

Novel technologies for clinical trial recruitment in Australia

# July 2023

Research reported in this publication was supported by the Medical Research Future Fund under grant number MRFTA000001

Engagement

Involvement

Participation

## Authors

Husna Begum<sup>1</sup>, Courtney Gee<sup>1</sup>, Nikolajs Zeps<sup>2</sup> and John Zalcberg<sup>1,3</sup>

Authors affiliation:

<sup>1</sup>Australian Clinical Trials Alliance, Melbourne, VIC 3205, Australia

<sup>2</sup> Monash Partners Academic Health Science Centre, Melbourne, VIC 3168, Australia

<sup>3</sup> Monash University, Melbourne, VIC 3004, Australia

## Abstract

Clinical trials are important for an improving healthcare system. They enable key questions in health to be answered. To ensure that the findings are generalisable to the wider community, they must be inclusive of and accessible to a broad population. Traditional methods of recruitment into clinical trials rely on direct contact between health providers and those that conduct trials, however, recent innovations mean that is changing. Technological innovations, particularly the adoption of electronic medical records and use of social media, have provided parallel and complementary approaches to identifying and connecting with potential trial participants. The COVID-19 pandemic has hastened the adoption of new approaches and technology, for example the expansion of telehealth. To assist researchers, the Australian Clinical Trials Alliance has undertaken a project to identify and summarise the approaches of the various providers of trial recruitment services in Australia.

## Keywords

Clinical trials, recruitment, technology

## Abbreviations

AI – Artificial Intelligence
ACTA – Australian Clinical Trials Alliance
ANZCTR - Australia and New Zealand Clinical Trials Registry
CALD – Culturally and Linguistically Diverse
CERA – Centre for Eye Research Australia
CRO – Contract Research Organisation
CTN – Clinical Trial Network
EHR – Electronic Health Record
EMR – Electronic Medical Record
GP – General practitioner
HCO – Health Care Organisations
HMRI – Hunter Medical Research Institute Register
ML – Machine learning
NLP – Natural Language Processing
RCT – Randomised Controlled Trial

## Introduction

Australia is a leading destination for clinical trials with over \$1 billion in direct expenditure<sup>1</sup> and accounting for 4.2% of global clinical trial activity.<sup>2</sup> From 2006 to 2020, around 18,000 trials started in Australia, with over 40% in the last five years, with an estimated 8.7 million trial participants.<sup>3</sup> Australia's world-class medical research infrastructure, high clinical standards and relatively straightforward regulatory framework incentivise clinical trial conduct.<sup>4</sup> Timely trial start-up together with meeting expected recruitment targets remains a global challenge but is subject to factors often beyond the control of individual sites. Nevertheless, conducting proper site feasibility is important to increase the likelihood of relevant population recruitment. According to a recent Australian analysis, finding eligible participants meeting the study's inclusion/exclusion criteria was the most significant barrier to trial recruitment.<sup>5-7</sup> Failure of current recruitment methods, including high screen-failure rates,<sup>8</sup> indicates need for improved mechanisms. It has been reported that 80% of clinical trials struggle with enrolment, with a 30% drop out rate after participant sign-up.<sup>9</sup> This highlights the importance of creating participant-centric trials that adopt more inclusive selection criteria reflecting real-world practice and cultural diversity, as well as improved methods of engaging with potential participants.

The COVID-19 pandemic has contributed to accelerated digitization and technological advances in clinical trial conduct, in addition to decentralised clinical trials (e.g. teletrials <sup>10</sup>) implementation that support hybrid recruitment models. Technological innovations may improve efficiency and productivity through novel tools to increase patient engagement, reduce patient burden, and improve trial management and cost.<sup>11, 12</sup> Yet expanded use of new technologies raises regulatory, operational, and usability concerns requiring consideration to avoid potential implementation barriers.<sup>11</sup> Technology benefits include the ability to search existing digital documents and data repositories, even in unstructured data formats such as electronic medical records (EMR).<sup>13</sup> These could increase recruitment, particularly of under-represented populations such as those residing in rural/regional/remote areas, from culturally and linguistically diverse (CALD) backgrounds, or those with rare diseases.

In Australia, Clinical Trial Networks (CTNs) conduct most of the investigator-initiated clinical trials. The Australian Clinical Trials Alliance (ACTA), the peak body representing such Australian CTNs, ran a workshop to identify how new and emerging technologies can be utilised to improve trial recruitment and increase trial activity. Prior to the workshop involving expert panellists, ACTA engaged with technology providers to map the landscape of current or evolving technologies being utilised for clinical trial recruitment, focusing on those employed in Australia. A summary of these recruitment technologies is provided here. *Please refer to the Supplementary material for more information on methodology*.

Out of scope was a review of consumers' role in trial recruitment, or how these technologies improve access or reduce burden for potential trial participants. ACTA encourages active involvement of consumers in trial design and recruitment to ensure clinical trials address issues and interventions that matter to patients, that trial participant burden is reduced and minimised, and participation rates improved.<sup>14</sup>

## Results

An online scoping search identified 22 technology providers that aim to actively increase participant recruitment into Australian clinical trials **(Table 1)**.

Almost half (41%) of the technology providers included were established in the last five years, perhaps prompted from the COVID-19 pandemic, which stimulated digital adoption in clinical trials.<sup>15</sup> Hence there is currently limited data available to demonstrate their contribution to clinical trial recruitment improvement. The remaining half were able to provide some evidence supporting their technologies' capabilities. As there

remains no independent mechanism to evaluate trial recruitment rates at a local, state, or national level in Australia, this report relies on their self-reported data.

# Approaches identified

Four main approaches have been identified; registers, artificial intelligence (AI), platform/framework, or other (including digital advertising methods).

Half of the providers included in our survey (50%) classify their technology under one approach, while others utilise several, possibly indicating growing need to utilise multiple approaches and tools to optimise recruitment strategies. More than half of providers (59%) classify themselves as registers, and a quarter (23%) utilise digital advertising methods.

Providers with international presence, for example TriNetX<sup>16</sup> and HealthMatch,<sup>17</sup> may be of interest, as their recruitment strategies are AI and data-driven based to identify suitable geographic locations for trial participants specific to particular studies, and provide advice to trial sponsors on how to recruit effectively and efficiently based on studies' inclusion and exclusion criteria.

## Experience in Australia

International technology providers noted greater success in trial recruitment with their Australian sites; Nativve Health Research<sup>18</sup> reports better Australian market uptake for trials in specific disease areas than international counterparts like the US. Local established providers, ClinTrial Refer<sup>19</sup> and Evrima Technologies,<sup>20</sup> report similar successes. For example, ClinTrial Refer has supported over 2000 trials, while Evrima Technologies launched GPConnect targeted at primary care providers, similar to Torch Recruit<sup>21</sup> which is already supporting 28 general practices in Australia (trial recruitment through primary care has been highlighted as an effective sector to target national clinical trial capability development, particularly in United Kingdom).<sup>22</sup> Another provider, Clinials,<sup>23</sup> is new to the market, with experience in recruiting participants for medical device and drug trials, although their approach and commitment needed from participants vary between trials.

Establishment of multiple academic or government driven registers addresses access gap for participants wishing to search or participate in clinical trials. These include Join Us,<sup>24</sup> StepUp for Dementia Research<sup>25</sup> and StepUp for Ageing Research,<sup>26</sup> Australian Cancer Trials,<sup>27</sup> and Hunter Medical Research Institute Register (HMRI)<sup>28</sup> (Table 1 and Figure 1). These technologies built their own brand and participant base due to work directly or indirectly involving patients of specific disease conditions, and their networks. They often target multiple health states with reported success (Table 1) while making information broadly accessible to people.

Another internationally used recruitment avenue is via the EMR. Technologies like CogStack <sup>29, 30</sup> have been implemented at major teaching hospitals amongst other sites and utilise techniques like natural language processing (NLP) to identify potential participants for open studies. Queensland is also adopting this approach <sup>31</sup> and can provide almost real-time data, although likely less relevant for trials not requiring hospital care. A Singapore-based technology provider, Oncoshot, <sup>32</sup> operates similarly integrating with hospital EMRs, allowing de-identified data sharing across international collaborative groups for clinical trial recruitment purposes.

Recruiting capabilities in rural/regional/remote areas of Australia was also explored, along with ensuring equity of access to trials for CALD populations. Torch Recruit, TriNetX and Oncoshot are working on improving equitable access to rural/regional/remote areas. Most technologies report they are in early stages of implementing trial information in different languages to target CALD populations. Specifically, Opin powered by Opyl Limited, has successfully completed enrolment campaigns in 4 languages across 6 countries.

## Participant recruitment journey

Clinical trial recruitment occurs at all stages of the participant's health journey, from otherwise healthy participants (when considering disease prevention trials or related to normal health states such as pregnancy) to participants who have entered the medical system needing various levels of care. We have attempted to map technologies available during a participant's health journey (Figure 1). It is anticipated that this figure will benefit those interested in understanding various clinical trial options available based on their health conditions, and to understand technologies' self-reported capabilities, provided in Table 1.

Table 1. Novel technologies used for clinical trial recruitment in Australia.

Provider Category of participant health journer (All, healthy, primary care, specialist care, tertiary care, post-discharge)	Year of establishment	Category (Register, AI, Platform/Framework, Other)	Number of organisations utilising technology	Number of trials utilising technology	Evidence of key capabilities
Join Us All health states	2020	Register	20+	14	Join Us has supported recruitment to >25 research studies to date. There is currently limited pilot data and impact modelling only.
Australian All Health state Cancer Trials/ANZCTR^	2010	Register	Unknown	As of 17/10/22, information for 5,130 studies is displayed on the Australian Cancer Trials website	<ul> <li>Of the studies displayed on the Australian Cancer Trials website, approximately 1/3 have provided a summary using lay language, describing the purpose of the trial, and what is involved for participants. These studies have provided information on time and costs associated with involvement in the study, and can be searched by the focus of their study (for example, surgery, chemotherapy, etc.), cancer type, and state or territory the trial is recruiting in.</li> <li>Key metrics include the following: <ol> <li>Visits to the website have increased over time, with the website being accessed an average of 3,558 times per month in 2022, triple the average from 2010. Website data indicate that the large focus of the Australian Cancer Trials website is to assist recruitment. For example, in May 2022, 7,750 searches for clinical trials were completed, and the information page 'Taking part in a trial' one of the top 5 accessed website pages.</li> </ol> </li> <li>A user survey of the website was completed in late 2018. Of the 1,828 users who responded, the majority (63%) were accessing the site to find a study for themselves, a family member/friend or their patient. Other reasons for visiting the website were to see what cancer-specific trials were available (18%) and for general interest (15%). When asked how well the website met their needs, 12% selected extremely well, 81% selected well to very well, and 7% selected not so well or not well at all.</li> </ul>

StepUp for Dementia Research and StepUp for Ageing Research	All health states	2019 (StepUp for Dementia) 2022 (StepUp for Ageing Research)	Register	26	30	Supported over 118 studies and over 25% are clinical trials. On average 50% of the final sample for a study were recruited from StepUp. A supportive listing of 18 publications/sites have utilised StepUp for recruitment (listed below this table) <sup>#</sup>
Victorian Cancer Trials Links (VCTL)	Specialist care	2009	Register	Approximately 46 clinical trial units who have trials listed as open to recruitment	Over 600 trials that are open to recruitment in Victoria listed on the platform	Key metrics include an average of 3000 users per month over the last 2 years. VCTL is a searchable platform that assists with the promotion and identification of cancer treatment clinical trials in Victoria.
ClinicalTrials.gov	All health states	2000	Register	NA	NA	NA. ClinicalTrials.gov is a Web-based resource that provides patients, their family members, health care professionals, researchers, and the public with easy access to information on publicly and privately supported clinical studies on a wide range of diseases and conditions.
Hunter Medical Research Institute Register (HMRI)	All health states	2003	Register	NA	1732 people on HMRI Research Volunteer Register and 736 active members on the Stroke Research Register	Organisational knowledge built over 18 years of running the register, and 6 years of running the Stroke Research Register Hunter. Experience in engaging with the community and with patients/consumers about the opportunity to participate in trials, as well as the routines, needs, priorities and workflows of the 1773 researchers who are affiliated with HMRI across their 19 different research programs. Their data shows that they have matched members with research participation spots across 240 discrete research projects (including clinical trials. Customisation and personalisation of process, evidenced by this publication derived from their Stroke register: <u>https://pubmed.ncbi.nlm.nih.gov/34629050/</u>
Evrima Technologies	Healthy Primary care (Evrima Technologies)	2019	Register Other: Digital advertising	114	61	<ul> <li>Evrima has successfully recruited across various therapeutic areas. Two notable case studies:</li> <li>1) Evrima conducted a high-volume Phase III Vaccine study where they onboarded 28 sites across 10 weeks in Australia and New Zealand. The integrated advertising campaign was delivered under budget and on sponsor's target time, with more than 1M as impressions leading to 418 referrals to site.</li> <li>2) Evrima recruited for a period of 5 months across 6 sites for a Sleep Disturbance Study, where they achieved the first referral</li> </ul>

						within 24 hours. They had 31k website views and 110 successfully enrolled participants (50% of total enrolments). Database of >80,000 people who have registered interest to learn about trial opportunities.
	Healthy Primary Care (Evrima Connect)		Register Platform	104	18	<ul> <li>Evrima Connect enterprise level recruitment analytics provide trial stakeholders with real-time visibility on recruitment progress. Key evidences are through the Sleep Disturbances Case Study:</li> <li>Evrima recruited for a period of 5 months across 6 sites</li> <li>Data-driven decisions were based on insights from Evrima Connect Platform</li> <li>Through the analysis of the Evrima Connect reporting dashboards, it was identified that there was a high level of participants being disqualified early on in the screening process</li> <li>The disqualification report highlighted why participants were being disqualified and through this identification, protocol inclusion/exclusion criteria amendments were made and resubmitted to ethics which resulted in a lower rate of disqualification at that stage of recruitment.</li> </ul>
	Healthy Primary Care (GP Search Tool)		Register Platform	26	6	<ul> <li>The GP Search Tool has successfully and easily identified potentially suitable patients. This has been evidenced through the Gout Case Study:</li> <li>Through the inclusion &amp; exclusion criteria search query, 393 patients were easily identified at 1 GP practice</li> </ul>
Torch Recruit	Primary care	2022	Register Platform/Framework Al	28 general practices	5 active trials, 2 trials in the process of roll- out, numerous others in discussion	As Torch Recruit <sup>™</sup> is in the early stages of active trial recruitment, reportable outcomes are not yet available. Torch Recruit is currently working on a <b>case study featuring The</b> <b>PARTNER Network and the IC3 trial</b> where Primary Care Collaborative Cancer Clinical Trials Group (PC4), Australia's largest primary care cancer clinical trials group, is leading the ' <u>Identifying cirrhosis and liver cancer in primary care</u> ' (IC3) trial. <sup>33</sup> Over 400 patients have already been recruited to the IC3 trial which is using Torch Recruit to identify people at increased risk of cirrhosis and trial a new biomarker test to identify people who require screening for liver cancer. Recruitment is occurring across four states, including rural sites in WA, Vic and Qld. The trial will recruit 2,800 patients and become the first exemplar trial in the PARTNER program - a national

						<ul> <li>collaboration between rural GP clinics and primary care</li> <li>researchers across Western Australia, South Australia, Northern</li> <li>Territory, Tasmania, Victoria and Queensland.</li> <li>PARTNER is part of the Australian Teletrials Program and is</li> <li>focused on bringing the trial to rural patients, where large</li> <li>populations are at risk of liver disease and liver cancer.<sup>34</sup></li> <li>PARTNER Network recruitment has commenced in South</li> <li>Australia and Victoria and will expand to Tasmania, Queensland</li> <li>and Western Australia this year.</li> <li>Torch Recruit has agreements to work with 200 general</li> <li>practitioners (GPs) including 90 GPs over the next year.</li> </ul>
Opin, powered by Opyl Limited	All health states	2019	Register Al Other: Trial recruitment and design predictive analytics	Numerous	>20 to date	<ul> <li>Key evidences include:</li> <li>(1) Completion of successful enrolment campaigns across 6 countries and 4 languages</li> <li>(2) Master Service Agreements with global Pharma companies</li> <li>(3) Partnerships with Australians CROs, clinical sites and research institutes</li> <li>(4) Successful grant recipient's and awards with academic partners e.g RMIT</li> <li>(5) Develop of Al-driven technology TrialKey as a decision- making support tool for protocol planning</li> <li>Corporate partnerships with specialist consent organisations</li> <li>(Consentic), patient advocacy groups and co-developers (RMIT University)</li> </ul>
Clinials	All health states	2021	Register Al Other: Digital marketing/advertising	NA	NA	Supported multiple vaccination studies from pneumococcal and COVID-19 to RSV, as well as deep dived into chronic conditions like type 2 diabetes, sciatica and cartridge defects. They have experience with recruiting for both medical device and drug trials, which vary greatly in their approach and commitment needed from the participants. In particular, there are four case studies highlighting this: (1) Over 32 days of advertising for a lumbar pain study in Adelaide alone, their campaign reached a total of more than 140k people, resulting in 47 eligible for trial with a lead cost of \$40 per participant (2) A time sensitive COVID-19 booster vaccine study, Clinials identified 136 eligible participants for clinicians to contact within 4 weeks of study requiring to close recruitment. Each eligible

						<ul> <li>participant cost \$28 to recruit and minimised the work needed to screen participants by over 4 times.</li> <li>(3) An international sponsor conducted a study in Australia using Clinials for severe eczema with a stringent protocol and only one site. Clinials marketing campaign reached 233 submissions, helping the sponsor to recruit over the protocol goal of 12 people.</li> <li>(4) Regent1 study for T2 Diabetes engaged with Clinials for recruitment, Clinials successfully identified 91 participants over 44 days of advertising, resulting in 54 final participants filtered by study criteria.</li> </ul>
HealthMatch	All health states	2019 (Australia) 2021 (US)	Register Al Platform/Framework Other: Digital advertising/marketing	Over 60+ sponsors Over 1500+ trial sites	Over 6500 trials hosted on site Over 100 commercially contracted trials have used HealthMatch (ranging from phase I to IV)	HealthMatch has ~40 million medical questions answered by patients, through which it can derive at minimum over 400 million further medical data. Re-engagement: HealthMatch can rapidly, accurately and effectively re-engage its existing user base to generate high quality, screened, patient referrals for clinical trials. Their hard churn rate is less than 0.5%, with mandatory questionnaire completions above 80% on average and of all patients that do not match to a trial (over 40% of patients match to 2 or more trials), 20% go on to add another condition. Their clickthrough rate (CTR) on email is 11.8 times higher than industry benchmarks and their campaigns across email, text and push notifications consistently engage more than 50% of targeted users on a per engagement basis. Over 63% of referrals in the last 180 days came from existing users in their user base.
Trialfacts	All health states	2006	Register Other: Digital marketing campaigns	300 (global)	600 studies (global)	Eight successful Australian case studies are featured on their website: 1) https://trialfacts.com/case-study/effective-clinical-trial- recruitment-plan-narrowing-field-from-500-to-24/ 2) https://trialfacts.com/case-study/how-outsourcing- recruitment-helped-one-study-get-from-20-successful- recruitment-to-83/ 3) https://trialfacts.com/case-study/trialfacts-recruits- prescreens-amp-provides-study-communications-for-over-3300- participants-in-flu-study/

						<ul> <li>4) https://trialfacts.com/case-study/trialfacts-helpsbridge-the- gap-in-oncological-studies/</li> <li>5) https://trialfacts.com/case-study/recruitment-was-more- challenging-than-i-thought-interview-with-dr-lynette-roberts/</li> <li>6) https://trialfacts.com/case-study/trialfacts-successfully- recruits-for-a-challenging-national-clinical-trial-involving-an- epidural-treatment-for-sciatica/</li> <li>7) https://trialfacts.com/case-study/from-zero-to-155- enrollment-one-researchers-road-to-successful-recruitment/</li> <li>8) https://trialfacts.com/case-study/when-the-tried-and-true- methods-fail-research-team-seeks-recruitment-help-and-finds- successt/</li> </ul>
Electronic Medical Record System (EMRS) - QLD	Tertiary care	2015	Platform/Framework	NA	Still starting (doing the first one)	Emerging, ability to sweep the EMR every 15 mins if needed.
CogStack	Primary care Tertiary care	2021-2022	Platform/Framework	3	2	Data collection ongoing, too early to provide details.
ClinTrial Refer	All health states	2013	Platform	700+	2000+	<ol> <li>2013 Pilot (Index App Haematology)- 19 participating hospital sites, data collected over a 4-year period demonstrated cross referrals increased from an average of one a month to 9 a month, 63% increase in recruitment, 60% increase in unit staffing.</li> <li>2014-2015 - Melanoma Institute Australia examined the use of the ClinTrial Refer app to support cross referral and recruitment into melanoma clinical trials between 2014 – 2015. Results reported a 23% increase in medical oncology and new patient referrals and a 127% increase in clinical trial participation. <i>Ref: Journal of Clinical Oncology- 'An App to Increase cross- referral and recruitment to melanoma clinical trials'</i></li> </ol>
Centre for Eye Research Australia (CERA)	Primary care Specialist care Tertiary care	1996	Other: Social media, support groups, industry publications, REDCap	NA	NA	NA. Specialised for eye conditions where recruitment is primarily through research referrals, managed and tracked within OpenEyes (EMR).
TriNetX	All health states	2013	AI Platform/Framework (NLP and machine learning (ML))	120+ (global) 4 (Australia)	No. of Global Feasibility Opportunities which include	Provide an avenue to query a rich anonymised data network of >220 million patients globally from USA, Japan, UK, Australia, India, and other locations. TriNetX uses real-world data using harmonised global data which is HIPAA and GDPR compliant.

	Crociolist says	2018		Quer 50	Australia = 18,500+	Over 800 Publications: https://trinetx.com/real-world-resources/publications/         Case Studies: https://trinetx.com/real-world-resources/case-studies/         Follow up the patient Roadmap for TriNetX:         https://trinetx.com/real-world-resources/events/         TriNetX Value Proposition including Diversity Lens (trying to support health care organisations (HCOs)/Pharma/contract         research organisation (CRO) do research based on ethnicity):         https://trinetx.com/products/features/#diversity-lens-overview.         Trials - Regional or Rural - The TriNetX platform allows         regional/rural hospitals to market themselves to global         HCOs/Pharma/CROs once they join our network and therefore         increasing their clinical trials, research, and         collaboration opportunities.
(Oncoshot)	Specialist care Tertiary care Post-discharge	2018	AI Platform/Framework (machine learning)	(global) 2 hospital networks/5 CROs (Australia)	400-500 (Australia)	<ul> <li>Experience in working with:</li> <li>Clinical Trial Networks (CTN)</li> <li>Hospitals with existing EHR infrastructure</li> <li>Linking CROs to rural/regional communities through access to these communities from genetic testing (OMICO) provided to rural populations in Australia.</li> </ul>
Nativve Health Research	All health states	2013	AI Framework Other: Digital advertising campaigns	200 (global) 10 (Australia)	25-30 trials (in Australia, with 9- 10 trials alone with The George Institute; ~15 studies still in grant/planning stage)	Health Research is based in the UK and has started recruitment in Australia over 24 months ago. They present an ongoing Australian COPD Case study from The George Institute which shows successful recruitment of more than 150 people within 3 months of digital advertising across NZ and Australia [original stats: 175,000 saw the ads, 4219 link clicks, 517 started the REDCap form]
TrialWire	All health states	2001	AI Platform/Framework (ML, advanced algorithms)	NA	NA	Australian Case studies listed on site: 1) https://trial-wire.com/case-studies/amd/ 2) https://trial-wire.com/case-studies/diabetes-injectable- phase-ii/
Antidote	NA	2016	AI	300+ partner organisations	NA	Two Australian case studies listed on website: 1) IBS: <u>https://www.antidote.me/antidote-case-study-ibs</u> 2) Psoriasis: <u>https://www.antidote.me/antidote-case-study-psoriasis</u>

Australian	All health states	Unknown	Register	Unknown	As at 5/6/2023,	NA. This site allows consumers to search for clinical trials that
Clinical Trials					there were 6093	are listed on the ANZCTR website. It also includes a listing of
					trials displayed	Australian clinical trial sites. It allows consumers to subscribe for
					on the Australian	clinical trial alerts and provides some clinical trial information in
					Clinical Trials	lay language.
					website	

Supporting information: NA = Not available

<sup>^</sup>Australia and New Zealand Clinical Trials Registry

\*StepUp Dementia supporting publications:

https://www.tandfonline.com/doi/abs/10.1080/07317115.2021.1929630

https://www.frontiersin.org/articles/10.3389/fpsyt.2021.710703/full

https://www.tandfonline.com/doi/abs/10.1080/10447318.2022.2109246 https://onlinelibrary.wiley.com/doi/abs/10.1111/jep.13551

https://www.cambridge.org/core/journals/international-psychogeriatrics/article/views-of-people-living-with-dementia-and-their-familiescare-partners-helpful-and-unhelpful-responses-to-behavioral-changes/40B74052441502BD72D669D091CB8FBE https://research-management.mq.edu.au/ws/portalfiles/portal/198191898/Publisher\_version\_open\_access\_.pdf

https://bmjopen.bmj.com/content/11/2/e041500

https://journals.sagepub.com/doi/10.1177/07334648221120082

https://eprints.qut.edu.au/209233/

https://journals.sagepub.com/doi/10.1177/10748407221101638

https://chsr.centre.uq.edu.au/files/4876/InterimGuidance.pdf

https://onlinelibrary.wiley.com/doi/10.1111/jep.13551

https://www.sciencedirect.com/science/article/pii/S2589958922000214

https://journals.sagepub.com/doi/10.1177/00048674211011699

https://bmjopen.bmj.com/content/12/5/e058237.abstract

https://content.iospress.com/articles/journal-of-alzheimers-disease/jad220827

https://onlinelibrary.wiley.com/doi/full/10.1111/ajag.13161 https://www.sciencedirect.com/science/article/pii/S245186542300025X



#### Figure 1. Trial recruitment technologies available during a participant's health journey.

## Discussion

We have identified several opportunities that offer potential solutions for clinical trial participant recruitment. However, Australia's national infrastructure for coordinated trial recruitment is still behind other countries such as the UK, particularly across all health care settings from primary care to tertiary care.<sup>35</sup>

Integration of technologies within existing systems, such as medical records, has been highlighted recently in Australia and internationally. A previous national report identified the need for a unified approach, jurisdictional cooperation and improved record linkage initiatives to support industry and sponsors to identify potential research participants.<sup>36</sup> Connecting EHRs, including clinical trials management systems, would allow sharing of information across jurisdictions and could improve the quality of data.<sup>36</sup> This has positively impacted participant recruitment and retention in the UK,<sup>36</sup> selection of trial participants in some European countries<sup>37</sup> and the US.<sup>38-40</sup> In the UK, longer-term interoperable EHR systems providing simple access to up-to-date datasets to facilitate trials is still too early in development to be used effectively for patient recruitment.<sup>40</sup>

Enhancing clinical trial capability and recruitment has mostly been focused within the tertiary sector, however the primary health care sector presents an opportunity to expand clinical trials access to a broader community population and in establishing a greater evidence base for the care they deliver. Whilst providing reimbursement to GPs and allied health professionals to support trial recruitment via referrals and contribute data is seen as a possible strategy towards further building clinical trial capability in this sector,<sup>7</sup> we identified technologies such as Evrima Connect and Torch Recruit that are providing important technological means to enhance the conduct of trials in the primary care. These approaches are similar to using EHRs in hospitals and although not possible at the present time, linking the two sectors to enable continuity of care would greatly benefit usual health management and clinical trial activity. The ATHENA Project in Queensland is another example of patient recruitment through EHR.<sup>41</sup>

We identified the use of AI and ML methods as an important means to improve recruitment through using predictive models across large health datasets to identify individuals who are likely to meet eligibility criteria for specific clinical trials.<sup>42</sup> As these methods advance, they may accurately predict participants who meet trial eligibility criteria, and identify key locations for trial participants. Technologies such as TriNetX and HealthMatch have already built an international network with large datasets to enhance participant recruitment and may offer the way forward in informing trial sponsors on optimal recruitment strategies, including refining eligibility criteria, target population demographics for specific disease conditions, and ability to recruit from CALD populations and remote communities.

Recent systematic reviews identifying comparative studies of digital tools for recruiting and/or retaining participants in health-related randomised controlled trials (RCTs) have been reported.<sup>43, 44</sup> While there is limited evidence on the efficiency of these tools and their impact on participants and investigators involved in RCTs,<sup>43, 44</sup> Opin powered by Opyl Limited, Clinials, Evrima Technologies, Trialfacts, and Nativve Health Research were identified in using digital tools to support successful recruitment strategies. As technology is advancing, more technology solutions may enter the recruitment space.

Academic driven participant registers utilised for trial recruitment have independently shown success, including Join Us, HMRI, and StepUp for Dementia and Ageing Research. These registers are participant driven and are mostly popular with specific disease conditions, with success evidenced by numerous publications. Similarly, certain technologies that are non-participant driven but have been notable for their success in the investigator-initiated clinical trial sector are trial search engines, including ClinTrial Refer, the Victorian Cancer Trials Link, Australian Cancer Trials and Clinicaltrials.gov. Some of these registers serve as a repository of trials so participants know who to contact for trial involvement.

Internationally, the US and the UK have invested substantially in EHR data as part of their national healthcare delivery system.<sup>45</sup> This has significant capacity to impact Australia's global clinical trial competitiveness by providing a data set that could identify potential populations for targeted recruitment to clinical trials.<sup>36</sup>

Utilising technologies to improve recruitment may have some limitations. Technologies that utilise digital advertising/marketing may be unsuccessful in groups lacking access to technology or necessary technological wherewithal to participate. Multiple approaches for optimal clinical trial recruitment and retention may be required for sub-populations. It is also worth considering what consumers prefer, as multiple technology vendors and registers used for recruitment may hinder consumer access to trials, and there may be preference for one trial platform.<sup>46</sup> Additionally, trial sponsors have different funding restrictions, capabilities and priorities, and identifying which technology is most appropriate is also an important consideration.

## **Concluding remarks**

In conclusion, novel technologies are rapidly emerging to improve the recruitment process for clinical trials in Australia. While multiple capabilities of novel technologies used for recruitment include the use of digital advertising, EHRs, and AI/ML, they offer benefits in identifying potential participants, improving accessibility, and enhancing retention in clinical trials. These technologies have potential to increase clinical trial success and ultimately improve patient outcomes.

## Acknowledgements

We gratefully acknowledge operational funding from the Australian Government's Medical Research Future Fund under grant number MRFTA000001.

## Supplementary methods and results (please refer to Supplementary section)

# References

1. MTPConnect. *Australia's clinical trials sector*. May 2021.

https://www.mtpconnect.org.au/images/MTPConnect\_Australia's%20Clinical%20Trials%20Sector%20report %202021.pdf.

2. Clinical Trials Arena. Australia accounts for 4.2% share of global clinical trial activity in 2021, (2022, accessed 30 March 2023).

3. Willson ML, Seidler AL, Aberoumand M, et al. *Latest update of the clinical trials landscape in Australia (2006 – 2020)*. 2022. <u>https://www.anzctr.org.au/docs/ClinicalTrialsInAustraliaUPDATE2006-2020.pdf</u>: Australian New Zealand Clinical Trials Registry (ANZCTR).

4. Frost & Sullivan. Australia – Preferred Destination for Early Phase Clinical Trials,

https://www.frost.com/files/6514/7374/3781/Novotech WP 20160701 v2.1.pdf (2016, accessed 14 February 2023).

5. CT:IQ. *Clinical Trial Site Recruitment Guide*. 2019. <u>https://ctiq.com.au/wp-content/uploads/Clinical-Trial-Recruitment-Guide-Final.pdf</u>.

6. Zahren C, Harvey S, Weekes L, et al. Clinical trials site recruitment optimisation: Guidance from Clinical Trials: Impact and Quality. *Clin Trials* 2021; 18: 594-605. 2021/05/28. DOI:

10.1177/17407745211015924.

7. Research Australia. *Clearing the pathway for global clinical trials*. 2021.

https://issuu.com/researchaustralia/docs/clinical\_trial\_reform\_report\_hr.

8. Harrer S, Shah P, Antony B, et al. Artificial Intelligence for Clinical Trial Design. *Trends Pharmacol Sci* 2019; 40: 577-591. 2019/07/22. DOI: 10.1016/j.tips.2019.05.005.

9. Clinials. 5 reasons why clinical trials fail to finish (and how to solve them),

https://app.hubspot.com/documents/20220561/view/325818133?accessId=b06f67 (2022, accessed 14 February 2023).

10. Australian Government. Australian Teletrial Program, <u>https://australianteletrialprogram.com.au/</u> (2022, accessed 01 May 2023).

11. Neuroscience Trials of the Future: Proceedings of a Workshop. In: *Forum on Neuroscience and Nervous System Disorders; Board on Health Sciences Policy; Health and Medicine Division; National Academies of Sciences, Engineering, and Medicine* Washington (DC), 19/08/2016 2016., National Academies Press (US).

12. DiMasi JA, Smith Z, Oakley-Girvan I, et al. Assessing the Financial Value of Decentralized Clinical Trials. *Ther Innov Regul Sci* 2023; 57: 209-219. 2022/09/15. DOI: 10.1007/s43441-022-00454-5.

13. Fitzer K, Haeuslschmid R, Blasini R, et al. Patient Recruitment System for Clinical Trials: Mixed Methods Study About Requirements at Ten University Hospitals. *JMIR Med Inform* 2022; 10: e28696. 2022/04/21. DOI: 10.2196/28696.

14. Angela L Todd DN. More and better clinical trials in health care: focusing on people, not just systems and processes. *Med J Aust* 2023; 218: 209-211. DOI: doi: 10.5694/mja2.51856.

15. Anderson M. How the COVID-19 pandemic is changing clinical trial conduct and driving innovation in bioanalysis. *Bioanalysis* 2021; 13: 1195-1203. 2021/07/20. DOI: 10.4155/bio-2021-0107.

16. TriNetX. <u>https://trinetx.com/</u> (2023, accessed 14 March 2023).

17. HealthMatch. <u>https://healthmatch.io/about</u> (2023, accessed 14 March 2023).

18. Nativve Health Research. <u>https://www.healthresearch.study/</u> (2022, accessed 14 March 2023).

19. ClinTrial Refer. <u>https://www.clintrialrefer.org.au/</u> (2013, accessed 14 February 2023).

20. Evrima Technologies: Clinical Trial Recruitment Solutions. <u>https://evrima.com/</u> (2023, accessed 14 March 2023).

21. Torch Recruit. <u>https://www.torchrecruit.com.au/</u> (2022, accessed 14 February 2023).

22. Clinical Practice Research Datalink. CPRD SPRINT (Speedy Patient Recruitment INto Trials),

https://cprd.com/cprd-sprint-speedy-patient-recruitment-trials (2022, accessed 14 March 2023).

23. Clinials. <u>https://clinials.com/</u> (2023, accessed 14 March 2023).

24. Join Us. <u>https://www.joinus.org.au/</u> (2021, accessed 14 March 2023).

25. StepUp for Dementia Research. <u>https://www.stepupfordementiaresearch.org.au/</u> (2019, accessed 14 February 2023).

26. StepUp for Ageing Research. <u>https://www.stepupforageingresearch.org.au/</u> (2022, accessed 14 March 2023).

27. Australian Cancer Trials. <u>https://www.australiancancertrials.gov.au/</u> (2023, accessed 14 March 2023).

28. Hunter Medical Research Institute Register. <u>https://hmri.org.au/participate-research/research-register</u> (2022, accessed 14 March 2023).

29. CogStack. <u>https://monashpartners.org.au/cogstack/</u> (2020, accessed 14 March 2023).

30. Australian Health Research Alliance. <u>https://ahra.org.au/our-work/data-driven-healthcare-improvement/</u> (accessed 14 March 2023).

31. Queensland Health. Integrated electronic medical record (ieMR),

https://www.health.qld.gov.au/clinical-practice/innovation/digital-health-initiatives/queensland/integratedelectronic-medical-record-iemr (1996-2023, accessed 14 March 2023).

32. Oncoshot. <u>https://www.oncoshot.com/</u> (2018-2023, accessed 14 March 2023).

33. Adams LE, Jon; Jeffrey, Gary; Thompson, Alex; Strasser, Simone; Crawford, Darrell; Gordon, Louisa; Reid, Christopher; Wallace, Michael; Chondros, Patty. The IC3 trial: Identifying cirrhosis and liver cancer in primary care, <u>https://research-repository.uwa.edu.au/en/projects/the-ic3-trial-identifying-cirrhosis-and-liver-cancer-in-primary-c</u> (accessed 14 March 2023).

34. Powell EE, Skoien R, Rahman T, et al. Increasing Hospitalization Rates for Cirrhosis: Overrepresentation of Disadvantaged Australians. *eClinicalMedicine* 2019; 11: 44-53. DOI: 10.1016/j.eclinm.2019.05.007.

35. National Institure for Health and Care Research (NIHR). Clinical Research Network,

https://www.nihr.ac.uk/explore-nihr/support/clinical-research-network.htm (2023, accessed 14 March 2023).

36. Australian Government Department of Health. *Scoping and analysis of recruitment and retention in Australian clinical trials - Final Report, June 2016*.

https://www1.health.gov.Au/internet/main/publishing.nsf/Content/EE207D978A44E4B8CA257FA90081B21 2/\$File/EY%20Final%20Report%20-

%20Recruitment%20and%20retention%20in%20Australian%20clinical%20trials%2030%20June%202016.pdf.

37. Laaksonen N, Bengtstrom M, Axelin A, et al. Success and failure factors of patient recruitment for industry-sponsored clinical trials and the role of the electronic health records-a qualitative interview study in the Nordic countries. *Trials* 2022; 23: 385. 2022/05/14. DOI: 10.1186/s13063-022-06144-9.

38. Cowie MR, Blomster JI, Curtis LH, et al. Electronic health records to facilitate clinical research. *Clin Res Cardiol* 2017; 106: 1-9. 2016/08/26. DOI: 10.1007/s00392-016-1025-6.

39. Mc Cord KA and Hemkens LG. Using electronic health records for clinical trials: Where do we stand and where can we go? *CMAJ* 2019; 191: E128-E133. 2019/02/06. DOI: 10.1503/cmaj.180841.

40. Sydes MR, Barbachano Y, Bowman L, et al. Realising the full potential of data-enabled trials in the UK: a call for action. *BMJ Open* 2021; 11: e043906. 2021/06/18. DOI: 10.1136/bmjopen-2020-043906.

41. Greaves K. The ATHENA COVID-19 Study Queensland Health.

42. Chow R, Midroni J, Kaur J, et al. Use of artificial intelligence for cancer clinical trial enrollment: a systematic review and meta-analysis. *J Natl Cancer Inst* 2023; 115: 365-374. 2023/01/24. DOI: 10.1093/jnci/djad013.

43. Brøgger-Mikkelsen M, Ali Z, Zibert JR, et al. Online Patient Recruitment in Clinical Trials: Systematic Review and Meta-Analysis. *J Med Internet Res* 2020; 22: e22179. Review 4.11.2020. DOI: 10.2196/22179.

44. Frampton GK, Shepherd J, Pickett K, et al. Digital tools for the recruitment and retention of participants in randomised controlled trials: a systematic map. *Trials* 2020; 21: 478. 2020/06/06. DOI: 10.1186/s13063-020-04358-3.

45. Australian Clinical Trials Alliance. *International Best Practice Towards a Learning Healthcare System. A scoping activity to map international approaches to embed clinical trials into the healthcare system.* 2018

(Updated 2022). <u>https://clinicaltrialsalliance.org.au/wp-content/uploads/2018/05/Embedding-International-Scan-August-updated-2022-Clean.pdf</u>.

46. Bowden J, Briggs, L. Searching for clinical trials: What patients want. Research4Me Report from a Think Tank Exploring the Issues Finding and Providing Information About Clinical Trials, and How They Might Be Solved. 2018. Research4Me.

47. nCoup - Volunteer. (accessed 28 March 2023).

48. nCoup - nCartes. (accessed 28 March 2023).