Hospital Network (LHN) by establishing a dedicated clinical research unit, embedding clinical trials within the service and promoting communication and collaboration between clinicians and investigators, including research coordinators, with positive impacts on recruitment and retention in clinical trials. The unit provides dedicated clinical space and has been effective in building a culture of trials within the hospital. The unit also shares staffing with the LHN to provide a dedicated trials workforce, that is the hospital employs a certain number of full time staff as well as managing a smaller number of contract staff. Staff are shared between trials and nurses are able to move across clinical areas whereas historically nurses could only run a trial in one clinical area. With workforce shared across the LHN, the unit is able to focus on the set-up, conduct and management of clinical trials, dedicating time to recruitment and retention.

Electronic health records

The capability and interoperability of EHRs varies across, and within, jurisdictions. In 2015, the Australian Government announced \$485m for further development and implementation of the My Health Record (MHR), including establishment of the Australian Digital Health Agency to strengthen digital health governance arrangements. While the status of development and utility of MHR will be impacted by the level of uptake by clinicians and consumers, the focus on digital health and the implementation of EHRs at the site and jurisdictional level presents the opportunity to enable recruitment through utilisation of EHRs to prioritise, and identify participants for, clinical trials within the health system.

Workshop participants agreed that EHRs have significant capacity to impact Australia's global competitiveness to undertake clinical trials by providing a data set that could assist to define research priorities and determine potential populations for targeted recruitment to clinical trials. The capacity of EHRs to share de-identified data with clinical trial registries, support feasibility assessments and impact positively on recruitment and retention, in relation to improvements in the efficiency of the recruitment process, was agreed. Stakeholders noted that the UK already successfully uses primary care and hospital data for this purpose. Further,

²⁰ Sinha G 2007, *United Kingdom becomes the cancer clinical trials recruitment capital of the world*, Journal of the National Cancer Institute. 99(6): 420-422.

²¹ NIHR 2016, *NIHR Clinical Research Network*, accessed 12 April 2016, <https://www.crn.nihr.ac.uk/>.

workshop participants identified a high need for jurisdictional cooperation and improved initiatives for record linkage to support industry and sponsors to identify potential research participants.

Research identified that connecting electronic medical records (EMRs), including clinical trials management systems or additional modules, with EHRs would allow for the sharing of information across jurisdictions and could improve the quality of data held on clinical registries. The literature noted the importance of EHRs to assist in accurately identifying potential participants and enabling recruitment. Enhancing the capability and interoperability of EMRs and EHRs would ensure appropriate distribution of resources and the opportunity for efficiency gains based on the prioritisation of clinical trials and potential for improved timeframes for recruitment.

In Brisbane, the Princess Alexandra Hospital uses an updated EMR with the capacity to identify potential and current clinical trial participants, as well as identify recruiting trials. Workshop participants agreed that this would be an enabler of recruitment to clinical trials, and provide the data required for feasibility assessments and performance reporting.

Investment presents a key barrier to the streamlined implementation of EHRs with capability to support the set-up, conduct and management of clinical trials, including recruitment. There is potential for industry and sponsors to redirect investment for clinical trial recruitment to funding additional clinical trials modules to EHRs at the site or jurisdictional level both as a measure to enable recruitment, and drive research and development priorities.

b. Strategies and initiatives

A number of existing strategies and initiatives that enable recruitment and retention to Australian clinical trials were identified throughout research and consultation, as presented in the national and international scan and consultation reports. Key success factors for innovations and initiatives included:

- Study design and patient selection;
- Engagement approaches with participants, community members and site staff;
- Networks and partnerships; and
- Technology and social media.

Research and consultation further identified a high need for coordination of initiatives and innovations nationally and across jurisdictions.

Mobile applications

A number of mobile applications enable recruitment by connecting clinicians and potential participants to open, or upcoming, trials. ClinTrial Refer, an application developed by the Haematology Clinical Research Network NSW/ACT, facilitates clinician and patient access to current information on local clinical trials to improve

trial participation by increasing referrals.²² Since its inception in 2013, there has been a significant and sustained increase in cross referrals for clinical trials, and a statewide increase of greater than 50% in recruitment from 300 to 460 from 2012 to 2014 and a 20% increase in unit staffing from 2013 to 2014.²³ The application has been revised for other networks and maintains a basic structure of listing currently recruiting trials. Updates for additional networks include providing niche options to specific potential population groups including adolescent-young adult networks. Users have reported that the application is easy to navigate and update. It has directly contributed to an increase in trial recruitment across sites.

Online patient recruitment

CTC is an online patient recruitment service where researchers can advertise their trials to clinicians and consumers. While other information pathways exist for clinicians and consumers to connect to trials, including ANZCTR and AustralianClinicalTrials.gov.au, CTC provides pre-screening features, and is targeted at consumer awareness. CTC assists researchers and sponsors by providing surge capacity for recruitment activities and seeks to provide an information and referral pathway for clinicians as a trusted source, or hub, to improve participant/clinician engagement and enable recruitment.²⁴

Consumer-led initiatives

Consumer involvement in trial design and conduct is a key enabler to recruitment and retention in clinical trials. The Miracle Babies Foundation supports premature and sick newborns, their families and hospitals. The Foundation works with investigators and research sponsors to design research questions and build awareness about better ways to approach families regarding trials and build relationships.

EY global SMRs reported significant growth in targeting potential participants through awareness campaigns with patient support groups. Sponsors have reported more return on investment in patient communities than in *ad hoc*, study specific, short-term recruitment campaigns. Early engagement with patient communities can help build stronger long-term relationships with potential participants, while input from the community can improve overall study design by providing insights into the questions that are important to that population.

Social media

Research and consultation identified that social media was an enabler to the recruitment of trial participants as well as the promotion of the value proposition and awareness of clinical trials. Despite differing levels of awareness of clinical trials revealed in consultations with participants and general public, EY Sweeney found that a wide range of sources contributed to people's knowledge of trials, including

²² Ristuccia R 2012, *ClinTrial Refer - a mobile application to connect patients with local clinical trials*, Cancer Institute, accessed 25 May 2016, <http://www.cancerinstitute.org.au/abstracts-2013/clintrial-refer>.

²³ Ristuccia R, Badoux X C, Gibson, M, Huseincehajic A, & Trotman J 2015, *Increasing Cross-Referral and Recruitment to Clinical Trials: A New Approach*, *Blood*. 126(23): 636.

²⁴ Clinical Trials Connect, accessed 20 April 2016, <https://www.ctc.asn.au/>.

advertisements on social media. A study of Facebook in 2015 concluded that social networks have potential when it comes to recruiting participants for clinical trials. One study ran a Facebook advertisement for five months and invited females aged 16-25 from Victoria to participate in a health study. The advertisement was accessed by 551 women who were then taken to the study's website; 462 subsequently agreed to complete a health-related survey, with 278 then completing the survey.²⁵

According to a 2014 study by the Center for the Study of Drug Development, Tufts University, 11% of studies globally were using social media for patient recruitment. The study acknowledged that social and digital media are gaining ground as important enablers of recruitment and retention through effective engagement of potential participant communities. Of those currently used, Facebook was the main channel, followed by patient community websites, YouTube and mobile applications.²⁶

Stakeholders reported that social media is used to promote breast cancer clinical trials, though wording is generic and always supported by a communications policy encouraging patients to seek advice from their treating physician. These trials communicate progress and results of the clinical trials, and promote recruitment to trials on YouTube. Stakeholders indicated that this was successful in setting expectations for potential participants, promoting clinical trials and supporting collaboration between consumers, investigators and clinicians. While no specific data has been collected in relation to the use of social media, there was positive anecdotal evidence that coordinators are using it successfully as an information resource though questions remain around who resources and who regulates this approach.

Stakeholders agreed that social media is a cost-effective solution to leveraging networks of social media followers, sustaining a long-term awareness campaign and enabling recruitment and retention. There were however a number of ethical, protocol, and demographic considerations that may limit its use. Social media could also present a number of risks to the trials themselves, as participants may take to social media for information on whether they are on a placebo or active arm of a trial, and they may post negative comments about the research.

Teletrials

Teletrials in Australia are also anticipated to extend research to regional and remote areas and overcome logistical issues that might otherwise impact recruitment and retention. From a Good Clinical Practice (GCP) perspective, further consideration will need to be given to the governance and regulation requirements of this

²⁵ Tyler D 2013, *Digital recruitment for clinical trials*, PMLiVE, accessed 18 April 2016, http://www.pmlive.com/blogs/digital_intelligence/archive/2013/december/digital_recruitment_for_clinical_trials_527335.

²⁶ Tufts Center for the Study of Drug Development 2014, 'Industry usage of social and digital media communities in clinical research', A Tufts Center for the Study of Drug Development White Paper, accessed 12 December 2015, http://csdd.tufts.edu/files/uploads/TCSDD_Social_Media_Final.pdf.

approach. The Clinical Oncology Society of Australia and the Cancer Institute NSW are collaborating on the development of an Australia/New Zealand teletrial model to enable the conduct of clinical trials in regional and rural areas. The model allows clinicians from larger centres, or primary sites, to enrol, consent and treat patients on clinical trials at regional and rural centres (satellite sites) using teleoncology in collaboration with clinicians from satellite centres.²⁷

Global initiatives - UK

The Salford Lung Study (UK), a collaboration between GSK, the National Health Service and the University of Manchester, is a new approach to assist doctors who prescribe medicines to understand how they work with a number of individual conditions or characteristics. This study had minimal exclusion criteria and was targeted at a broad demographic. This approach to protocol design, through partnerships and collaboration between industry, government and research entities, relied on long-term investment by GSK including supporting local infrastructure and training.²⁸

c. Strategies for specific population groups

Culturally and Linguistically Diverse (CALD) groups

A lack of access to language services for people from a CALD background is a key barrier to recruitment, both in the design of trials and exclusion criteria, and the way information about clinical trials is presented and disseminated. Research and consultation identified the general exclusion of CALD populations from protocol design due to constraints on budgets for translation services, with impacts on representation of particular population demographics in clinical research. In consultations held in NSW, stakeholders indicated that in the OPAL lung cancer study conducted by the University of Newcastle, the exclusion of CALD people equated to 30% of the potential participant population not even being considered for the study. This group is further excluded by being unable to access patient information, consent forms and, for some, technology.

Research and consultation identified a high need for interpreters, though the costs associated with these services are a prohibitive factor for both commercially-sponsored and investigator-led trials. Stakeholders indicated that sites needed to communicate with sponsors about demographics during site selection to support the inclusion of CALD populations. A cost-benefit analysis of the potential of translation services in clinical trials as a recruitment and retention measure could support prioritisation of funding for interpreters.

Youth

Research and consultation identified a high need to engage youth and adolescents in clinical trials. Targeted consultation with CanTeen highlighted a number of enablers for recruitment of youth to trials, including a workforce skilled in communicating

²⁷ Clinical Oncology Society of Australia (COSA) 2015, 'Progress in regional and rural oncology', accessed 28 May 2016, <http://cancerforum.org.au/wp-content/uploads/2016/03/COSA.pdf>.

²⁸ GSK 2014, Clinical trials meet the real world, accessed 20 May 2016, <http://www.gsk.com/en-gb/our-stories/everyday-health/clinical-trials-meet-the-real-world>.

with young people, engaging them in treatment and clinical trials, raising awareness to parents and patient groups, and further streamlining ethics and governance approval processes at the site level.

Rural and remote communities

While distance was continually disputed by stakeholders as a barrier to participation in clinical trials, stakeholders identified a high need to engage with rural and remote communities in relation to research. Research and consultation indicated that in some cases patients would travel across jurisdictions to be in a trial that they perceived would be lifesaving or would improve their condition, with the willingness to travel often in correlation with the severity of the illness being treated. Enablers of recruitment and retention in rural and remote areas included opportunities for relationship building and collaboration between rural and remote clinicians, metropolitan-based clinicians and pharmaceutical companies. Logistics are key barriers, particularly where specimen collection is required. However, telehealth and opportunities for alternative methods of data collection were identified as potential strategies to overcome these issues.

Indigenous Australians

Low levels of health literacy, including low levels of understanding in relation to research and clinical trials, a culture of mistrust of clinical trials and institutions more broadly, lack of engagement in protocol design, and complexity of trials failing to provide flexibility for Indigenous people are key barriers to recruitment, as evidenced by a poor history of success or completion in clinical trials in this context.

Research and consultation identified the need for sponsors and sites to partner with Aboriginal Medical Services as integral to encouraging Indigenous communities to participate in clinical trials. Registries, 'front of house' consent measures and use of EHRs at the site level could also enhance recruitment.

Other enablers to recruitment and retention of Indigenous Australians to clinical trials included utilisation of informal networks within communities to build trust and making participants feel part of the research rather than a 'patient'. Stakeholders also suggested providing information and consent forms that used alternative communication approaches, including pictorial representations, and that could be made available in local languages.

Stakeholders identified a high need for the establishment of an Indigenous clinical trial network to support trial design, recruitment and conduct.

Cognitively impaired

State and territory governments may appoint guardians for people who are incapable of making their own decisions about their lifestyle, including decisions about medical treatment. Consent and guardianship orders are a barrier to the recruitment of cognitively impaired participants to clinical trials. This is exacerbated by the variability in legislation in the eight states and territories in relation to the level of consent required for a person under guardianship orders to participate in

clinical trials. Stakeholders agreed that legislation could be streamlined nationally to enable participation of cognitively impaired persons in clinical trials and research.

2.3.3 Leading practice and performance

a. Leading practice guidelines for clinical trials

The *Clinical Trials Framework for Action 2015* (the Framework) sets out the aims and activities identified as critical to improving the Australian clinical trials environment, and considers the foundations required for a leading practice, quality driven clinical trials sector. The Framework identifies a number of operational objectives including building capacity and capability of the clinical trials sector, enabling the sector to deliver on commitments in a repeatable and predictable manner and embedding continuous quality improvement in clinical trials.

The safe conduct of clinical trials was recognised by all stakeholders as the key principle for a successful and sustainable clinical trials industry in Australia. Further, participants and community members held expectations that standard principles and procedural guidelines govern the conduct of clinical trials in order to protect patient safety and minimise adverse events.

Stakeholders identified a lack of leading practice principles for the design, conduct and management of clinical trials. Stakeholders generally agreed that there is a high need to define leading practice for clinical trials and that these are vital if Australia is to remain globally competitive. Participants and general public maintained that they had confidence in the Australian system and expressed an assumption that there would be more laxity around these procedures in other jurisdictions, such as the USA, indicating a high level of trust in the health system that could be leveraged and extended to clinical trials. Stakeholders acknowledged that funding priorities across government, and jurisdictional differences, would be ongoing issues in relation to development and streamlining of principles or guidelines.

While stakeholders acknowledged that leading practice guidelines would be valuable, they further acknowledged that they would need to meet the NHMRC guidelines and not duplicate the GCP. They would provide a practical set of principles and tools for the set-up, conduct and management of leading practice clinical trials. Stakeholders also noted a high need for mentorship to support implementation of leading practice principles and noted that opportunities were limited due to the short-term contract nature of the workforce. A study of surgical clinical trials and the factors impacting recruitment found that when less successful recruiters, in this case surgeons, were offered individualised coaching on communication to potential participants, the recruitment rate increased from 35% to 65%.²⁹

²⁹ Blaseby JM 2012, *Recruiting patients into randomised clinical trials in surgery*, British Journal of Surgery. 99(3): 307-308.

Acknowledging that incentives are a sensitive issue, emerging consensus among stakeholders was that clinical trials participants should be reimbursed not only for the costs associated with participation but also for their time. Stakeholders suggested the development of a set of principles about incentives, for stakeholder consideration.

While financial incentives for participants may be perceived as a key personal motivator for clinical trials, participants and community members were divergent in their views over the role of incentives in recruiting and retaining clinical trials participants. In general, incentives were not expected and were felt to have minimal influence, particularly where participants had a greater health-related need for the intervention. Community members felt that incentives were necessary when individuals were taking part in a trial which offered them no personal benefit.

b. Measuring clinical trial participation and performance reporting

Research and consultation identified a high need for standardised performance metrics for clinical trials and research. Greater visibility is required at the national, jurisdictional and site level in relation to performance of clinical trials, recruitment and retention, the number of trials currently recruiting and the number of participants currently enrolled in trials.

Stakeholders indicated that many sites lack visibility on the number of trials being conducted at their site. Performance metrics would need to be supported particularly by an increased focus on research KPIs at a site level. Currently, hospital KPIs are silent on research, with no imperative to report research activities, possibly suggesting a lack of buy-in from government regarding the importance of research. In NSW however, stakeholders indicated that the NSW Government did have a set of KPIs for clinical research, related to ethics and governance, patient recruitment and others, that linked to research infrastructure funding.

Research and consultation identified a lack of reliable data underpinning feasibility assessments, demonstrating a high need to leverage the capability of EHRs, as well as a need to develop streamlined tools, resources and standards for undertaking feasibility assessments, supported by the availability of potential participant data and transparent research metrics.

Commercial sponsors highlighted concerns with the lack of transparent data and audit mechanisms for trials at the site and jurisdiction level, with no central approving authority for clinical trials. They agreed that implementation of metrics would need to consider the administrative burden so that sites were not disadvantaged.

While the CTJWG has identified the need to establish a metrics system and promote ICT interoperability as a key priority area for its work, the collection and reporting mechanisms for metrics require consideration over the longer term. The needs of sponsors and the Australian economy must be balanced with maximising the benefits of clinical trials to the community and creating a culture of continuous improvement across the sector.

2.3.4 Awareness of clinical trials

Consultation identified a lack of clinical trial awareness among clinicians, consumers, LHNs, and philanthropists as a key barrier to recruitment and retention.

Stakeholders suggested that this was underpinned by a lack of a clinical trial culture at a national, jurisdictional, site, and community level.

Research and consultation identified an overwhelming need to define the value proposition for clinical trials and communicate the benefits to participating in trials to both clinicians and consumers, noting that there are systemic issues that also need to be resolved.

a. Consumers

Consultations with clinical trial participants and community members, as well as other groups (such as the CHF and Miracle Babies), identified a number of key enablers for recruitment and retention to clinical trials. A high need for targeted campaigns focusing on the promotion of the value proposition and benefits of clinical trials, as well as targeted recruitment and retention campaigns, were identified. A number of other factors also contribute to developing trial-seeking behaviour in consumers and clinicians including embedding clinical trials within the broader healthy system and normalising conversations about research between patients and health care professionals.

Consultations conducted with clinical trial participants, including withdrawers and refusers, and members of the general public, identified a number of factors which contributed to whether people felt able to participate in a clinical trial. Appendix C provides a detailed overview of the enablers and barriers influencing participation in a clinical trial. The research identified that while overall awareness of clinical trials in the community is low and patients may feel apprehensive before consenting to take part in a trial, retention of these patients is not a key issue for clinical trials. This finding supports the evidence collected in research and consultation. Participants and community members felt that based on their experiences and awareness of clinical trials there is scope to improve trial recruitment and retention. Appendix D presents their suggestions for improvements that would enable recruitment and retention in clinical trials.

Consultations with consumer representatives suggested that education of the community is vital to encouraging participation in clinical trials and that it should include reassurances regarding privacy and safety. Stakeholders further agreed that education and awareness raising should be supported by normalising conversations between clinicians and participants regarding clinical trials, and that there is a high need to engage consumer groups in improving perceptions of research, understanding the benefits of clinical trials and developing trial-seeking behaviour in the community. Stakeholders suggested that information on how important clinical trials are to the general wellbeing of communities should be disseminated to address myths and build trust in clinical trials, research, and innovations in health care.

Stakeholders suggested that messaging include that clinical trials research can be translated into better outcomes for patients, and a more effective health system.

Research and consultation identified differing views on the use of mass advertising or awareness campaigns. Stakeholders provided an example of a clinical trial where \$8,000 was invested in four advertisements in a Victorian newspaper. It resulted in over 270 phone calls, 65 follow ups, and 20 potential participants invited for screening. In this case, one participant was randomised into the trial. Another example of limited outcomes for participation was seen in organ and tissue donation where expensive promotional campaigns delivered increased participation rates in the short term only. Workshop participants did agree that there was a need for holistic, long-term strategies for consumer engagement that not only directed patients to clinical trial registries but also engaged them in the value proposition of clinical trials.

Stakeholders agreed that consumer bodies such as the CHF, Diabetes Australia and the Cancer Council Australia had a role to play in education and awareness raising, and in building integrated networks of researchers and consumer groups to increase awareness. Stakeholders suggested utilising the National Prescribing Service 'My Medicines' community announcements for clinical trials and patient support groups.

The CHF supported these initiatives although indicated that awareness campaigns should not raise consumer expectations. The CHF also suggested that consumer factsheets outlining the benefits and risks of clinical trials be provided to all potential trial participants during the recruitment phase.

b. Clinicians

Research and consultation identified a high need to promote clinical trials to clinicians and to engage primary care clinicians, including GPs, in trials and networks to enable recruitment and retention. Further, it identified that the relationship between the site and the primary care clinicians is critical to the success of recruitment and retention in clinical trials. Sponsors and sites often misunderstand the work or business model of these clinicians and place unreasonable expectations on their capacity in relation to awareness raising about clinical trials.

Consultation identified a high need to include GPs in the method of care delivery and protocol design. Workshop participants agreed that while GP advice is often not formally required for enrolment, patients often seek their GP's advice prior to deciding whether or not to participate in a clinical trial. Stakeholders regularly noted that while clinical trial participation should be encouraged by GPs, that they are often not in a position to discuss clinical trials recruitment with patients due to their daily business and appointment times. Stakeholders suggested that it was critical that the burden on GPs be kept to a minimum in order to facilitate recruitment.

Research and consultation identified that clinicians have a general role in communicating the benefits of clinical trials and encouraging trial-seeking behaviour. However GPs and specialists are not necessarily engaged in clinical trials and do not know where to direct their patients to find out about clinical trials.

Stakeholders identified a high need for a comprehensive strategy to engage GPs and other clinicians in clinical trials, and educate sponsors on how to engage and educate clinicians on the benefits of clinical trials to patients and the practice. The ASPREE³⁰ trial was an example provided of a trial that had engaged with GPs to successfully recruit and retain clinical trial participants. Greater awareness of clinical trials networks and registries is also needed for this sector.

Stakeholder consultations also revealed concerns in relation to access to training for new site investigators, agreeing that in terms of participant recruitment and retention, site staff training is critical. Staff need to fully comprehend what a trial involves, otherwise they risk recruiting participants who are not fully informed. Workshop participants agreed that ongoing education and support to all parties involved in the conduct of clinical trials is critical. Stakeholders indicated that GCP training is burdensome. While this training is required for compliance, stakeholders noted a significant gap in provision of practical experience and engagement with trials. The Department of Industry, Innovation and Science has commissioned a Vocational, Educational and Training (VET) accredited course to be delivered to hospital staff who oversee clinical trials, and researchers who submit clinical trials applications, to assist in improving the timeliness of clinical trial applications. Opportunities to extend this course to include design and conduct of trials to enable recruitment and retention should be explored.

c. Philanthropists

While investigators generally look to government and industry for investment, very few consider approaching philanthropic organisations, or have the knowledge of how to access this type of funding. In the USA, investigators engage with philanthropy successfully to gain investment for research. Workshop stakeholders identified a high need for opportunities for engagement with philanthropic organisations to build awareness and increase investment.

2.3.5 Regulation and safety

Research and consultation indicated strong agreement that participant safety is paramount in relation to clinical trials.

Stakeholders indicated that FDA regulations frequently limit the available potential population for a clinical trial based on strict and often unyielding inclusion and exclusion criteria. A specific example of inclusion criteria is the need for double barrier methods for contraception. To meet the inclusion criteria of the clinical trial one method is required to be a spermicide. This is an infrequently utilised method in Australia causing issues for trial participation.

While inclusion and exclusion criteria need to be balanced with safety for participants, ultimately regulatory requirements drive trial design. This may be

³⁰ ASPREE 2015, *About the ASPREE study*, accessed 18 July 2016, <http://www.aspree.org/aus/about-us/the-aspree-study/>.

outside the CTJWG's remit, however the issues are all encompassing and a consistent theme through the project.

3. Key findings

Leadership and coordination

Leadership and coordination at national, jurisdictional and institutional level will establish clinical trials as an important component of Australia's health care system, driving increased support for clinical trials, awareness, leading practice and performance. Leadership and coordination will impact recruitment and retention through consistent awareness raising and promotion of benefits of clinical trials in the community, continuous improvement, and enhancement of existing clinical trial recruitment and retention initiatives nationally.

Streamlined coordination of clinical trials architecture, initiatives and infrastructure is an enabler of recruitment and retention in clinical trials as it limits duplication of effort, drives prioritisation of investment, enhances efforts to build awareness, and enhances the clinical trials environment at the national, jurisdiction and institutional level.

COAG recognises that national coordination across the jurisdictions is needed to address fragmentation and inefficiencies in clinical trials. Together with an increase in sponsor engagement, national coordination will improve trial outcomes, including recruitment and retention.

Engaging jurisdictions in awareness raising and participant safety in clinical trials, aligned with adequate systems for the conduct of clinical trials and associated quality assessments will maintain, and potentially improve, levels of participation in clinical trials.

Support for clinical trials

The success of a clinical trial, including recruitment and retention, can be significantly impacted by its design, conduct and management. Involving trained clinicians experienced in research, consumers, and patient advocacy groups in research networks can ensure that trials meet consumer and community priorities and are designed with both research and participants in mind. Support for clinical trials is required from clinicians, investigators, sponsors and networks including clinical trial registries, EHRs and a dedicated research workforce.

Registries and EHRs enable recruitment and retention by providing visibility of potential participant groups. For these to be effective measures for identifying potential participants, clinicians and consumers need to be aware that they exist and trust that they are well maintained and up to date. EHRs have the capability to identify potential participants for trials, and trials for potential participants, and save significant amounts of time for research coordinators, clinicians and participants in the overall recruitment process.

Research and consultation identified significant issues related to the non-ongoing nature of research coordinator roles, noting that dedicated trial recruitment staff

are more successful at achieving recruitment targets than those involved in trials sporadically. A dedicated, trained research workforce is a key enabler to recruitment and retention based on the development of relationships between key research staff and participants.

Specific population groups, including CALD communities, Indigenous Australians, people with a mental illness, youth, rural and remote communities, and cognitively impaired people, are generally excluded from meaningful participation in clinical trials in Australia. Strategies to address participation in clinical trials for each of these groups, including consideration of trial design and conduct, eligibility criteria and recruitment measures are required.

Leading practice and performance

Leading practice principles for the design, conduct and management of clinical trials are an important enabler of clinical trials in Australia, including recruitment and retention. Defining and promoting leading practice for clinical trials will assist to maintain Australia's global competitiveness, as well as community confidence, and enable more effective recruitment and retention.

Research and consultation identified a high need for practical, leading practice principles for clinical trials to support streamlining of expectations for clinical trials at a national, jurisdictional and institutional level. These leading practice principles should not be intended to duplicate existing GCP guidelines, rather provide a practical 'how to' guide for trials and be complemented by training and mentorship for site staff in recognition of research as a specialised skill set that requires experience for all clinicians.

Leading practice principles should also extend to the use of financial incentives for participants in clinical trials. Incentives for time, rather than solely for expenses such as transport, were generally supported in both the consumer and stakeholder consultation. Financial incentives for time spent will enable recruitment and retention by allowing participants the opportunity to make decisions about trials that are not impacted by potential loss of income.

Leading practice principles may include:

- Early involvement of GPs in study design where they are likely to be involved in recruitment;
- Use of different forms of trial data collection to reduce the need for participant travel;
- Use of rural centres to manage rural clinical trial participants;
- Use of social media to recruit participants; ongoing use of social media in the conduct of clinical trials;
- Communication between clinicians, potential participants and participants;
- Regular feedback to participants on the results of trials;
- Use of incentives;
- Shared success factors for patient recruitment, including engaging early with target populations;

- Use of supportive techniques such as newsletters, reminders, birthday cards to establish a sense of belonging with other trial participants;
- Employment standards for research coordinators and other clinical trials staff; and
- Specific leading practice principles for trials conducted outside of the hospital setting such as trials conducted in primary care and community settings.

Standardised metrics and mechanisms for data collection and reporting are required to track performance of clinical trials activities, including recruitment and retention rates and the success of targeted strategies or initiatives. While the CTJWG has identified the need to establish a metrics system and promote ICT interoperability as key priority areas for its work, the collection and reporting mechanisms for these metrics require consideration over the longer term so that the needs of sponsors and the Australian economy are balanced against maximising the benefits of clinical trials to the community, and creating a culture of continuous improvement across the sector. Consideration could also be given to leveraging existing networks such as LHNs or websites such as AustralianClinicalTrials.gov.au, that is, where government, sponsors, clinicians and consumers already seek health, or research-related, information.

Metrics for performance reporting to include:

- Time for ethics and governance approval;
- Time to recruit participants;
- Clinician time dedicated to research;
- Number of trials conducted on site;
- Number of participants;
- Retention rates; and
- Adverse events.

Awareness

Research and consultation identified an overwhelming need to define the value proposition for clinical trials and communicate the benefits of participating in trials to both clinicians and consumers, noting that there are systemic issues that need to be resolved.

Awareness of clinical trials, including where to go for information on trials and how to access trials, is required for clinicians, consumers and alternative funding providers such as philanthropists. These groups need to be engaged in clinical trials at a national, jurisdictional, institutional and personal level to affect recruitment and retention. Strategies targeted at awareness and education could leverage existing initiatives and information networks or websites, for example LHNs, AustralianClinicalTrials.gov.au.

Regulation and safety

The safe conduct of clinical trials is recognised by all stakeholders as the key principle for a successful and sustainable clinical trials industry in Australia.

Research conducted by EY Sweeney found that clinical trials participants and community members held expectations that principles and procedures govern the conduct of clinical trials in order to protect patient safety and minimise adverse events.

In consultations with clinical trials participants and members of the general public, respondents maintained that they had confidence in the Australian system and expressed an assumption that there might be more laxity around these procedures in other jurisdictions, such as the USA. This indicates a high level of trust within the Australian health system that could be leveraged and extended to clinical trials. Perceptions of safety are a key enabler to recruitment and retention in Australian clinical trials.

Feedback also suggests that international regulations can limit the potential participant population for a clinical trial based on strict, and often unyielding, inclusion and exclusion criteria over and above the requirements needed to protect participant safety. While participant safety remains paramount, it is ultimately regulatory requirements that are driving trial design. It is noted that this may be outside the CTJWG's remit, however the issue is an all-encompassing and consistent theme throughout the project, and could impact recruitment.

4. Recommendations

EY has presented a total of 14 recommendations for consideration by the CTJWG to improve recruitment and retention in Australian clinical trials.

Leadership and coordination

Recommendation 1: The CTJWG/AHMAC to clarify leadership roles at the national, state and territory level to provide oversight and coordination of clinical trials initiatives to maximise the realisation of benefits of participation in clinical trials for health consumers and clinicians. This should involve the enhancement of existing national clinical trials roles and/or the establishment of dedicated structures at national and individual state and territory levels to improve clinical trial coordination across Australia.

***Reason for recommendation:** As recognised by COAG-HC, national coordination of clinical trials is required across jurisdictions to overcome fragmentation and inefficiencies. Clearer definition of roles and established, dedicated structures are required to ensure that clinical trials remain a significant aspect of Australia's health care system. Research and consultation indicated that jurisdictions should identify opportunities to streamline the coordination of trials, including recruitment and retention efforts, to reduce duplication, allow for greater focus on the prioritisation of investment in trials, and build a culture of clinical trials nationally.*

Recommendation 2: The CTJWG, on behalf of the nine jurisdictions, to recommend to the Independent Hospital Pricing Authority (IHPA) to introduce activity based funding to hospitals for public hospital clinical trial activity utilising trial completion as an output measure. This would further encourage and embed research KPIs within the hospital setting and link specific funding to research activity.

***Reason for recommendation:** The introduction of activity based funding for clinical trials could enable coordination of initiatives and investment for clinical trial recruitment and retention at the institutional level, and further embed research within the hospital setting nationally.*

Support for clinical trials

Recommendation 3: Over the short term, the CTJWG, the Australian Government Department of Health, the NHMRC, and ACTA, to formalise the structure, roles and support for clinical trials research networks, ensuring that they reflect national, consumer and community priorities for research. This will include promotion and encouragement of:

- Health consumer involvement in networks, via the Consumers Health Forum (CHF) and other patient advocacy groups, in the development of national research questions and involvement in appropriate clinical research networks;
- Access to Medical Research Future Fund (MRFF) or other sources of funding for support for clinical trials networks including resources for secretariat, data management and trial coordination;
- Research networks to utilise existing and future patient registries to

encourage clinical trial participation, leveraging the opportunity to improve recruitment and retention through coordinated use of clinical quality registries to identify potential participants; and

- Involvement of primary care focused networks in design and conduct of research, recognising that recruitment of participants from primary care settings will need to involve primary care research networks.

Reason for recommendation: *The emphasis on clinical trials networks in the recommendations reflects the significant impact that networks may have in ensuring that national, consumer and community priorities for research are met and that these are considered by sponsors in the design, management and conduct of trials. Networks also provide the opportunity to coordinate clinical trial activity nationally, including recruitment and retention of participants, and form an important link with sponsoring bodies. While there are a number of very well performing networks in Australia, there are many opportunities available to improve the networking of key researchers in a number of areas of clinical trial research, as well as interaction between existing networks.*

Recommendation 4: The CTJWG to provide input regarding required enhancements to the Australian New Zealand Clinical Trials Registry (ANZCTR) to improve its relevance for participants and researchers and ensure it is regularly updated, noting the current limitations in ANZCTR's scope and functional capabilities. This could include advice on consolidation of ANZCTR with AustralianClinicalTrials.gov.au and a strategic framework on how these registries continue to work simultaneously.

Reason for recommendation: *Research and consultation identified a high need for a central registry of commercially-sponsored and investigator-led clinical trials in Australia, noting that this provides an efficient means of recruitment to trials. Clinicians and consumers indicated that they did not access available registries as they were often outdated and did not provide a comprehensive view of open trials. Stakeholders suggested that duplication of registries and trial sites further drove fragmentation and was a barrier to recruitment and retention by making it difficult to access accurate information and disabling efforts to raise awareness of trials for both clinicians and consumers.*

Recommendation 5: Over the short term, the Australian Government Department of Health and the Australian Digital Health Agency to build the capability of the My Health Record to facilitate clinical trial recruitment and retention. Furthermore, the states and territories health departments and governing bodies of private sector health organisations should ensure that Electronic Medical Records implemented in the public and private hospital and health service systems facilitate the recruitment and retention of participants in clinical trials.

Reason for recommendation: *My Health Record presents significant opportunities for Australia's health care system, including clinical trials, particularly in relation to recruitment and participation. Building the capability of My Health Record, as well as the Electronic Medical Records implemented in public and private hospitals and*

health services nationally, could assist clinicians to identify potential participants for currently recruiting trials. This would lead to improved efficiency in clinical trial recruitment, and would further embed research into clinician and consumer behaviours.

Recommendation 6: Over the medium term, jurisdictions to address sensitivities of secondary use of data and work with industry and sponsors to pursue opportunities to utilise existing data linkage regimes, through a central agency/ies, to identify prospective trial participants.

Reason for recommendation: Research and consultation identified a high need to utilise existing data sources to identify prospective trial participants. Secondary use of data presents sensitivities for jurisdictions, industry and sponsors and continued engagement across these groups is required to address these issues.

Recommendation 7: The CTJWG to work with jurisdictions to progress ongoing and long-term roles for research nurses, support the inclusion of clinical research into job descriptions for clinicians, and embed the need for ongoing site training and mentorship in running clinical trials.

Reason for recommendation: Ongoing and long-term positions for research staff are necessary to achieve recruitment goals and ensure a safe clinical trials sector. Research and consultation identified that a dedicated research workforce is a key enabler for recruitment and retention in clinical trials, particularly by relationship building between clinicians and potential participants. Research coordinators and other staff require the capability, skills and experience to manage clinical trials, including recruiting and retaining trial participants.

Recommendation 8: The CTJWG to consider opportunities to build on existing innovations and initiatives as outlined in Appendix B. Initiatives that present opportunities for the CTJWG.

Reason for recommendation: Research and consultation identified a number of existing initiatives that present opportunities for the CTJWG to consider for promotion and/or development to improve recruitment and retention in clinical trials.

Recommendation 9: The CTJWG, the NHMRC and research entities to focus on clinical trial recruitment and retention strategies in special groups such as culturally and linguistically diverse (CALD) communities, youth, Indigenous Australians, rural and remote communities, and people with a mental illness. Focused strategies to also be developed for cognitively impaired potential trial participants, supported by advice to jurisdictions on guardianship legislation as an enabler of recruitment.

Reason for recommendation: Inadequate participation, and unnecessary exclusion, of these groups in Australian clinical trials indicates a high need for focused strategies to increase recruitment and retention. Research and consultation

indicated that these groups were often excluded in trial design or limited in their opportunities to participate.

Leading practice and performance

Recommendation 10: Over the short term, the CTJWG to work with the NHMRC and the Australian Government Department of Health to devise an online leading practice guide to the successful design, management, administration and conduct of clinical trials starting with the creation of a culture that embeds clinical trials within leading practice clinical care and reflecting the primary consideration of safety for clinical trial participants. This resource should be continuously reviewed and updated, and could include a set of tools for practical implementation.

***Reason for recommendation:** Research and consultation identified a high need for the development and utilisation of leading practice guidelines for clinical trials to streamline the design, management and conduct of clinical trials nationally, and to continue to position Australia as a safe place to conduct trials to trial sponsors within the global market. Furthermore, stakeholder consultation indicated that well managed and delivered clinical trials have much higher rates of recruitment and retention.*

Recommendation 11: The NHMRC to devise guidelines for the consistent use of financial incentives for trial participants, to appropriately recognise the time commitment, rather than solely expenses incurred, of participants in clinical trials.

***Reason for recommendation:** Research and consultation highlighted the need for revised guidelines on the use of incentives to ensure consistency across the sector. Providing financial incentives for time and effort, beyond expenses such as transportation, means that loss of income does not present a barrier for potential trial participants.*

Recommendation 12: The CTJWG, in consultation with clinical trial sponsors, to continue to expand on national clinical trials metrics to support continuous improvement in clinical trial recruitment efforts, and consider the merit of future annual publication at LHN and individual research entity level.

***Reason for recommendations:** Research and consultation identified a high need for transparent performance reporting in relation to clinical trials, including recruitment and retention data. Currently, there is no central repository of clinical trials data nationally. Reporting of metrics will drive a culture of continuous improvement within the clinical trial environment. Expansion of national trial metrics over the longer term will assist jurisdictions to realise and build awareness of the economic and health benefits of trials to consumers, clinicians and the broader community.*

Awareness

Recommendation 13: The CTJWG to work with the NHMRC and other relevant stakeholders and advocacy groups to define the value proposition for clinical trials, and design and implement strategies to raise awareness of the role and value of

clinical trials amongst the general public, health care practitioners (including primary care clinicians), Local Hospital Networks(LHNs), and the philanthropic community, including promotion of a more distinct profile for the AustralianClinicalTrials.gov.au website.

Reason for recommendation: *The value proposition for clinical trials, including the benefits and value of clinical trials to clinicians, consumers and the economy is required to increase engagement in clinical trials. Research and consultation identified that lack of awareness was a key barrier to recruitment and retention in clinical trials.*

Regulation and safety

Recommendation 14: The CTJWG to;

- reaffirm the primacy of safety in clinical trials across the sector; and
- consult organisations that conduct commercially-initiated and investigator-initiated clinical trials over impediments to recruitment that are derived from Food and Drug Administration (FDA), European Medicines Agency (EMA) or other requirements and to seek resolution with the relevant foreign authority through the Therapeutic Goods Administration (TGA).

Reason for recommendation: *Stakeholders agreed that safety is the primary enabler of recruitment and retention in clinical trials. Public consultation identified a high level of confidence in the clinical trials system in Australia, although stakeholders warned that this had the potential to change should a major adverse event occur. Stakeholders also suggested that international regulation presented limitations to clinical trial participation and that these required resolution.*

5. Conclusion

This report provides synthesis of findings and proposed solutions and future approaches for the CTJWG based on extensive research and consultation undertaken throughout this project.

Recruitment and retention cannot be considered in isolation of the systemic, structural and cultural factors shaping the Australian clinical trials environment at the national, jurisdictional and institutional level. Research and consultation has identified that there is no single strategy that will improve recruitment and retention in Australian clinical trials, rather a coordinated approach is required. The recommendations set out in this report provide consideration of these factors.

The greatest impact for recruitment and retention will come from a focus on innovative and collaborative approaches underpinned by national leadership and coordination, strengthened clinical trials networks, increased uptake of digital health and data initiatives, and the development of leading practice guidelines for the design, conduct and management of Australian clinical trials.

Appendix A. Glossary

ACTA	Australian Clinical Trials Alliance
AHMAC	Australian Health Ministers' Advisory Council
ANZCTR	Australian New Zealand Clinical Trials Registry
ASPREE	ASPIrin in Reducing Events in the Elderly - led by Monash University in Australia and the Berman Centre for Outcomes and Clinical Research in the USA, the ASPREE trial is focused on determining the balance of aspirin's effects in healthy older people. ³¹
CALD	Culturally and linguistically diverse
CHF	Consumers Health Forum of Australia
Clinical quality registry	The Australian Commission on Safety and Quality in Health Care defines a clinical quality registry as 'an organisation which systematically monitors the quality (appropriateness and effectiveness) of health care, within specific clinical domains, by routinely collecting, analysing and reporting health-related information. The information is used to identify outcome benchmarks, significant outcome variance, and inform improvements in healthcare quality.' ³²
Clinical trial registry	ACTA defines a clinical trial registry as an 'organisation or website that either: <ul style="list-style-type: none"> • lists clinical trials being conducted (or that have recently been conducted) in Australia (or internationally, including Australia); • provides a mechanism for patients or others to register their interest in participating in an Australian clinical trial; and • provides a link between potential participants and Australian clinical trials.'³³
COAG	Council of Australian Governments

³¹ ASPREE 2015, *ASPIrin in Reducing Events in the Elderly*, accessed 30 June 2016, <http://www.aspree.org/aus/>

³² Australian Commission on Safety and Quality in Health Care 2014, Framework for Australian clinical quality registries, ACSQHC, accessed 30 June 2016, <http://www.safetyandquality.gov.au/wp-content/uploads/2014/09/Framework-for-Australian-Clinical-Quality-Registries.pdf>

³³ Australian Clinical Trials, accessed 30 June 2016, <https://www.australianclinicaltrials.gov.au/clinical-trials-registries>

COAG-HC	Council of Australian Governments - Health Council
CRN	Clinical Research Network
CTAC	Clinical Trials Advisory Committee
CTAG	Clinical Trials Advisory Group
CTC	Clinical Trials Connect
CTJWG	Clinical Trials Jurisdictional Working Group
DIIS	Department of Industry, Innovation and Science
EHR	An Electronic Health Record provides a history of medical and clinical care across a number of health care providers and is digitally stored in one place. An EHR can generally be accessed and updated by authorised health care providers, and the individual patient, at different institutions and sites in real-time.
EMA	European Medicines Agency
EMR	Electronic Medical Record - an electronic medical record is a patient's record of medical and clinical care, gathered by a single health provider.
FDA	Food and Drug Administration
GCP	Good Clinical Practice guidelines are internationally accepted standards for the design and conduct of clinical trials, and set out minimum requirements for reporting. ³⁴
ICU	Intensive Care Unit
LHN	Local Health Network
NHMRC	National Health and Medical Research Council
TGA	Therapeutic Goods Administration

³⁴ Therapeutic Goods Administration (n.d), *The Australian clinical trial handbook*, accessed 30 June 2016, <https://www.tga.gov.au/publication/australian-clinical-trial-handbook>.

Appendix B. Initiatives that present opportunities for the CTJWG

Initiative	Details	Opportunities for the CTJWG
Sunshine Coast Hospital & Health Service - Clinical Research Unit	Dedicated Clinical Research Unit; nurses communicate and collaborate with clinicians, ensure that clinical trials and research is visible across the health service and build ownership of trials among staff. Taking a risk-based, benefits management approach supported by the executive means that dedicated resources are available to communicate with clinicians.	<ul style="list-style-type: none"> • Develop good practice case study supporting clinical trials - demonstrate the success of the Sunshine Coast model of permanent staff available in a "staff pool" model to support projects. • Promote the benefits of clinical trials to hospital executive to gain buy-in. • Consider and develop leading practice principles for the conduct of clinical trials at the hospital, LHN and jurisdiction level. • Consider development of metrics, identify and consider leveraging existing data measurement tools to measure participation and conduct of clinical trials.
ClinTrial Refer	Mobile application connecting clinicians and patients to clinical trials.	<ul style="list-style-type: none"> • Consider development of a streamlined application to connect clinicians and patients to clinical trials. • Consider coordination of awareness raising relating to different mobile applications and promote adaptations of ClinTrial Refer through a national directory of innovations. This would require investment to ensure regular updating.
Clinical Trials Connect	Online patient recruitment service.	<ul style="list-style-type: none"> • Build AustralianClinicalTrials.gov.au to support online patient recruitment, considering whole-of-trials approach to connect networks, trial sites, and consumers. • Build online presence of the website through social media.

Melbourne Health - "Ask Me About Research" Campaign	Melbourne Health campaign to encourage patients to ask their clinicians about research and clinical trials. Staff wear badges and other information is provided around the care sites e.g. posters.	<ul style="list-style-type: none"> Consider national campaign, led by jurisdictions. Consider relevant dates such as International Clinical Trials Day to focus promotion on consumers and clinicians (e.g. GPs). This could be considered jointly with the CTJWG Communications Working Group.
Medicare	A sponsor approached the Australian Government Department of Human Services (Medicare) to identify and contact potential trial participants on behalf of the sponsor, inviting patients to contact their health professional or the trial coordinator to discuss potential eligibility. The Department of Human Services managed patient contact; patient data was not supplied to the sponsor. Stringent ethical and legislative arrangements apply to these arrangements, and fees may be payable.	<ul style="list-style-type: none"> Consider private-public partnerships for the funding and development of EHRs or other large scale infrastructure projects that would enable recruitment and provide greater return on investment.
Critical Care Trials Network	Characterised by strong and consistent communication, leadership, strategy and coordination, working together to develop questions, coordinate studies and distribute workload across site.	<ul style="list-style-type: none"> Develop leading practice case study for promotion on AustralianClinicalTrials.gov.au. Consider a dedicated structure to support creation of clinical trial networks and identify areas (e.g. by geography or disease group) that would benefit from a network.
Electronic health records	Determine capability of electronic health records to identify potential and current clinical trial participants, and identify currently recruiting trials.	<ul style="list-style-type: none"> Consider suggestion to the Department to build in prompts for clinical trials in My Health Record. Consider leading practice principles in relation to systems capabilities to support jurisdictions and sites to make informed choices about software purchases.

Appendix C. Enablers and barriers to clinical trial recruitment and retention (findings from participants and general public consultations)

Enabler or barrier	Influence on participation in a clinical trial
Nature of intervention	<ul style="list-style-type: none"> • People have different levels of tolerance for pain, discomfort and needles, and different perceptions of the level of risk involved in a given study. • They were most likely to agree to participate in a trial when the intervention did not exceed the level of discomfort they would be willing to tolerate, and when they judged that the benefits outweighed the risks.
Prognosis and need for the intervention	<ul style="list-style-type: none"> • People with serious or terminal illness were generally more willing to take part in a trial, viewing the intervention as their "last hope". They were therefore more willing to tolerate risks and side effects than those whose illness was less severe or not life threatening.
Accessibility of medical and nursing team	<ul style="list-style-type: none"> • The extent to which people could access the medical and nursing team if they had any questions about the trial, or if they developed any side effects. • People were most willing to take part in a trial when they felt that the medical and nursing team were accessible should they have any questions or encounter any problems. The relationships that patients developed with these staff also aided retention in trials.
Accessibility of the trial venue	<ul style="list-style-type: none"> • The lack of ease with which people could access the trial venue (or hospital) meant that people who lacked transport and/or lived a long distance from a trial were less likely to take part.
Trust in medical and nursing team	<ul style="list-style-type: none"> • Although most patients met the medical and nursing team for the first time when they were invited to take part in the trial, they consistently nominated trust in these health professionals as one of the main reasons they decided to proceed.
Voluntary nature of participation	<ul style="list-style-type: none"> • When first invited to participate in a trial, patients felt that the decision to participate was theirs alone, and did not feel in any way pressured by the hospital staff to consent. • Knowing that they had choice and control over participating left them feeling more likely to agree to take part in the trial. • The knowledge that they could withdraw from the trial at any time was cited as a factor supporting retention in the trial, as it meant that they did not feel

	“trapped”.
Time commitment/ frequency of follow up	<ul style="list-style-type: none"> • People were generally willing to take part in a trial when the time commitment involved (including frequency of visits and length of the trial) was not too onerous and would present only a minor inconvenience to their lifestyle.
Flexibility	<ul style="list-style-type: none"> • People valued having a degree of choice around trial start dates and follow up appointments; this helped them to feel in control of the trial process. • Some community members felt that trials would be more attractive if clinics offered appointments after hours and on weekends to accommodate participants in full time employment.
Incentives	<ul style="list-style-type: none"> • There were quite divergent views over the role of incentives around the recruitment and retention of trial participants. • In general, incentives were not expected, so were felt to have minimal influence when patients had a greater need for the intervention (such as when their health status was poor). • Community members felt that incentives were necessary when people were taking part in a trial which offered them no benefits (such as a trial for a condition they did not have).

Appendix D. Opportunities for improvements to recruitment and retention (findings from the participants and general public consultations)

Issue	Rationale
Eligibility for trials	<ul style="list-style-type: none"> To increase the available pool of eligible people to take part in trials, consider assessing the eligibility of people who have a pre-existing condition and/or who take prescribed medication on a case by case basis, rather than applying a blanket exclusion approach.
Information around clinical trials	<ul style="list-style-type: none"> Most people with no prior involvement in clinical trials had relatively low awareness of the clinical trial process; some people had significant knowledge gaps. Any interventions to raise awareness of clinical trials in the community should emphasise the range of trials available (i.e., that they are not just used for drugs), that participation is voluntary, that participants do not incur any up-front costs (such as for the intervention), and expectations of participants in relation to their involvement. It is also important to inform prospective participants of the value of clinical trials, for example, the support the trial staff will provide throughout the trial and their access to the team, and that the monitoring process will provide them with some assurance that they can get assistance if any issues are identified.
Use of incentives	<ul style="list-style-type: none"> Incentives are an important motivator for healthy young people considering participating in a Phase 1 trial, however when people are seriously unwell, incentives have a negligible influence in terms of recruitment. Most community members who have had no involvement in clinical trials have an expectation of payment for taking part in a study, but once patients commence a trial, the strength of interpersonal relationships with the trial team provides them with a greater incentive to remain in the trial than a monetary incentive. The research did not find support for incentivising all trial patients; there was a preference to incentivise participants with no health benefits likely to be derived from participating in a trial. Research supported continuation of financial assistance to clinical trial participants to offset expenses such as travel and parking costs.
Travel, and accessibility of trial sites	<ul style="list-style-type: none"> People living in outer metropolitan and regional locations suggested that trial sites consider running clinics in these areas to minimise the times and costs associated with travelling into metropolitan areas. A related suggestion was where feasible, to make use of

	telemedicine to minimise travel times and costs.
Use of technology	<ul style="list-style-type: none"> • Younger people supported greater use of technology by clinical trials, for example, providing an option for questionnaires to be completed online instead of in hard copy only.

About EY

EY is a global leader in assurance, tax, transaction and advisory services. The insights and quality services we deliver help build trust and confidence in the capital markets and in economies the world over. We develop outstanding leaders who team to deliver on our promises to all of our stakeholders. In so doing, we play a critical role in building a better working world for our people, for our clients and for our communities.

EY refers to the global organisation and may refer to one or more of the member firms of Ernst & Young Global Limited, each of which is a separate legal entity. Ernst & Young Global Limited, a UK company limited by guarantee, does not provide services to clients. For more information about our organisation, please visit ey.com.

© 2016 Ernst & Young, Australia
All Rights Reserved.

ED 0616

In line with EY's commitment to minimise its impact on the environment, this document has been printed on paper with a high recycled content.

Ernst & Young is a registered trademark. Our report may be relied upon by Department of Health for the purpose of our engagement only pursuant to the terms of our signed official work order. We disclaim all responsibility to any other party for any loss or liability that the other party may suffer or incur arising from or relating to or in any way connected with the contents of our report, the provision of our report to the other party or the reliance upon our report by the other party.

Liability limited by a scheme approved under Professional Standards Legislation.

ey.com