Aboriginal and Torres Strait Islander People with Cancer - Clinical Trial Access Initiative

Consultancy Report for the ReViTALISE Project, 2022

menzies
school of health research

Acknowledgement of Country

Menzies School of Health Research and the Border Medical Oncology Research Unit (BMORU) acknowledge the traditional owners and custodians of the lands on which we conduct our services/research across Australia and we recognise and value their continuing cultural heritage, beliefs and deep connection with the lands and waters.

This report is supported by funding from the Australian Government under the Medical Research Future Fund, grant ID MRFRR000023.

First printed in March 2022

For citation: Green M and Cunningham J, 2022. *Consultancy Report to inform the Steering Committee of the ReViTALISE Project: Aboriginal and Torres Strait Islander People with Cancer - Clinical Trial Access Initiative*. Report prepared for Border Medical Oncology Research Unit by the Menzies School of Health Research, March 2022. Border Medical Oncology Research Unit, Albury Wodonga, and Menzies School of Health Research, Melbourne.

Consultancy Report provided to the Steering Committee of the *Aboriginal and Torres Strait Islander People with Cancer - Clinical Trial Access Initiative ('the Initiative')*, part of the ReViTALISE project: **Re**gional **Vi**ctorian **T**rials **A**lliance **L**inkages, **I**nnovation, **S**pecial populations, **E**quity Project.

Menzies School of Health Research was commissioned to undertake this work by the ReViTALISE team in October 2021. The purpose was to provide guidance to the *Aboriginal and Torres Strait Islander People with Cancer - Clinical Trial Access Initiative* Steering Committee, to inform planning and implementation using the following components:

1. Key principles to guide the approach;
2. Summary of the 2019 VACCHO Desktop Review[1] and updated literature review (2019-2021), focusing on strategies that may improve recruitment and retention of Aboriginal and Torres Strait Islander people in Victorian regional cancer clinical trials;
3. Strategy mapping: Key challenges and potential strategies to meet the aims of the *Aboriginal and Torres Strait Islander People with Cancer - Clinical Trial Access Initiative*. Recommendations incorporate findings of both the VACCHO Review and the updated literature review.

TABLE OF CONTENTS

LIST OF TABLES

TERMINOLOGY

The term ‘Aboriginal people’ is used in this report to refer to both Aboriginal and Torres Strait Islander peoples. We respectfully recognise the diversity of cultures, identities, perspectives, and experiences of the First Peoples of Australia. Other terms may be used when referring to specific documents that have used different terminology. Consultation with Aboriginal people from regional Victoria should inform ongoing terminology.

GLOSSARY

TERM	EXPLANATION
Aboriginal Health Worker (AHW)	An Aboriginal and/or Torres Strait Islander person who has gained a Certificate II or higher qualification in Aboriginal and/or Torres Strait Islander Primary Health Care from the Health (HLT) training package[2]
Aboriginal (Health) Liaison Officer / (ALO / AHLO)	An Aboriginal and/or Torres Strait Islander person (usually an Aboriginal Health Worker) who assists multidisciplinary teams to provide culturally appropriate health care and support for individuals and families visiting hospitals and health clinics[2]
Cultural safety[3]	The National Cultural Respect Framework for Aboriginal and Torres Strait Islander Health[3] defines cultural safety as follows: Cultural safety '*identifies that health consumers are safest when health professionals have considered power relations, cultural differences and patients' rights. Part of this process requires clinicians to examine their own realities, beliefs and attitudes. Cultural safety is not defined by the health professional, but by the health consumer's experience – the individual's experience of care they are given, ability to access services and to raise concerns. The essential features of cultural safety are:* • *An understanding of one's culture;* • *An acknowledgement of difference, and a requirement that caregivers are actively mindful and respectful of difference(s);* • *Informed by the theory of power relations; any attempt to depoliticise cultural safety is to miss the point;* • *An appreciation of the historical context of colonisation, the practices of racism at individual and institutional levels, and their impact on First Nations people's living and wellbeing, in both the present and the past;* • *Its presence or absence is determined by the experience of the recipient of care and not defined by the caregiver*.'[3,p.18]
National Scheme[4]	The National Registration and Accreditation Scheme (NRAS) was established so there would be one scheme for registered health professionals in Australia. The scheme started in 2010 and now covers 15 professions including Aboriginal and Torres Strait Islander health practitioners, medical practitioners, nurses and midwives, and allied health professionals.
National Standards[5]	The National Safety and Quality Health Service (NSQHS) Standards were developed by the Australian Commission on Safety and Quality in Health Care (ACSQHC) in collaboration with the Australian Government, states and territories, private sector providers, clinical experts, patients and carers. The primary aims of the NSQHS Standards are to protect the public

	from harm and to improve the quality of health service provision. The eight NSQHS Standards provide a nationally consistent statement about the level of care consumers can expect from health services.
NICaN[6]	The National Indigenous Cancer Network (NICaN) is a web-based network of individuals and organisations interested in improving outcomes for Aboriginal and Torres Strait Islander people with cancer.
Person-centred care (PCC) as defined by The Picker Institute[7]	The fundamental underpinning of the Picker Institute's Principles of PCC is: '*Understanding and respecting people's values, preferences and expressed needs is the foundation of person-centred care*' The principles of person-centred care are: • *fast access to reliable health advice;* • *effective treatment delivered by trusted professionals;* • *continuity of care and smooth transitions;* • *involvement of and support for family and carers;* • *clear, comprehensive information, support for self-care;* • *involvement in decisions and respect for preferences;* • *emotional support, empathy and respect;* • *attention to physical and environmental needs.*[7]
Various group terms	Authors use a range of terms when publishing research or commentary about people who experience health, social and economic inequities, influenced by the author's location. Literature emerging from the USA frequently uses the terms 'racial / ethnic minorities', 'Black, Indigenous and People of Color (BIPOC) or 'racial and ethnic minority groups (REMGs)'. Other commonly used terms are 'underrepresented groups' and 'underserved groups'. This report uses the terms from the relevant article, but will specify if the population under study is First Nations peoples or Aboriginal and Torres Strait Islander people.
Yarning[8]	Yarning is a widely used term for '*an Indigenous style of conversation and storytelling*'.[8,p.51] Yarning is an accepted form of research and may include the Research Yarn, the Social Yarn, Collaborative Yarn and the Therapeutic yarn.[9] Also, the Clinical Yarn '*is used in clinical consultations with patients to build rapport and trust. It is a conversational, relaxed, open-ended style of communication that privileges storying as a vehicle to understand a patient's health issue within the context of their life, and as a way to communicate health information*.'[10,p.378]

ABBREVIATIONS

ACSQHC	Australian Commission for Safety and Quality in Health Care
AWH	Albury Wodonga Health
BMORU	Border Medical Oncology Research Unit
CALD	Culturally and linguistically diverse
CBPR	Community Based Participatory Research
CT	Clinical trial
DH	Department of Health (Victoria)
DHHS	Department of Health and Human Services (Victoria) (now DH)
GVH	Goulburn Valley Health
HRQOL	Health Related Quality of Life
NHMRC	National Health and Medical Research Council
PREM	Patient Reported Experience Measure
PRO	Patient Reported Outcome
PROM	Patient Reported Outcome Measure
RCT	Randomised controlled trial
SES	Socioeconomic status

EXECUTIVE SUMMARY

Menzies School of Health Research was commissioned to undertake this work for the '*Aboriginal and Torres Strait Islander People with Cancer - Clinical Trial Access Initiative'* Steering Committee, to inform planning and implementation of the Initiative. This report builds on the VACCHO Desktop Review[1] by updating key principles and guidelines relevant to the ReViTALISE project (Section 1) and the literature review (2), and synthesising strategies that may increase Aboriginal people's clinical trial participation in regional Victoria (3).

Barriers to the full participation of Aboriginal people in clinical trials relate to study design, gatekeeping, and mistrust of research and health institutions due to the historical context of colonisation combined with harmful research practices, amongst other barriers. The issue is widely recognised as one of equity and social justice, in addition to compromising scientific validity when clinical trial findings do not represent the population affected by the condition.

Many strategies devised to address the barriers are reported in the literature, primarily, though not exclusively, from the USA regarding racial and ethnic minority groups. Australian and international governance and strategy documents aimed at addressing the lack of equitable access to clinical trials are summarised in Section 2, in addition to commentary following the COVID-19 pandemic, which has highlighted disparities in clinical trial participation. Consistent themes emerged, with commonalities between Australian and international literature including the centrality of addressing

the issue of mistrust of research and health institutions. Further, recognising the culturally bound nature of healthcare for Aboriginal people is integral to the success of strategies.

There are a number of ways to conceptualise strategies that have been reported as successful at increasing diversity in clinical trial participation. Although there is considerable overlap, for the purposes of this report, strategies have been categorised as presented in Figure 1. It is important to note that in addition to the overarching themes, strategies related to *2.2.3.3 Community outreach and engagement* apply across the entire project. The strategies have been identified for the *Aboriginal and Torres Strait Islander People with Cancer - Clinical Trial Access Initiative*, however they have relevance to other ReViTALISE streams.

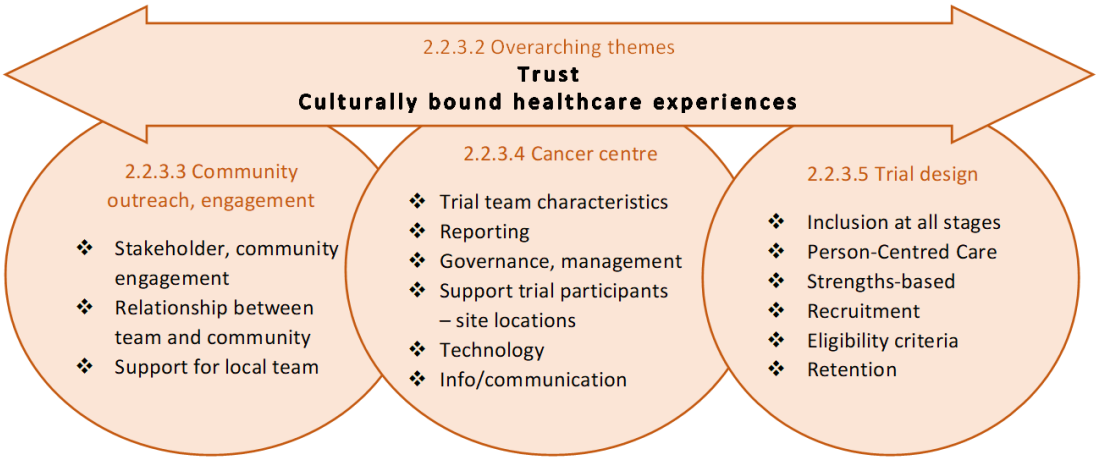

FIGURE 1 FRAMEWORK FOR CONCEPTUALISING EVIDENCE

Critical issues for the design and implementation phases of this project include: the meaningful involvement of Aboriginal people from the beginning; improved reporting of Indigenous status; overcoming gatekeeping and addressing key aspects of study design. Models of care and strategies that have potential to address identified barriers are presented in Section 3, along with potential linkages to other streams of the ReViTALISE project. There is no single solution and the Steering Committee will need to consider the most appropriate mix to meet the aims of the *Aboriginal and Torres Strait Islander People with Cancer - Clinical Trial Access Initiative*.

PREAMBLE

This report has been written by researchers who are not Aboriginal or Torres Strait Islander people. Although the authors have many years of experience working with Aboriginal and Torres Strait Islander people in clinical and research settings, it is possible that our presence as non-Aboriginal researchers has the potential to distort representation of the voices of the Aboriginal and Torres Strait Islander people involved in, and affected by, the work. It is critical that ongoing implementation of the ReViTALISE project is guided by Aboriginal people.

1. KEY PRINCIPLES AND GUIDELINES

The key national policy documents which guide best practice research involving Aboriginal and Torres Strait Islander people (hereafter respectfully referred to as Aboriginal people) in Australia reflect the strength and centrality of Aboriginal voices. Efforts to improve health outcomes for Aboriginal people require recognition that the experience of healthcare is culturally bound, and that direction from Aboriginal people is critical. This section lists key documents which have particular relevance to the ReViTALISE project regarding: research ethics and practice; health service delivery; and cancer specific documents. An expanded table with more information about each of the documents is in Appendix 1. National policy and framework documents specific to clinical trials are in Section 2.2.1.

TABLE 1.1 KEY DOCUMENTS: PRINCIPLES AND GUIDELINES

INSTITUTION, YEAR	DOCUMENT NAME	SUMMARY
RESEARCH ETHICS AND PRACTICE		
National Health and Medical Research Council (NHMRC) 2018a	Ethical conduct in research with Aboriginal and Torres Strait Islander Peoples and communities: Guidelines for researchers and stakeholders[11]	Six core values: spirit and integrity; cultural continuity; equity; reciprocity; respect; responsibility. Contains acknowledgement of connection to Country and definition of health.
NHMRC 2018b	Keeping research on track II[12] (Companion document to above.)	Implementation of values and ethics in 8 steps of the research journey. Discusses rights held by Aboriginal and Torres Strait Islander people regarding research.
NHMRC 2018c	Road Map 3[13]	Strategic framework to guide NHMRC's efforts to improve outcomes for Aboriginal and Torres Strait Islander people. Key areas: workforce development;

		community engagement; and identified research priorities.
The Australian Institute of Aboriginal and Torres Strait Islander Studies (AIATSIS) 2020	Code of Ethics[14]	Emphasises four principles which underpin appropriate research with Aboriginal and Torres Strait Islander people: Indigenous self-determination; Indigenous leadership; Impact and Value; and Sustainability and Accountability.
Jamieson et al. 2010	Ten principles regarding health research among Indigenous Australian populations[15]	Recommends that researchers consider five essential and five desirable principles from the initial design phase.
Harfield et al 2020	Quality Appraisal Tool (QAT)[16]	A checklist to guide research quality assessment from Aboriginal and Torres Strait Islander people's perspectives.
Huria et al. 2019	CONSIDER statement: CONSolIDated critERtia for strengthening the reporting of health research involving Indigenous Peoples[17]	International collaborative effort that aims to strengthen research praxis and advance Indigenous health outcomes. Provides checklist for the reporting of research involving Indigenous peoples.
HEALTH SERVICES		
The Wardliparingga Aboriginal Research Unit of South Australian Health and Medical Research Institute, 2017	National Safety and Quality Health Service (NSQHS) Standards User Guide for Aboriginal and Torres Strait Islander Health[18]	The NSQHS Standards require health services to improve health care provision for Aboriginal and Torres Strait Islander people; the User Guide is designed to support health services to meet the standards.
Commonwealth of Australia, 2016	Cultural Respect Framework for Aboriginal and Torres Strait Islander Health, 2016-2026[3]	Aims to ensure accessible, responsive and safe health services for Aboriginal and Torres Strait Islander people through embedding cultural respect principles in health systems.
The Australian Health Practitioner Regulation Agency, 2020	Aboriginal and Torres Strait Islander Health and Cultural Safety Strategy 2020-2025[4]	Aims to eliminate racism from the health system and aims to make cultural safety, as defined by Aboriginal and Torres Strait Islander people, 'the norm'.
CANCER SPECIFIC		
Cancer Australia, 2015	National Aboriginal and Torres Strait Islander Cancer Framework[19]	Established strategic direction to address disparities and improve cancer outcomes for Aboriginal and Torres Strait Islander people with cancer.
Cancer Australia, 2018	Optimal Care Pathways (OCP) for Aboriginal and	Designed to complement the tumour-specific OCPs, focusing on aspects of the care pathway that need to be responsive

	Torres Strait Islander people[20]	to the needs of Aboriginal and Torres Strait Islander people with cancer. Contains detailed guidance for health practitioners and service planners on optimal care across the cancer continuum. Includes clinical trials.
Cancer Australia, 2020	A Guide to Implementing the Optimal Care Pathway for Aboriginal and Torres Strait Islander People with Cancer[2]	Suggests activities to support OCP implementation at health system and health service levels, and health professional training. Overarching activities: 1) Culturally competent workforce 2) Integrated planning and care delivery 3) Culturally appropriate care coordination and support.

An important shift in the orientation of health programs aimed at improving health outcomes for Aboriginal people has been the adoption of strengths-based approaches. Two reports published by the Lowitja Institute examine the impact of deficit discourse on health policy[21] with reference to health of Aboriginal people, and contribute to moving the narrative away from a focus on deficit.[22] A strengths-based approach is described as rejecting the discourse that '*narrowly situates responsibility for problems with the affected individuals or communities, overlooking the larger socio-economic structures in which they are embedded*'.[22,p.vi] Strengths-based approaches recognise the strengths and capabilities of Aboriginal people and can incorporate a number of different elements:[22]

- privileging Indigenous ways of knowing and being;
- use of decolonising methodologies; shift to an Indigenous worldview;
- recognition of protective factors e.g. family and culture connectedness;

- viewing factors such as knowledge, skills, networks, extended family and cultural identity as assets;

- recognition of structural factors that influence health and wellbeing; and

- recognition that outcomes valued by Aboriginal people may be more influenced by cultural values than outcomes anticipated by the health system.

The best practice guidance outlined in this section constitutes important baseline knowledge for development and implementation of research involving Aboriginal people. The next section summarises the VACCHO Review[1] and the recent literature relevant to the aims of the ReViTALISE project.

2. SUMMARY OF THE LITERATURE

2.1 VACCHO DESKTOP REVIEW 2019

2.1.1 BACKGROUND

The VACCHO Desktop Review[1] (the VACCHO Review) was commissioned in early 2019 to inform the *Improving Cancer Outcomes for Victorian Aboriginal Communities Working Group*, which was established by the Department of Health and Human Services (DHHS, now Department of Health (DH)) and VACCHO. The Review reported on existing evidence and knowledge in three areas: 1) Improving Aboriginal participation in clinical trials and research; 2) Improving culturally safe and effective cancer treatment for Aboriginal people with cancer; and 3) Improving Aboriginal people's self-identification and the quality of cancer data. Evidence was collected from peer reviewed and grey literature from 2010-2019 focussing on Aboriginal and Torres Strait Islander people in Australia, supplemented by information about First Nations people in other countries and other underrepresented groups. The summary below focuses on aspects of Item 1, which contained 3 questions relevant to the ReViTALISE project:

1.1 What is the current level of participation by Aboriginal and Torres Strait Islander people in clinical research? What are the current issues in collecting this information?

1.2 What is the evidence that inclusion and exclusion criteria are a barrier for Aboriginal people to participate in research?

1.3 What are effective best practice models for improving Aboriginal people's participation in clinical research

The information to follow includes the VACCHO Review findings in general, findings related to eligibility criteria, barriers and facilitators to participation, models of care that may improve participation of Aboriginal people in clinical trials and a summary of recommended next steps.

2.1.2 SUMMARY OF VACCHO REVIEW FINDINGS

National and state level policy documents, strategic plans and guidelines summarised in the VACCHO Review reflected the revised agenda regarding clinical trials, aimed at making Australia a 'destination of choice' for trials. Most documents addressed the need to increase access to clinical trials in the general population. While striving for equity of access was evident in some documents, the participation of Aboriginal people in clinical trials was not the focus. A tension was noted between the aim of streamlining ethics approval processes, and the opportunity of Aboriginal people to participate in research that is culturally safe. In addition, ensuring the confidentiality of Aboriginal trial participants is an aspect that requires management due to small numbers of Aboriginal patients in cancer treatment centres.

2.1.2.1 Current level of participation in clinical research

In an effort to summarise the current level of participation of Aboriginal people in clinical research, distinction was made between (i) clinical research not specific to Aboriginal people (e.g., international cancer treatment trials)

and (ii) clinical research designed to include Aboriginal people either solely or substantially.

(i) No information was available about the level of participation of Aboriginal people in clinical trials that are not specifically aimed at Aboriginal people. Investigators were either not reporting or not collecting data on the Indigenous status of participants. It was noted that National Cancer Collaborative Trials Groups are required to demonstrate participation of Aboriginal people in clinical trials, however there was no information regarding whether this was currently happening. No information about ethnic background is provided on the Australian New Zealand Clinical Trials Registry (ANZCTR) website. No direct information was found regarding interest and/or willingness of Aboriginal people to participate in clinical research. Variability in clinical trial participation rates between urban and rural areas in NSW and Victoria was reported, however figures were not provided for Aboriginal patients specifically.

(ii) The numbers of trials specific to Aboriginal people, and the number of Aboriginal people participating in them, has increased since ~2010. At the time of the VACCHO Desktop Review (2019), the ANZCTR records indicated that over 50 trials relating to Aboriginal health had been completed and another 81 trials were in progress. Most were not cancer related, however it has become evident that Aboriginal participation in clinical research studies can be high in the right circumstances.

2.1.2.2 Eligibility Criteria and Participation of Aboriginal People in Clinical Trials

No evidence was publicly available on inclusion and exclusion criteria as a barrier to participation by Aboriginal people; a highly relevant analysis by Cunningham and Garvey[23] which was underway at the time of the VACCHO report will be included in section 2.2. International reviews which identified strict exclusion criteria as a barrier to trial participation by under-represented groups were located and are summarised below. It was noted that exclusion based on English language proficiency may be a factor in the reduced participation of Aboriginal people in clinical trials, however the relevant research was not focussed on Aboriginal people. Exclusion due to lack of English language proficiency was evident in 21% of trials assessed in one review[24] examining this issue, though it was less common for cancer trials. It is unclear which factors contributed to differences in culturally and linguistically diverse (CALD) patients enrolling in clinical trials: English language proficiency as an explicit exclusion criterion; or the difficulties and costs of including participants for whom English is not their preferred language.

2.1.2.3 Barriers and Facilitators to Participation

The literature around barriers to and facilitators of participation in clinical trials for ethnic minority populations primarily comes from the USA and there are a number of frameworks through which to examine them, e.g., consideration of 1) awareness; 2) opportunity and 3) acceptance/refusal (decision-making).[25] Interpreting the evidence for the Australian context

requires caution, particularly regarding the health insurance system. However, many barriers and enablers reported from the USA are similar to those identified in a systematic review of randomised controlled trial (RCT) participation for Indigenous peoples in Australia, New Zealand, Canada and the USA by Glover et al.[26] Key barriers identified included: lack of access; mistrust of health and research institutions; inappropriate research materials; and loss to follow-up.[26] From the large number of barriers identified in the literature (see Box 1), amongst the most important were those related to gatekeeping and study design, both of which are barriers to opportunity.

BARRIERS TO PARTICIPATION OF ABORIGINAL PEOPLE IN CLINICAL TRIALS

Gatekeeping	Whether or not a care provider actually discusses possible trial participation with a given patient.
Study design	Stringent inclusion and exclusion criteria;
	Timing, duration, location and focus of the study.
Other	Mistrust of health and research institutions;
	Lack of knowledge about trials;
	Perceived harms/fear;
	Ineffective cross-cultural communication;
	Patients' lack of English proficiency;
	Lack of staff diversity;
	Inappropriate materials with respect to language, literacy level, and cultural beliefs/practices;
	Logistical and cost factors; and
	Lack of care provider knowledge about relevant open trials.

BOX 1 SUMMARY OF BARRIERS TO PARTICIPATION OF ABORIGINAL PEOPLE IN CLINICAL TRIALS[1]

In the review by Glover and colleagues,[26] facilitators were broadly consistent with elements cited as improving participation in clinical trials of under-represented groups as summarised in Box 2. In summary, key enablers include a commitment to inclusion, building long-term (and meaningful) relationships with community, greater flexibility in study design and implementation, and employing appropriate staff.

FACILITATORS OF PARTICIPATION OF ABORIGINAL PEOPLE IN CLINICAL TRIALS

Inclusion	Commitment to inclusion by both individuals and institutions;
	Building inclusion into study design, increased protocol flexibility.
Partnerships	Partnership, relationship building, early engagement, community-identified priorities/needs, Indigenous leadership and guidance.
	Creating community partnerships and involving the community throughout the research process. Allowing time for this.
Cultural competency	Increasing cultural competency of clinicians and researchers.
Recruitment	Targeted recruitment; Indigenous led, through Indigenous health services and Indigenous schools, via Indigenous media;
	Active targeting and recruitment of under-represented groups.
Practical barriers	Assisting with logistical and cost barriers;
Study location	Conducting trials in community settings;
Study teams	Employing Indigenous research staff; Appropriate bicultural/bilingual staff, training and supporting researchers from diverse communities;
Study design	Shifting the balance towards pragmatic clinical trials that focus on the needs of groups that are disproportionately affected by cancer(s) rather than on particular types of cancer;
	Drawing on Indigenous traditions, incorporating on Indigenous worldview / knowledge systems into intervention design;
Study materials	Appropriate language(s) and appearance, input from community/Indigenous staff on materials.

BOX 2 SUMMARY OF FACILITATORS OF PARTICIPATION OF ABORIGINAL PEOPLE IN CLINICAL TRIALS[1]

2.1.2.4 Improving Aboriginal People's Participation in Clinical Research: Best Practice Models

Three models were identified as worthy of consideration in the Victorian context: patient navigation, tele-trials and Community-Based Participatory Research (CBPR).

2.1.2.5 VACCHO Review recommendations for ongoing work

The VACCHO Review[1] outlines recommendations regarding clinical trials on pages 8-9. Areas requiring further research and collaboration were identified and will be incorporated into the findings of this report. In brief, further work is needed around: health services' collection of Indigenous status; clinical trial inclusion and exclusion criteria; community knowledge of clinical trials; balancing streamlining of ethics approvals, cultural safety and confidentiality; meaningful opportunities for Aboriginal community engagement in all aspects of clinical trials; and investigation of different models of care, which will be discussed in more detail in the following section.

2.2 PUBLISHED LITERATURE 2019-2021

There is consensus in the literature that diversity in clinical trial participation is a critical factor that will help reduce health disparities and promote health equity. Justifications to increase diversity in clinical trials include: reasons of social justice, given the historical context and the health disparities experienced by First Nations people and other minority populations; the compromised credibility of clinical trials that do not represent the relevant

population; and to facilitate scientific discovery.[27] Efforts to increase the participation of diverse populations in clinical trials have become prominent internationally and within Australia, with the issue brought into sharp focus due to the disproportionate effects of the COVID-19 pandemic.

A large body of research has reported various mechanisms to address the lack of diversity in clinical trials, however the key messages, particularly regarding the broad approach, are consistent. Strategies need to be powerful and sustained enough to lead to the endpoint of addressing health disparities, which means they need to address the social determinants that shape individual health.[28] Targeted strategies are required at all levels of the health system: a piecemeal approach is unlikely to achieve meaningful and sustained change.[29, 30] Being guided by an Indigenous worldview and accepting that Western science is not the only consideration will require genuine and longstanding partnerships with Aboriginal stakeholders.

The methods used in the literature search covering 2019 – Nov 2021 were based on the VACCHO Review Item 1 and are detailed in Appendix 2. Section 2.2.1 will first present recent policy, guideline and framework documents that have emerged from government and research group activities and that are specific to clinical trials. To build on the summary of barriers to participation in clinical trials outlined in Box 1, recent research will be presented in terms of broad implications for health policy (Section 2.2.2). Strategies that may improve opportunity for Aboriginal people to participate in clinical trials will then be presented according to relevant aspects of clinical trials (Section 2.2.3). Finally, research and commentary that has emerged

from the COVID-19 pandemic will be summarised according to its relevance to the ReViTALISE project (Section 2.2.4). Further details about articles from which the evidence is extracted is tabulated in Appendices 4, 5 and 6.

2.2.1 Clinical trial policy, guideline, framework documents (post 2019)

There have been several significant developments at the national level in Australia since 2019 and internationally, which are detailed in Appendix 3 across three tables:

Appendix 3.1 Recent Australian developments and their implications for the ReViTALISE project. This table includes a brief overview of the National Clinical Trials Governance Framework (CTGF) and Guide for Implementation,[31] and national guidance on tele-trials[32-34] (though these contain limited consideration of Aboriginal people specifically), amongst other references;

Appendix 3.2 Extraction of items which are directly relevant to the *Aboriginal and Torres Strait Islander People with Cancer - Clinical Trial Access Initiative*, from the National Clinical Trials Governance Framework (CTGF) User Guide (also named 'Guide for Implementation'); and

Appendix 3.3 Relevant International framework/policy documents.

Key areas of concordance between the CTGF and the Indigenous Trials Access Project include the core governance principles of 'Equity' and

‘Organisational culture, partnerships and collaboration’, which articulates the centrality of ‘Partnering with consumers’ and other stakeholders.

The CTGF Actions, which are accompanied by strategies, key tasks, and examples of supporting evidence to help address each Action, *‘are also mandatory for health service organisations that provide a clinical trials service’*.[31,p.8] CTGF items with implications for the ReViTALISE project are extracted in Table 2.2. The CTGF Guide for Implementation[31] specifies the roles and functions of different stakeholders, for example, for the category of Patient Safety and Quality Improvement Systems:

- Boards/CEOs; ‘*ensure availability of data and information to support quality assurance and review of CT services across the health service organisation or trial site’*;[31,p.48]
- Managers; ‘*ensure that safety and quality systems for undertaking CTs reflect the role of the health service organisation within a wider network of other health services and providers’*;[31,p.48]
- Clinical trial workforce; ‘*communicate with clinicians in other health service organisations to support good clinical outcomes, for trial participants’*;[31,p.48]
- Clinical trial sponsors; ‘*support quality processes and reporting as required on the conduct of CTs within the health service organisation or trial site’*;[31,p.49]
- Consumers, patients’ trial participants, carers and families; ‘*use opportunities to take an active role in providing feedback, complaints and compliments about experiences in CT participation and,*

communicate with the organisation about any opportunities for improving CT services'.[31,p.49]

Although not specific to clinical trials, a recently developed Culturally Adaptive Governance Framework has been included in Appendix 3.1 (and further discussed in 'Governance of clinical trials') due to its potential for use in the ReViTALISE project.

2.2.2 Barriers and their implications

In the literature review (2019-2021), barriers to clinical trial participation were consistent with those found in the VACCHO review: mistrust of health services and research; lack of knowledge about trials; perceived harm or fear; communication issues, particularly related to cultural aspects; lack of English language proficiency; lack of staff diversity; inappropriate study materials; logistical factors; lack of care provider knowledge about relevant open trials; and a mismatch between where people receive their care and where studies are conducted.

A directly relevant study, published since the VACCHO Review, examined barriers to Aboriginal and Torres Strait Islander people's participation in clinical trials.[23] The analysis of online documents aimed to identify factors that may systematically reduce opportunities for Aboriginal and Torres Strait Islander people's participation in clinical trials. The study examined 365

Phase 3* (n=266), Phase 4* (n=11), or Phase N/A* (n=88) cancer interventional studies with at least one Australian site, that were registered on ANZCTR between 2014-2018. The findings suggested that barriers related to opportunity are relevant to Aboriginal and Torres Strait Islander people in Australia, including: study design (rigid inclusion/exclusion criteria, study location, focus, timing and duration); and gatekeeping (whether a care provider discusses potential trial participation with a given patient).[23] These factors are outlined in more detail below:

- Location of residence: 89% of eligible trials had only major city/inner regional sites; 39% of Aboriginal and Torres Strait Islander people live outside these areas. This applied to Phase 3/4 trials and Phase N/A. Although many Aboriginal and Torres Strait Islander cancer patients are required to travel to major centres for treatment, the follow-up visits required by trials would make it difficult if not impossible for them to participate. Though internet based trials may increase participation by those living away from urban areas, reliable access to and affordability of digital technology may compromise access to such trials. Teletrials may address the distance issue in part, however digital access may be an issue for these trials also.
- Cancer types addressed by trials: Between 2009-2013, seven cancer types (lung, breast, colorectal, prostate, head and neck, uterine and liver) accounted for 58% of new cases among Aboriginal and Torres Strait Islander people. These cancer types were studied in 46% of Phase 3/4 trials in 2014-2018, compared with 60% of Phase N/A trials. Even if the diagnosed cancer type is being studied, restrictions to enrolment such as

* Phase 3: aim to test if the new treatment is better than the current best standard treatment. Participants are randomised to the new or the standard treatment groups. New treatments generally need to go through more than one Phase 3 trial to be accepted. Phase 4: long-term monitoring after a drug has been licensed for use – assesses long-term side-effects. Phase N/A: trials without phases (e.g. non-drug trials). https://www.australiancancertrials.gov.au/about-clinical-trials.aspx .

specific tumour type, response to prior treatment, or time since diagnosis, further reduce eligibility. Cancer types with late-stage presentation and low survival cancers (e.g. lung cancer) are likely to be understudied, due to the emphasis on breast and prostate cancer, and the nature of Phase 4 interventions.

- Exclusion from trials due to comorbidities/health status was very common, especially in Phase 3/4 trials. Given the higher levels of comorbidity in Aboriginal and Torres Strait Islander people (both cancer patients and in general), these exclusions impact Aboriginal and Torres Strait Islander patients more than non-Aboriginal patients. The advantages of using narrow eligibility criteria may be outweighed by reduced generalisability of results and may restrict knowledge of diversity in response to treatment.
- Exclusion for other reasons were noted in the report: '*Language proficiency was more likely to be stated as a requirement in Phase N/A trials, especially those involving treatment with psychotherapy. Very few trials specified exclusion on the basis of smoking status. About one in eight Phase 3/4 trials (12%) included a statement to indicate that 'other criteria may apply'; that is, the documentation provided online did not include all relevant information*'.[23,p.42] The authors found that '*Nearly one in five trials included an exclusion relating to psychological and/or psychiatric conditions and/or a history of substance abuse, with similar proportions for Phase 3/4 (24%) and Phase N/A trials (23%). A substantial minority of trials (38% of Phase 3/4 and 35% of Phase N/A) included a statement to indicate that investigator judgment or opinion should be used in deciding on patient eligibility'*.[23,p.42] This raises the possibility that some Aboriginal patients will be seen as too 'difficult' and therefore excluded. Implicit bias is possibly a factor here also.

Streamlining of ethics and governance approvals underway in Australia may compromise efforts to ensure cultural safety for Aboriginal and Torres Strait Islander trial participants. The authors highlight the need for systematic

collection and reporting of Indigenous status of potential and actual trial participants, as part of a national minimum data set.

Strategies reported in the literature that have successfully, or that may, address the barriers described above are outlined in the next section.

2.2.3 Strategies for improved diversity in clinical trial enrolment

2.2.3.1 Introduction

The drive towards increasing diversity in CTs as a way of improving health outcomes needs to be underpinned by awareness that the lack of diversity in CT participation is not the result of deficits in particular populations, e.g., due to their education, awareness or biology. Minority populations have been systematically excluded from research, or only included in research done 'to' the population in question using damaging and disrespectful practices.[15, 35] Neither approach produces a benefit to the population and the result is mistrust in the health system and research. One response to this history has been the incorporation of 'decolonising methodologies' in research, including in Australia with Aboriginal and Torres Strait Islander people.[36] The seminal publication 'Decolonizing Methodologies' by Linda Tuhiwai Smith more than 20 years ago, is now into its third edition.[35] The latest edition acknowledges that significant progress has been made, however, 'research' remains a dirty word for many Indigenous people in the world. Decolonising methodologies seek to redress the power imbalance, by centring Indigenous knowledge and voices, creating meaningful partnerships with Indigenous people, ensuring

that the research agenda is driven by Indigenous people and that outcomes benefit Indigenous people.[35, 36]

Overarching themes that align with decolonising methodologies will be presented in Section 2.2.3.2: they are integral to the work to be undertaken. There are different ways to conceptualise the evidence regarding effective or proposed strategies;[29, 37, 38] a useful organisational framework by Regnante and colleagues[29] was identified and adapted as presented in Figure 2. Strategies have been grouped under categories of: Community outreach and engagement (2.2.3.3), which apply across the entire project; Cancer centre (2.2.3.4); Trial design (2.2.3.5). The use of overlapping shapes is deliberate, e.g., both 'site locations' and 'Info / communication' could be considered an aspect of both 'Cancer centre' and 'Trial design'. Section 2.2.3.6 will summarise models of care that may be particularly relevant to the ReViTALISE project. Strategies have been identified for the *Aboriginal and Torres Strait Islander People with Cancer - Clinical Trial Access Initiative*, however they have relevance to each ReViTALISE stream.

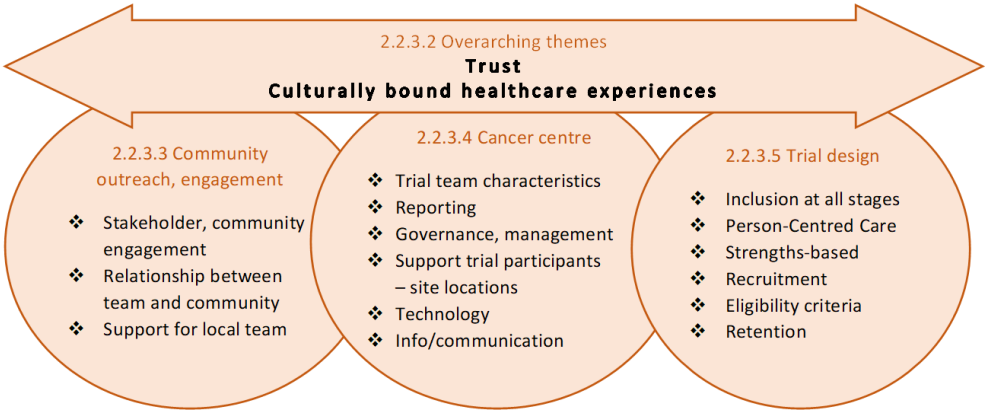

FIGURE 2 FRAMEWORK FOR CONCEPTUALISING EVIDENCE

2.2.3.2 OVERARCHING THEMES

Trust

The issue of (mis)trust of health and research institutions was evident in many studies;[38-46] this issue is widespread, multilayered and challenging to address in Australia given the context in which the mistrust emerged and ongoing colonisation. Commentary from the USA regarding the COVID-19 pandemic identified trust as a critical issue and recommended focussed strategies to build and sustain trust (Appendix 6). Using COVID-19 to enhance individual knowledge and awareness of clinical trials was proposed,[40] however the focus was on strategies that address research practices and infrastructure such as: commitment to ongoing engagement and partnership with communities;[47] acknowledging the past, recognising personal bias and systematic inequalities, and addressing barriers through effective policies and procedures;[40] and recognising that researchers cannot simply ask Black communities to '*simply be more trusting*'[48,p.e121(2)] as structural racism has been created and sustained primarily by white people. Addressing other barriers such as appropriate trial sites (Section 2.2.3.4) and less restrictive study designs (as outlined in Section 2.2.3.5), was also reported as going some way to enhance trust in health institutions.

Culturally bound healthcare

A highly consistent, overarching theme evident in the literature about clinical trial participation of diverse populations is that successful strategies recognise the culturally bound nature of the health care experience and that this needs to be evident throughout the intervention and/or study design. Napoles[49] expressed this succinctly: the success of strategies was dependent on "*a culturally-informed investment of resources that required key stakeholder input via the establishment of genuine partnerships with the targeted populations and their providers*".[49,p.11] This takes time, attention and resources, all of which are usually underestimated.[49] Inherent in such an approach is the importance of addressing cultural safety and cultural issues, which needs to be integrated into the study design. Community engagement is necessary from the beginning and at all project levels (governance, management, implementation). Culturally congruent study design was reported to be one of several facilitators in enrolment of minority populations in gynaecological cancer clinical trials in the USA.[50] Other facilitators were benefits to participation, such as appropriate compensation and/or access to care, and a desire by participants to help their families and communities. However, the authors cautioned that these facilitators will be expressed and interpreted differently by each community, geographic region, language group, or disease type, hence the centrality of community engagement and patient-oriented design of clinical trials, regardless of the area of study, as mechanisms to meaningfully address minority enrolment disparity.

Understanding the importance and implications of trust and culturally bound healthcare needs to underpin health services research with Aboriginal and Torres Strait Islander people. The following section (2.2.3.3) outlines community outreach and engagement strategies: this issue is intentionally listed first, as it is of critical importance and applies across the project.

2.2.3.3 COMMUNITY OUTREACH AND ENGAGEMENT

Stakeholder and community engagement

This aspect of CT management is closely linked to the relationship between the trial team and community, but highlights the need for genuine engagement at the organisational or formal level, in addition to the level of individual community members,[30, 50-53] which is likely to mean longer timeframes and higher costs. The findings were consistent across adult and paediatric studies.[30, 50-52, 54] A collaborative review aimed at describing best practice for conducting paediatric clinical trials with Indigenous communities in the USA described three best practice strategies, each of which require strong engagement: 1) *early and sustained engagement* 2) *building Indigenous research capacity*, and (3) *supporting community ownership and oversight of research*.[54,p.1650]

Involvement of stakeholders and development of strong partnerships entail an acceptance that this will impact or shape the trial design and conduct. In a report on how community involvement affected a RCT about childhood hearing loss in rural Alaska,[55] community involvement was strengthened by

the use of multiple modalities of involvement and inclusion of lead stakeholders on the study team. This engagement and participation resulted in changes to the research question, comparators, outcomes and measures, telemedicine protocols, and recruitment and retention (further detail is in Appendix 4, Robler et al.).[55]

This approach was consistent with the experiences of using CBPR to design, conduct and evaluate three RCTs with American Indian communities;[42] the researchers emphasised that respect for the importance of diverse knowledge systems that account for both Indigenous knowledge and colonial science contributed to the RCT's success. Other factors were: long standing partnerships characterised by learning between tribal members and researchers; establishing trusted partnerships and receiving tribal approval before embarking on the RCTs; ensuring trial design facilitates opportunity for all eligible tribal members to take part; and hiring tribal members. Attention to the inclusion of women as key stakeholders and decision-makers for their family was also reported as an important component of increasing diversity in CT participation.[56]

Relationship between trial team and community

An unequivocal message was that the relationship between clinical trial teams and the community needs to be actively built from the beginning, with consistent efforts made to build and maintain a strong relationship between the research team and community staff.[26, 38, 57] Indeed, this was described as

the most significant undertaking in the preparation phase in a study involving a qualitative RCT in Canadian Indigenous communities.[57] Developing an understanding of community issues, expectations and priorities will require meaningful engagement. Non-judgemental staff are an important aspect of building respectful relationships, demonstrated by e.g., acceptance of the culture at local clinics regarding pace and tone, or collaboration regarding the appropriateness of the wording of text messages. Maintaining a strong relationship requires availability to meet with various community members and community groups (not only gatekeepers), cocreating community presentations, reports or follow-up plans, and taking part in community events such as sharing of food or community feasts. Other strategies included: working with trusted community partners,[38] tribal and health service leaders; including family in decision making, while maintaining confidentiality;[58] and learning about the local community, which may include community beliefs around illness, tribal customs regarding illness and death, and modifying communication styles if required.

A CBPR framework was used to understand information needs of African American women regarding participation in cancer CTs.[56] The CPBR framework was integral to reaching the outcomes of interest and was found to have potential to strengthen the long-term relationship between researchers and the community, and ensure community perspectives are reflected in research design and implementation.[56]

Support for local team

Employing staff from the relevant population in the study team, and providing appropriate support to them, was integral to recruitment of minority populations. In Maar and colleagues'[57] secondary analysis of RCT qualitative data to identify culturally safe research practices in Canadian Indigenous communities (mentioned in 'Relationship between trial team and community'), good relations between the research team (who were based outside the community) and community staff was very important, and supportive communication was key to this, with timely, open responses to questions, kindness, respect and support. Incorporation of professional and personal staff development was a positive strategy. This project was about hypertension and community staff were trained in blood pressure monitoring or management; task shifting from nursing staff to community staff in turn supported recruitment.[57] (also see 'Recruitment / enrolment).

2.2.3.4 Cancer Centre

Characteristics of trial teams (cultural background, language, training)

Training of research personnel was consistently described in the literature as a mechanism to improve enrolment of minority participants to clinical trials.[41, 51, 52, 59, 60] Niranjan and colleagues conducted 91 interviews with oncology researchers and clinicians and identified a number of aspects that are likely to contribute to increased minority enrolment in CTs. The team identified

training and educational needs,[60] examined bias and stereotyping amongst health professionals regarding minority enrolment in CTs[61] and summarised institutional barriers and facilitators.[62] Participants in this study acknowledged the need for, and benefits of, training of research professionals to increase cultural awareness, particularly regarding appropriate communication skills. The authors recommended flexible learning options including classroom training, live online classes, training on demand and self-study courses and evaluation of the education programs. Respondents also identified the need to allow for sufficient time for potential participants to process important and complex information as a vital component of oncology CT recruitment. Bias and stereotyping of minority populations were evident, leading to withholding of CT opportunities from potential minority participants,[61] though participants also commonly described addressing research misconceptions to build trust.

A similarly strong message was to create trial teams that better represent who is being recruited, for impact on recruitment as well as community trust of research generally.[26, 35, 41, 52, 58, 59] (also see ‘Recruitment /enrolment).

Reporting clinical trials

It is critical to categorise, measure and report on participation in clinical trials to maximise the credibility of results, for reasons of social justice and to facilitate scientific discovery. The gap in the collection and reporting of Indigenous status in clinical trials in Australia and the need for multilevel action to address this is well documented.[23] Articles from the USA consistently call for transparent reporting of racial composition on RCTs;[44, 63]

one author proposed that journals and editors be **required** to include detailed information on race/ethnicity in publications and on trial registration websites, even if the numbers are underpowered, to show differential outcomes or treatment effects.[63]

Governance of clinical trials

Appendix 3.2 outlines recent developments regarding governance of clinical trials in the Australian context, with implications for the ReViTALISE project extracted. The framework strategies are consistent with the literature and include involvement of Aboriginal people at all levels, and ensuring communication and study materials are culturally safe.

This information needs to be considered alongside Duke et al.'s Culturally Adaptive Governance Framework (CAGF),[64] which is summarised in Appendix 3.1. Using the CAGF, '*building relationships begins with First Nations people working across the research stakeholder network',*[64,p.11] not simply in advisory or consultative roles. Figure 3 illustrates what encompasses '*community'* under this framework. The Framework is currently being utilised in at least one national trial, which has commenced recruitment: the Flash GM Study[65] (continuous blood glucose monitoring in type 2 diabetes), which incorporates Rumbalara Aboriginal Cooperative as a pilot site and Goolum Goolum Aboriginal Cooperative (Horsham, Victoria) as a satellite site.

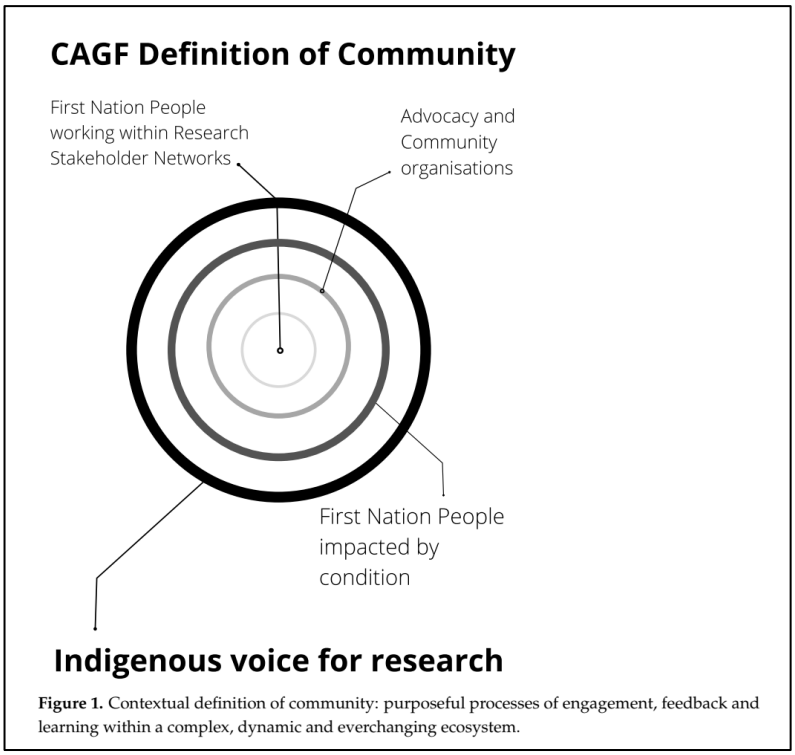

FIGURE 3 GRAPHIC REPRESENTATION OF COMMUNITY IN THE CAGF[64,p.12]

Management of clinical trials

The drive towards systematic data collection in research and healthcare, including that which will enable monitoring of progress and inform appropriate strategies, requires consideration of whether the measures are meaningful to the population in question. Involvement of an appropriate patient advisory group during all phases was identified as a notable practice in the management of CTs.[27, 29] Maar and colleagues[57] analysed a large qualitative dataset (n=142) collected during a 5-year pragmatic RCT designed to achieve improvements in blood pressure control across six culturally diverse Indigenous communities in Canada. A combination of reflection and face-to-

face visits helped address areas that needed improvement, particularly regarding cultural safety aspects such as understanding who speaks for the community, and that community priorities may not align with the trial topic. An important aspect was in-person visits to the community by the Principal Investigator and other staff, which facilitated trouble shooting of technology, recruitment and clinical issues throughout the study. *Building* and *maintaining* respectful relationships were key messages, along with good communication and support for the local team, commitment to co-design, supporting task shifting (see 'Support for local team') and reflecting on mistakes or areas for improvement that support learning and cultural safety.[57]

Strategies that support trial participants

The evidence strongly supports flexible scheduling of clinical trial arrangements as a mechanism to increase diverse participants.[38, 51, 53, 58, 66] This may include: extended hours; variable data collection mechanisms; choice of interview location and follow-up arrangements – e.g., home recruitment visits with phone follow-up; and avoiding scheduling appointments during important community events. Use of strategies that make it easier to participate by addressing cost and logistical barriers was a consistent message e.g., providing transport, child care, incentives, travel vouchers, multiple forms of contact and consideration of appointment scheduling.[40, 50, 53, 58, 59, 66] Building of relationships was also mentioned by many researchers, with an acknowledgement that this will require additional staff time.[59]

The location of study sites is critical and identifying centres that are more accessible to minority populations (e.g. regional medical centres) is more likely to improve participation.[23, 40] Incorporating consideration of cultural issues, such as awareness of cultural practices and norms regarding food or communication, or consideration of cultural festivals in planning recruitment,[58] was also viewed as an essential component to overcome identified barriers. Other strategies include making personal contact (face to face or patient navigators by phone), engagement through community groups, appropriate communication, engaging investigators or study team members from the relevant population, and improving cultural awareness of the study team. The use of incentives was a commonly reported strategy to aid recruitment and retention,[38, 50, 51, 67] or to complete baseline measures,[38] however it was important to ensure the amount was respectful, not coercive.

Use of novel technological strategies

Novel technological solutions were proposed for different phases of clinical trials such as: social media for recruitment;[68] multimedia approaches to aid informed consent to improve participation of culturally and linguistically diverse (CALD) populations; use of data collection to inform strategies[35, 38, 51] or to assess participants' motivation for participating;[38] use of Apps depending on the age of potential participants;[66] e-health data, social media, gamification in CVD CTs;[41] and telehealth or teletrials.[23, 40, 59]

Information / communication – Language, appropriateness of study materials

Development of appropriate study materials was a consistent strategy to increase enrolment of underrepresented populations. This includes meeting the appropriate level of reading comprehension and health literacy[35,69] and ensuring that materials are culturally relevant and appropriate through considerations of Indigenous traditions and worldview.[26, 30, 70] Merely translating existing instruments may not be sufficient, due to lack of cultural appropriateness or relevance.[71,45] In their commentary about the challenge of language in increasing diversity in trial populations, Willis and colleagues[45] advocated for the need to distinguish between trials in which obtaining informed consent is the primary language requirement, compared with trials where use of language is part of the intervention, such as communicating symptoms. These authors advocate for robust translation methods if existing instruments are used, including forwards-backwards translation, and input from multiple translators and clinical reviewers. In an Australian study which examined barriers to clinical trial participation for Aboriginal people, a requirement of language proficiency was more likely to be stated in Phase N/A trials, especially those involving psychotherapy treatment (see Section 2.2.2 for more on this study).[23]

Consideration of communication with the patient's family and community,[43, 56, 58] study invitation processes[58], and study branding[51] is required. Respondents in the study examining information needs of African American women (also see 'Relationship between trial team and community') indicated

that decisions to participate would be made by the individual in consultation with the family, and that recruitment should occur in community settings. Information tools need to: have cultural relevance (e.g., more stories with African American women); reflect both positive and negative aspects of CT participation; outline the nature of involvement (consent, enrolment and participation); and use appropriate language.[56]

Information / communication - Education

Three key factors emerged in this area: i) lack of awareness of CTs was considered a barrier to participation in the general population and diverse populations (including patients, families, communities); ii) health professionals' awareness of the need and justification for diversity in CTs warranted education; and iii) specific issues relating to paediatrics, including trust.

i) Strategies to increase awareness and acceptance of CTs were consistent in advocating relevant community involvement at the earliest stages of developing such interventions and ensuring materials used were culturally relevant.[30] The study mentioned in 'Relationship between trial teams and community' highlighted the importance of including the perspectives of African American women, as key stakeholders and decision-makers for their family, and the need to provide research information in a way that facilitates family discussion and decision-making regarding CCTs.[56] As mentioned earlier, the COVID-19 pandemic may be a mechanism to enhance knowledge and awareness of RCTs.[40]

ii) The importance of building a trusting relationship between trial investigators and clinicians was identified in an Intervention Mapping approach aimed at modifying recruitment behaviours of investigators to increase diversity in CTs: this 6 step trial is yet to be evaluated but may be informative for this aspect of the project.[72] In a qualitative study involving 91 interviews with health professionals at 5 US cancer centres, some respondents viewed racial and ethnic minorities as 'less promising' participants, or in some cases withheld trial opportunities based on these perceptions,[61] suggesting the need for education of staff regarding cultural awareness, bias and stereotyping in order to increase enrolment. Although not specifically about clinical trials, recent work in the Australian context[46] identified practical tools and approaches that could form the basis of professional education for clinicians when communicating with Aboriginal people about cancer and its treatment.

iii) In paediatrics, education of families about the merits of clinical research as a mechanism to improve trust in medical researchers was one of the main facilitators reported in two qualitative studies involving health professionals[43] and parents[39]. Following the latter work, a formative research process has been conducted to design a culturally appropriate cancer CTs education program for African American and Latino communities.[73] This work, which is not focussed on paediatrics, is summarised in Appendix 4.

2.2.3.5 TRIAL DESIGN

Reconsidering all aspects of CT design was a consistent theme in the literature, with inclusion to be considered at all stages[45] and a balance

needed between community interests and the 'colonial scientific rigor' of RCTs[42]. There is evidence that working with the community to co-design the intervention, to ensure it is relevant to and accepted by the community, has potential to improve inclusion of diverse populations,[57] and strengthen the trial's patient-centredness.[63] The importance of community involvement from the earliest stages was consistent, e.g., interviewing patients to inform the study protocol.[51] Inclusion of outcomes considerate of tribal community concepts of success, as well as those found in standard colonial scientific research practices, were proposed to measure the success of CBPR RCTs and increase trial participation amongst American Indian populations.[42] This is consistent with strengths-based approaches as described in Section 1.[22]

Recruitment / enrolment

Key messages around recruitment strategies that may increase enrolment of diverse populations in clinical trials consistently centred on culturally and linguistically appropriate strategies[70] (e.g. awareness that Western individual informed consent processes may not align with decision-making for non-Western cultures[41] and respect for preferences related to privacy and gender), the importance of site selection where the target population is, and allowing sufficient time for the development of relationships necessary for successful recruitment[51]. Input from the relevant community in the development of recruitment materials and strategies was also identified as an important strategy. Regnante and colleagues[29] reported on strategies used by multiple US cancer centres that facilitated participation of racial/ethnic minority groups in cancer trials. These included: cultural competence training

for staff that includes information about motivators, challenges, and barriers to research participation; community advisory boards composed of diverse stakeholders to guide the development, feasibility, and implementation of research studies; lay community representatives—ambassadors—from the communities to cultivate community talent and tap into their expertise and networks to reach potential research participants; and transparency in sharing research findings, using plain language summaries to help participants understand their contributions to science and their community. These measures served to strengthen community partnerships with patients and care partners. This report noted that the actual invitation to participate in a study (particularly an intervention treatment study) must come from an investigator or coordinator involved in the study, not from community representatives. Ensuring the composition of research staff represents the population served also contributed to successful recruitment.

This information is consistent with an analysis of barriers and strategies regarding recruitment of low income racial/ethnic minorities to childhood obesity RCTs in the USA,[38] which collated a useful list of strategies. Trial staff were surveyed about successful strategies used in different trial stages and asked to nominate their top three strategies (and barriers). Strategies reported were (1) careful planning, (2) working with trusting community partners, (3) hiring recruitment staff who were culturally sensitive, personality appropriate, and willing to work flexible hours, (4) contacting potential participants actively and repeatedly, (5) recruiting at times and locations convenient for participants, (6) providing incentives to participants to complete baseline measures, (7) using a tracking database, (8) evaluating

whether participants understand the activities and expectations of the study, and (9) assessing participants' motivation for participating.[38]

Inclusion / exclusion criteria

Modification of inclusion and exclusion criteria was consistently advocated in the literature as a strategy to enhance participation and ensure the trial population reflects those who are most likely to receive the therapies.[23, 29, 40, 59, 74] Regnante and colleagues[29] proposed that in order to support recruitment and retention of minority populations in CTs, consideration of inclusion and exclusion criteria should be part of established practices, and include whether such criteria disproportionately affect the relevant population, but are not clinically relevant in a specific trial.

Retention

Evidence for improving retention included community engagement throughout the process, recognition of the longer time frames and higher costs incurred, and research collaborations. Relationship centred retention was successfully used to help build a study team community whose needs and input were valued and incorporated, in an effort to enrol African Americans into a renal risk variant clinical trial.[51] To address commonly reported practical barriers to retention, multiple strategies have been reported

as successful including: use of incentives; travel vouchers; multiple forms of contact; building relationships; and flexibility in scheduling.

A systematic review of strategies for recruitment and retention of racial/ethnic minorities to Alzheimer's disease research reported three major themes used by studies with the highest participant retention rates: follow-up communication (e.g. mailing reminders); maintaining the community relationship (e.g. hiring a community outreach worker, hosting regular volunteer events); and convenience (e.g. conducting annual assessment in homes).[75]

2.2.3.6 MODELS OF CARE

Patient navigation

As reported in the VACCHO Review,[1] there is some evidence to indicate that patient navigation may be an effective model to increase participation of Aboriginal people in CTs. Reported benefits of this model include recruitment of underrepresented groups,[30, 76] increased retention and fewer treatment interruptions,[30] improvement in HRQOL of Latinos with cancer,[77] higher satisfaction with care after cancer treatment guided by a patient navigator[76] and the provision of a link between researchers and underserved communities.[78] Barriers overcome by patient navigators regarding access to CTs amongst the general population include fear, communication issues, transportation difficulties and perceptions about treatment and providers.[79]

Nickell and colleagues[78] used a prospective RCT of a patient navigator intervention within a CBPR project, to increase the access of ethnically diverse low-income breast cancer patients to information about research participation opportunities. The work was conducted within an established community organisation that provided health navigation services primarily in non-clinical settings, the Shanti's Margot Murphy Women's Cancer Program (Shanti). Earlier work developed a Health Research Engagement Intervention (HREI) that provided general education about breast cancer research and resources to independently find participation opportunities on an online breast cancer resource that matches patients to research studies (broader than clinical trials due to negative associations with the term). Language-concordant Shanti Care Navigators (SCN), who were trained in peer support using a non-directive, client-centred mode of communication, were involved in every stage of the RCT which tested the efficacy of the HREI. Study participants' access to the online breast cancer resource was increased through a multilingual helpline and by reducing the literacy demands of the website. The study found no significant difference between intervention and control groups' health seeking behaviour. Competing priorities, such as accommodating demanding jobs, commutes, family caregiving, treatment side effect and comorbidities, limited the motivation of participants to seek enrolment information. Participants did not view research as a priority in the context of their busy daily lives, compared with the typical activities that SCNs assisted with, e.g., food, financial assistance and emotional support, however they were willing to participate in research if the study protocols were convenient and addressed relevant issues. The study demonstrated

that factors other than knowledge and awareness may influence trial participation decisions. Importantly, study participants' trust in the SCNs did not translate to trust in doctors and the 'research enterprise' and the authors concluded that additional efforts are required to address this issue.

Community Based Participatory Research (CBPR)

Community Based Participatory Research (CBPR) is a method to improve community health outcomes that establishes community and research stakeholders as equal partners in the research project.[27] Community involvement in all areas of leadership and decision making is facilitated as an integral aspect. Although there is widespread support for this approach as a mechanism to improve health outcomes amongst underserved groups, what 'participation' means is variable.[27] The processes necessary to undertake CBPR require strong community engagement, as discussed above in 'Stakeholder and community engagement' and 'Relationship between trial team and community'. Recent studies have examined this approach in relation to: COVID-19 vaccine trials;[47] a prospective RCT in the context of CBPR as discussed above in 'Patient navigation';[78] a systematic review focussing on elements of CBPR which improved the rate of accrual of racial and ethnic minority community members;[27] using CBPR to design RCTs with American Indians;[42] and developing a framework for evaluating CBPR for Indigenous people with gout in New Zealand[80].

Recent Australian work employing CBPR with Aboriginal communities outside the cancer sphere include community-based responses to alcohol

related harms,[81] and an evaluation of a CBPR project aimed at working towards elimination of rheumatic heart disease.[82] The latter assessed project alignment with the NHMRC principles for conducting research with Aboriginal and Torres Strait Islander people (Reciprocity; Respect; Equality; Responsibility; Survival and Protection; Spirit and Integrity) (see Appendix 1). Challenges for facilitators and community researchers in adhering to the principles were identified and exposed the '*pervasive effects of colonial power dynamics, even in a project seeking to be highly responsive to community needs*'.[82,p.46] It was noted that shifts in power relations, which are to be expected using a CBPR approach, do not impact infrastructure and socioeconomic challenges. The authors recommended that process indicators be key aspects of evaluation of CBPR projects rather than outcomes, with a commitment to 'both way' learning being integral to success. CBPR was found to promote equitable partnerships through key elements including: complementary expertise of researchers and Aboriginal communities; openness to learning; trust; and local community leadership.[81] The use of decolonising principles, and the promotion of Indigenous knowledge, experience, perspectives and control (e.g. through 'both-way' learning) were critical.[82] Implementation of CBPR required regular communication using multiple modes, local decision making power and the provision of direct benefits to communities (e.g. training of community researchers,[82] paid employment of community members, access to funding for program implementation and access to data).[81]

The VACCHO Review[1] referenced a strategic plan developed through extensive consultation in the US to apply CBPR to clinical trials. The plan,

'*Communities as Partners in Cancer Clinical Trials: Changing Research, Practice and Policy*'[83] can be translated to the Australian setting. The plan recommended the inclusion of both community representatives (ideally affiliated with a community-based organisation) and patient advocates (who have experience as a patient with cancer, carer or family member) as an essential part of the research process. The plan is summarised in Seifer et al[84] and the full report [83] details an Action Guide for implementation across seven categories, outlining the recommendations, target audience, proposed steps and resources.

Tele-trials

The use of telemedicine and teletrials is commonly recommended as a mechanism to improve inclusion in CTs; development and acceptance has been accelerated by responses to the COVID-19 pandemic.[40, 55, 59, 74, 85] The VACCHO Review[1] highlighted that teletrials programs must be purposefully designed to facilitate inclusion of Aboriginal patients, and evaluated to assess their performance in improving opportunities for participation.

Optimal Care Pathways (OCP)

The recent '*Optimal Care Pathway for Aboriginal and Torres Strait Islander people with cancer*' and accompanying *Guide to Implementing the Optimal Care Pathway for Aboriginal and Torres Strait Islander people with cancer*[2] may be useful resources to inform program design (also see Section 1 and Appendix 1). The two documents complement the tumour-specific OCPs and

focus on the aspects of cancer care that need to be responsive to Aboriginal and Torres Strait Islander people. The OCP is underpinned by the Aboriginal and Torres Strait Islander Cancer Framework[19] (also outlined in Section 1 and Appendix 1) and follows seven steps (though it recognises that not all patients will follow every step):

1. Prevention and early detection
2. Presentation, initial investigations and referral
3. Diagnosis, staging and treatment planning
4. Treatment
5. Care after initial treatment and recovery
6. Managing recurrent, residual and metastatic disease
7. End-of-life care

The importance of connection to clinical trials is one of the evidence-based principles that has been considered in developing the OCP. Steps 3 - 7 contain general reference to clinical trials and further resources are given.

The *Guide to Implementation* aims to support implementation of the OCP at different levels of the health system, and identifies three overarching priorities: 1) Culturally competent workforce; 2) Integrated planning and delivery of care across services; and 3) Culturally appropriate care coordination and support. The *Guide to Implementation* recognises connection to culture and the principles necessary for culturally appropriate and responsive cancer care, in addition to evidence-based principles that guide quality care in the health system more generally, such as person-centred care. Check lists to monitor progress towards each of these priorities

are included (e.g., does the service '*routinely seek and act on feedback from Aboriginal and Torres Strait Islander people on their experience*?',[2,p.14] with pointers to how the OCP can help).

Pathway-specific implementation activities (according to the steps identified in the OCP) also include information provision, checklists to monitor progress, how the OCP can help and activities across different health system levels. As an example, for Steps 3 and 4 *'Diagnosis, staging and treatment planning'* and *'Treatment',* the system / policy level consideration is '*Consideration by national clinical trial organisations about ways to increase access to and participation in cancer clinical trials by Aboriginal and Torres Strait Islander people*'. A number of health service activities are suggested, including '*Implement strategies to encourage and facilitate Aboriginal and Torres Strait Islander participation in clinical trials and research'*. Cancer statistics for Indigenous and non-Indigenous people and illustrative health services case studies are presented, as well as definitions, links to resources such as the National Standards[5] and references.

2.2.4 Summary of relevant commentary emerging from the COVID-19 pandemic

Although the recent articles discussed in this section are not directly related to increasing cancer clinical trial participation for Aboriginal people, they have been included as some of the strategies and approaches are likely to be relevant. Further detail about the literature mentioned here is contained in Appendix 6. The changes to clinical trial implementation necessitated by the COVID-19 pandemic have been discussed in commentary or perspective articles[40, 48, 74, 85] and presentation of USA COVID-19 vaccine trial data[47]. Concerns were expressed that the pandemic may exacerbate the existing disparities in RCT participation of diverse populations and may impact vaccine generalisability.[40] Doroshow and colleagues[74] outlined the aspects of clinical trials that have demonstrated prompt adaptability due to the pandemic including: electronic informed consent; reduction of travel requirements by transferring clinical care to local providers; availability of oral agents at local sites; decreasing the impact of minimal protocol deviations on assessment of CT site performance; remotely auditing CT documents; and accepting the validity of telehealth CT assessments. While some changes have potential to improve access to clinical trials for communities that have been under-represented in trials (e.g. engagement,[47] telemedicine and remote informed consent procedures[74]), other mechanisms suggested may be at odds with approaches that are imperative for research with Aboriginal people, such as harmonization and standardisation of documentation,[74] as study materials need to be understandable and relevant to the population.

There are concerns about the disproportionate effect of the COVID-19 pandemic on diverse populations, combined with the existing lack of participation in clinical trials by African Americans, American Indians / Alaskan Natives and other marginalised groups in the USA.[40, 48] Distinct from the impact on individual outcomes, this may also jeopardise external validity of trial results.[40, 48] Lackland et al.[40] described COVID-19 as providing an opportunity for clinical researchers to address negative perceptions of RCTs amongst minority communities, recognise personal bias and systemic inequalities, and consequently to build trust and awareness of RCTs amongst groups who have had negative past experiences. Developments in telehealth, building competencies in the community based health workforce and other strategies necessitated by the pandemic are also described by several authors as opportunities to enhance access to clinical trials by underserved populations.[40, 48, 85] Modification of eligibility criteria is also recognised as a mechanism to enhance participation.[40, 48] Some recommendations are USA specific, however the proposal of Warren et al.'s[48] that clinicians, investigators and pharmaceutical companies must produce convincing evidence that they are trustworthy - and overcome extensive historical evidence to the contrary - is relevant in the Australian context. They note that the ideas and practices that create today's 'structural racism' were primarily created by white people, hence are not primarily the responsibility of Black people to fix.[48] Potential strategies for demonstrating trustworthiness include exemplary informed consent processes with maximum transparency, and ensuring priority access to vaccines for people considered to be most disadvantaged.[48]

Following COVID-19 vaccine trials, Andrasik et al.[47] advocated for setting clear established goals for Black, Indigenous and People of Color (sic) (BIPOC) enrolment from the beginning of the study, to prevent these enrolment slots being absorbed by enrolment of white people, due to their enrolment outpacing that of BIPOC communities in the USA. Population-specific trials and setting of recruitment goals according to established frameworks were also proposed by Andrasik et al.[47] to ensure the inclusion of under-represented populations in research that could be beneficial to them. This is consistent with the American Society of Clinical Oncology's (ASCO) 2020 '*Policy Statement on Cancer Disparities and Health Equity'*,[86] which proposed stratified recruitment as a strategy to ensure adequate representation of groups at risk of disparate outcomes for the disease or treatment of interest (Appendix 2.3). Prolonged and directed engagement with communities also aided inclusive enrolment in these trials; the ASCO authors saw ongoing commitment to such partnerships as potentially helping research and research institutions to be viewed by communities as trustworthy.

2.2.5 OTHER STUDIES OF INTEREST

The studies flagged in this section have relevance to particular aspects of CT design, which may inform potential ReViTALISE project/s. More detail about the studies is contained in Appendix 5.

A survey and framework development around 'return of value' in research[87] could inform how feedback to participants is incorporated in study designs, at

their inception. This may include asking potential participants and local advocacy groups what information they would like to receive during / after the study and in what format. Researchers would need to consider, design and articulate what the study will give back, such as skills, personalised response to the study (e.g., medication / intervention response), or an understanding of what their contribution has meant. Other benefits may include feedback on identification of genetic risk, the impact of cancer on other conditions, or potential benefit to the community due to increased numbers of Aboriginal people being involved in trials.

A systematic review of the use of translated Patient Report Outcome Measures (PROMs) in CTs[71] may be useful. The authors recommend using recently developed guidance (the 'SPIRIT-PRO extension') for reporting in CT protocols where PROs are a primary or key secondary outcome. The SPIRIT-PRO extension provides international consensus-based guidance on protocol content. The 16-item checklist includes consideration of whether PROs have been translated and/or culturally adapted.

Development and evaluation of a web-based decision support tool for minority populations in the USA found significantly improved readiness to take part in a cancer CT.[88, 89] Although rigorous development and assessment in the *Aboriginal and Torres Strait Islander People with Cancer - Clinical Trial Access Initiative* context is necessary, there may be relevant learnings from this work.

An Australian qualitative study,[46] which aimed to identify practical tools and approaches around communication with Aboriginal and Torres Strait Islander

people about cancer and its treatment, could form the basis of professional education for clinicians.

3. STRATEGY MAPPING

This section aims to present options that may increase enrolment of Aboriginal people in clinical trials, and what would be required to implement them, to inform decision making of the Steering Committee (SC). Issues that are critical to address will be outlined initially (3.1), based on evidence cited in Sections 1 and 2 of this report. To varying degrees, these issues cannot be solved by the ReViTALISE project, however strategies that recognise and address them can be integrated. A suite of potential activities will then be outlined (3.2), followed by evidence-based guidance regarding the design and implementation of specific aspects of clinical trials (3.3).

Key decisions / actions for the SC include:

- Engage the right stakeholders including consideration of background and other information required to enable informed decision making and participation;
- Establish the mechanisms through which to achieve the project aims
    - increase participation of Aboriginal people in an existing single CT i.e., set within a specific trial?
    - increase participation across a range of trials e.g., via general awareness raising and education and/or patient navigation?
    - create new CT/s with the primary aim of recruiting Aboriginal people using evidence-based mechanisms?
- Decide which institution is most appropriate to oversee the work (to be named on ethics applications etc);

- Establish the SC governance role for the *Aboriginal and Torres Strait Islander People with Cancer - Clinical Trial Access Initiative* as compared with the Advisory Group;
- Establish roles and responsibilities, and clear lines of accountability and reporting for the SC, the project manager and the project team.

3.1 KEY CHALLENGES AND CRITICAL ISSUES

3.1.1 INVOLVEMENT OF ABORIGINAL PEOPLE AT ALL STAGES

The broad understanding of health (Appendix 1, NHMRC 2018a) of many Aboriginal people, connection to Country, and the culturally bound experience of healthcare make this issue critical. Recognition of Aboriginal people's history of negative experiences with the health system and with research is required, accompanied by transparent strategies to ensure positive experiences. This will require additional time and resources. It is important to not rely on a single voice: a range of organisations and representatives is necessary, including both community members (which entails paying patients and carers as part of the project team, as per Table 3.2, p.62) and community leaders. It is strongly advised to aim for establishment of long-term relationships with relevant organisations and individuals, and ensure participants are allowed equal voice. It is expected that changes to clinical trial design will result from this.

3.1.2 Reporting of Indigenous status

This is a larger scale challenge than this project alone can address, however the collection and reporting of the Indigenous status of patients is critical to measuring impact. Raising awareness of the critical nature of the issue at the highest levels of the health system, as well as the local level, may contribute to improving performance in this area i.e., from board members to administrative staff and patients. Points to raise include that this is part of health services' adherence to the National Standards,[5] and that there is a '*User Guide for Aboriginal and Torres Strait Islander health*'[18] to help health services achieve acceptable implementation of the Standards. Reporting of Indigenous status needs to occur at multiple levels: national, hospital, primary health care and trial documents including resultant publications.

3.1.3 Overcoming gatekeeping and improving study design

Implicit and explicit bias and systematic inequalities should be addressed through continuous education of health professionals involved in CTs. Locate study sites in local services and locations that Aboriginal people use. Rigid inclusion and exclusion criteria are consistently cited as a significant barrier to participation of Aboriginal people in clinical trials. It is important to identify trials in which these criteria can be modified or influenced and possibly design new trials to address this barrier.

3.2 SUITE OF ACTIVITIES

This section presents a range of activities across different areas of the health system for the SC to discuss. The first two ('3.2.1 Establish network' and '3.2.2 Collect baseline information') are foundational and will require further development by the SC. Subsequent activities are not linear or mutually exclusive; some are likely to be complementary. A distinction has been made between large multinational clinical trials initiated and run by pharmaceutical companies, and investigator-initiated trials (including registry trials), as these will require different strategies.

3.2.1 ESTABLISH NETWORK AT GOVERNANCE AND PROJECT LEVEL

Establishment of a network of organisations and staff to implement the ReViTALISE *Aboriginal and Torres Strait Islander People with Cancer - Clinical Trial Access Initiative* should be guided by Aboriginal people involved in regional health services, the non-Aboriginal people who work alongside them, clinical trial staff and consumers.

3.2.1.1 Steering Committee

As discussed at the first SC meeting (membership as per Table 3.1), the following additions would strengthen the committee: Senior Rumbalara Aboriginal Cooperative staff (preferably two positions); additional organisations as advised by Rumbalara Aboriginal Cooperative; other ReViTALISE streams as appropriate (e.g., telehealth and registry trials); and VACCHO representative/s.

TABLE 3.1 EXISTING STEERING COMMITTEE MEMBERS (21 JANUARY 2022)

NAME	ROLE	NAME	ROLE
Dr Javier Torres (JT)	Aboriginal and Torres Strait Islander People with Cancer - Clinical Trial Access Initiative Co-lead	Ms Carole Mott (CM)	Clinical Trials Coordinator, Goulburn Valley Health
Associate Professor Craig Underhill (CU)	Aboriginal and Torres Strait Islander People with Cancer - Clinical Trial Access Initiative Co-lead	Ms Karen Matheson (KM)	Clinical Trials Coordinator, Goulburn Valley Health
Ms Donna Long	ReViTALISE Project Manager	Ms Leah Lindrea (LL)	Aboriginal Research Assistant, Melbourne University, Shepparton
Professor Joan Cunningham (JC)	Menzies School of Health Research	Ms Tennille Lewin (TL)	Program Manager, Regional Research Teaching Hub
Dr Monica Green (MG)	Menzies School of Health Research	Ms Cynthia Scott (CS)	Aboriginal Liaison Officer, Goulburn Valley Health
Mr Ron James (RJ)	Consumer Representative	John Davies (JD)	Consumer Representative

3.2.1.2 Project implementation team

Establish the groundwork for a project team, with the aim of developing a detailed implementation plan, led by the ReViTALISE project officer, then putting it into action. Membership of the project team would be guided by the activities planned and advice from the SC. The connection and relationships between the SC, the project team and community need to be strong and culturally safe, with clearly defined roles. Areas of overlap between the SC and the project team need to be addressed. Formal and paid positions for patients, family and carers should be integrated, with reflective

communication practices and support for community workers. The information needs of external stakeholders require identification and may include regular communications, meetings and/or workshops.

TABLE 3.2 POSSIBLE PROJECT PARTNERS

ORGANISATION / PERSON	POSITION	POTENTIAL INVOLVEMENT*
The ReViTALISE project	Project Officer	Link between SC and project team.
The ReViTALISE project		Other ReViTALISE project hubs e.g. teletrials.
Shepparton Hospital/GVH	ALO / AHW Clinician/s	Link between project team and community.
Rumbalara Aboriginal Cooperative	Clinician/s	Advice on patient pathways, opportunities for interaction with community members.
Peter Copulas Cancer and Wellness Centre	CT nurse/s	
Consumers, families, carers		Provide input from Aboriginal and Torres Strait Islander people affected by cancer.
Private providers (e.g., Genesis Care, Shepparton Private)		
Trial site		Identify local people with necessary skills.
Academic institutions		Ethics approval, research staff support.
Other relevant organisations		TBA

* *To be determined based on Steering Committee decisions and negotiations.*

3.2.2 COLLECT BASELINE INFORMATION

Approximately six - twelve months for collection of baseline information to understand what is happening in the region and inform design of the *Aboriginal and Torres Strait Islander People with Cancer - Clinical Trial Access Initiative*.

TABLE 3.3 PROPOSED BASELINE INFORMATION

BASELINE DATA	LOCATION OF INFORMATION	FORMAT	ACCESS (WHO?)	STORAGE	PURPOSE
CANCER AND CLINICAL TRIAL DATA					
Cancer data re Aboriginal people in regional Victoria: case numbers; cancer types; locations.					
Characteristics of recent CTs: teletrials or face-to-face.					
Characteristics and number of trials currently open in regional Victoria.					
Characteristics of planned/future CTs					
Number Aboriginal and Torres Strait Islander people enrolled in regional Victorian CTs.					
Recent, current and proposed CTs: - Features of recruitment processes. Identify barriers and opportunities. - Features of eligibility criteria; identify possible barriers					
INFORMATION TO INFORM TRAINING / AWARENESS RAISING ACTIVITIES					
Staff currently involved in CTs in regional Victoria – location and role.					
Identify enablers of change eg CT investigators / coordinators.					
Current activities to inform Aboriginal people about open CTs.					
Community: Knowledge, perceptions and willingness to participate in CTs.					

Note: Shaded row indicates a study which requires ethics application and approval.

3.2.3 EDUCATION CAMPAIGN FOR CLINICIANS, PATIENTS, COMMUNITY

Using the information collected above, develop deeper understanding of the knowledge and attitudes of trial staff and gatekeepers towards participation of Aboriginal people in CTs, and design, implement and evaluate an information

campaign based on these results. This may involve working with the Regional Research Teaching Hub using a multipronged approach that addresses needs of health professionals and gatekeepers, as well as patients and community, to enable them to make decisions about CT participation that is right for them. This may complement the recent Australian work[46] which identified successful strategies used by health professionals when communicating with Aboriginal people about cancer and its treatment, and may assist in targeting subsequent activities.

Consideration of a promotional campaign based on the kidney transplant 'Am I on the list?' campaign (https://www.svhm.org.au/our-services/departments-and-services/n/nephrology/kidneytransplant) may be warranted, though an evaluation of this program is not evident.

3.2.4 Develop mechanisms to connect people to trials

The literature suggests that programs that employ multiple strategies are more successful than a single strategy at increasing participation of minority groups in clinical trials, however they are not likely to be effective without addressing systematic barriers in research infrastructure and conduct of trials. As an example for the regional Victorian setting, this could mean combining patient navigation with use of the *OCP for Aboriginal and Torres Strait Islander people*, which may provide opportunity for evaluation of the OCP implementation guide in practice. Complementary activities may include adaptation of CT materials to ensure they are culturally relevant and education / training of clinical staff regarding cancer disparities and bias.

3.2.4.1 Patient navigation (PN)

As a patient-centred approach to care, patient navigation has strong potential to increase the participation of Aboriginal people in clinical trials if guided by the principles described in Section 1. The literature suggests that interventions should facilitate outreach and inclusion on the part of researchers, not only rely on building CT awareness among Aboriginal people and communities, although this would be helpful. Patient navigation has potential to bring together disconnected resources or other aspects of the health system and connect them to patients. Considerations in designing a PN program and strategies to address them are presented below.

TABLE 3.4 PATIENT NAVIGATOR PROGRAM: CONSIDERATIONS AND STRATEGIES

CONSIDERATION	POSSIBLE STRATEGIES
Patient navigator role clarity: specific to project or more general role.	Past studies have trialled PNs in cancer screening and diagnosis, enrolment, retention, awareness and education about clinical research. Also care coordination generally.
Qualifications of PN: trained 'lay' navigators; RN; AHW/ALO; other.	Decision connected to sustainability of the model and types of training required. Training required regardless of the qualifications.
Training of the PN (influenced by qualifications)	Connect with ReViTALISE education Hub (and other Hubs?).
Support for PN	Identify types / levels of support. Identify and document clear processes for PN to access support. What resources will be available to PN, e.g., car, location of office.
Workforce shortages	Set pay and conditions at an appropriate level to make the positions attractive. Appropriate workplace support.
Sustainability of the model	Integrate ongoing evaluation mechanisms to enable demonstration of efficacy of the model.
Matching open trials, PN and patients' eligibility / interest	Strong PN link between specialist and patient, and CT networks.

3.2.4.2 Community Based Participatory Research (CBPR)

The strategic plan developed in the US to improve diversity in CTs using CBPR[83] (as mentioned in Section 2, p49) has informed Table 3.5, which identifies categories and strategies adapted for the Australian setting.

TABLE 3.5 USING CBPR TO INCREASE DIVERSITY IN CTS*

CATEGORY	POSSIBLE STRATEGIES – MOST APPLY ACROSS MULTIPLE CATEGORIES
Meaningful role for community representatives	Prioritise Aboriginal voices. Provide multiple options for involvement and develop a multidisciplinary team. Regular communication using multiple modes. Ensure direct benefits to communities based on their preferences.
Community perspectives in ethics approval processes	Local decision making power. Stay updated regarding VACCHO Research Accord (Victoria)
Improving the informed consent process	Promotion of Indigenous knowledge, experience, perspectives and control. See below
Community perspectives in protocol development, trial design and implementation	inclusion of community representatives and patient advocates in the study team, in formal, paid positions. Engage community in research design through focus groups and integration of stakeholders into study team. Enable feedback to amend trial design and document resultant changes.
Improving recruitment and retention	To be determined.
Enhancing local community support for cancer research	'Both-way' learning and openness to learning. Ensure complementary expertise of researchers and Aboriginal communities
Enhancing community interpretation, dissemination and implementation of trial outcomes	Training of community researchers, employment of community members, access to funding for program implementation and access to data. Local community leadership

* *Adapted from 'Communities as Partners in Cancer Clinical Trials: Changing Research, Practice and Policy'* [83]

Challenges identified in the CBPR process include the additional time needed for implementation, concerns about a limited evidence base regarding participatory approaches, compensation for community representatives and patient advocates, and a lack of CBPR training or

experience in the clinical trial workforce (whether this exists locally would need to be determined).

3.2.4.3 Teletrials / Extension of COSA tele-oncology

The work presented in Table 2.1 on teletrials is likely to be a useful guide. Opportunities for linkage with ReViTALISE teletrials stream should be pursued as appropriate.

3.2.4.4 Linkages with / leveraging other ReViTALISE projects

Though this report has been written predominantly for the *Aboriginal and Torres Strait Islander People with Cancer - Clinical Trial Access Initiative*, the principles and strategies outlined here also have relevance to other ReViTALISE project streams, as outlined in Table 3.6:

TABLE 3.6 POTENTIAL LINKAGES WITH REVITALISE PROJECT STREAMS

BROAD ACTIVITY AREA	REVITALISE STREAM
DIRECT CONNECTIONS	
Trial sites – number and location Access to CTs	Aboriginal and Torres Strait Islander People with Cancer - Clinical Trial Access Initiative Regional Research Teaching Hub Registry Trials Expansion Project Teletrials program
Trials for cancer types common in Aboriginal people	Teletrials program (focussed on Ca types) Regional Trials Network
Eligibility criteria	Registry Trials Expansion Project Teletrials program
Address implicit / explicit bias	Regional Research Teaching Hub Registry Trials Expansion Project
Health worker training and education	Regional Research Teaching Hub

Communication	
Health literacy / Knowledge gap	Regional Research Teaching Hub (jointly with RTN / CCV / DH?)
OTHER POSSIBLE CONNECTIONS	
	Immunotherapy Trials Project
	Geriatric Oncology Research Project
	Palliative and Supportive Care Research Project

3.2.4.5 Optimal Care Pathway (OCP) and Guide for Implementation

There is strong potential to use the *OCP for Aboriginal and Torres Strait Islander people with cancer* and the *Guide for Implementation* and evaluate their capacity to improve CT access for Aboriginal people.

3.2.4.6 Promote greater flexibility in design of investigator driven trials

It is beyond scope to detail options for this category, but it could be considered by the SC based on knowledge of existing and future trials.

3.2.4.7 Pharmaceutical trials

Consider an education campaign targeting decision-makers involved in multinational clinical trials in Australia. Leverage the CTGF and its promotion of equitable access to CTs, using multiple channels, events, forums etc.

3.3 SPECIFIC ASPECTS OF CTS

3.3.1 GOVERNANCE AND ETHICS

The documents outlined in Section 1 (detailed in Appendix 1) 'Key principles and guidelines' will inform this aspect of CTs. Governance and ethics processes, confidentiality and data storage will need to be in accordance with the overseeing institution. Multiple HREC applications will likely be required: relevant academic institution/s; AH&MRC (which has jurisdiction in NSW); Rumbalara Aboriginal Cooperative; AWH; GVH. Governance applications will be necessary at every site involved. Victoria is in the process of developing a body along the lines of AHMRC, the Victorian Aboriginal Research Accord Project (VARAP),[90] and this may occur during the life of the ReViTALISE project, affecting all studies involving Aboriginal and Torres Strait Islander people undertaken in Victoria. Mechanisms to help improve efficiency of this process include engaging Aboriginal people at the earliest stages, in addition to engaging staff with experience of local requirements, striving for consistency of teams, and appropriate wording of study materials as guided by Aboriginal people. Data sovereignty is also an aspect of research that will need to be addressed.

Explore the use of Duke et al.'s Culturally Adaptive Governance Framework[64] which may involve consultation with the authors at the Shepparton site regarding important lessons and recommendations. Implementation of this framework will entail investment in community priorities and Indigenous leadership capacity, facilitation of collaboration between Indigenous

knowledge systems and Western scientific traditions, fostering goodwill and meaningful connections, and integrating evaluation of governance using the framework.

3.3.2 Characteristics of trial teams

Strong, formal representation of the Aboriginal community is required at each level of the project: governance, management, design and implementation. Identification of education and training needs may require a preliminary survey of research staff, followed by measures designed to address gaps identified, as mentioned in Section 3.2.3. Linking this with the ReViTALISE Regional Research Teaching Hub may be an appropriate model; attention to cultural safety will be required.

3.3.3 Trial design

Build inclusion and active engagement of community members into the trial design, including increased flexibility in trial protocols. Facilitate robust reporting of effectiveness by building in evaluation of the strategies used.

3.3.4 Monitoring and evaluation

Consider review points as they relate to the ReViTALISE project and people who need to be involved in this to monitor progress. Key considerations regarding choosing the right PROMs / PREMs for monitoring include: reliability of measure; that it covers all relevant outcomes – must include

cultural issues; length (12 secs per item; no longer than 20 mins at baseline, shorter thereafter) and mode of administration; language; cultural appropriateness (including mode and place of administration), who completes the Patient Reported Outcome (PRO) (same participants as those evaluated for all endpoints); timing of measurement (clinically meaningful); and avoiding missing data. More detailed information is available on the COnsensus-based Standards for the selection of health Measurement Instruments (COSMIN) website.[91]

Regarding adaptation of screening and outcome measures, if existing measures are to be used, forward/backwards translation involving bilingual staff, with cultural adaptation as appropriate. If new measures are to be devised, Aboriginal people need to be integrally involved in their design. Significant work to develop measures for Aboriginal people is completed or underway in the following areas: wellbeing;[92, 93] supportive care needs;[94, 95] social and emotional wellbeing;[96] health related quality of life;[97, 98] inpatient experience;[99] and inpatient cultural safety.[100]

3.4 RISKS

This is a dynamic area and needs to be informed by the Risk Management Plan (Appendix 5) in the Regional Trial Network Victoria Project Plan, and the implementation plan of the *Aboriginal and Torres Strait Islander People with Cancer - Clinical Trial Access Initiative*.

REFERENCES

1. Cunningham J, Green M, Jaenke R, Garvey G. Desktop Review to consolidate the knowledge and evidence for three priority issues in the cancer care system: 1) Improving Aboriginal participation in clinical trials and research; 2) Improving culturally safe and effective cancer treatment for Aboriginal people with cancer; and 3) Improving Aboriginal people's self-identification and the quality of cancer data. Report prepared for VACCHO by the Menzies School of Health Research, July 2019. 2021. Victorian Aboriginal Community Controlled Health Organisation and Menzies School of Health Research, Melbourne. Accessed 15 March 2022. https://www.vaccho.org.au/research-resources/research-cancer-care-system/

2. Cancer Australia. A Guide to Implementing the Optimal Care Pathway for Aboriginal and Torres Strait Islander People with Cancer. Commonwealth of Australia 2020. Accessed 16 March 2022. https://www.canceraustralia.gov.au/publications-and-resources/cancer-australia-publications/guide-implementing-optimal-care-pathway-aboriginal-and-torres-strait-islander-people-cancer

3. National Aboriginal and Torres Strait Islander Health Standing Committee. National Cultural Respect Framework for Aboriginal and Torres Strait Islander Health 2016-2026. Australian Health Ministers' Advisory Council 2015. Accessed 16 March 2022. https://nacchocommunique.files.wordpress.com/2016/12/cultural_respect_framework_1december2016_1.pdf

4. ABSTARR Consulting. National Scheme's Aboriginal and Torres Strait Islander Health and Cultural Safety Strategy 2020-2025. The Australian Health Practitioner Regulation Agency, 2020. Accessed 16 March 2022. https://www.ahpra.gov.au/About-AHPRA/Aboriginal-and-Torres-Strait-Islander-Health-Strategy/health-and-cultural-safety-strategy.aspx

5. Australian Commission on Safety and Quality in Health Care (ACSQHC). The National Safety and Quality Health Service (NSQHS) Standards. Australian Commission on Safety and Quality in Health Care. Accessed 16 March 2022. https://www.safetyandquality.gov.au/standards/nsqhs-standards#:~:text=The%20National%20Safety%20and%20Quality%20Health%20Service%20%28NSQHS%29,care%20consumers%20can%20expect%20from%20health%20service%20organisations.

6. National Indigenous Cancer Network. Accessed 3 May 2021. http://www.nican.info/.

7. Picker Institute. Principles of Person Centred Care. Picker Institute. Accessed 16 March 2022. https://www.picker.org/about-us/picker-principles-of-person-centred-care/.

8. Laycock A, Walker D, Harrison N, Brands J. Researching Indigenous Health: A Practical Guide for Researchers. 2011. The Lowitja Institute Melbourne. Accessed 16 March 2022. https://www.lowitja.org.au/page/services/resources/health-policy-and-systems/aboriginal-and-torres-strait-islander-leadership/Researching-Indigenous-Health-Guide

9. Bessarab D, Ng'andu B. Yarning About Yarning as a Legitimate Method in Indigenous Research. International Journal of Critical Indigenous Studies. 2010;3(1).

10. Lin I, Green C, Bessarab D. 'Yarn with me': applying clinical yarning to improve clinician-patient communication in Aboriginal health care. Aust J Prim Health. Nov 2016;22(5).377-382. doi:10.1071/PY16051.

11. National Health and Medical Research Council. Ethical conduct in research with Aboriginal and Torres Strait Islander Peoples and communities: Guidelines for researchers and stakeholders. 2018. Accessed 16 March 2022. https://www.nhmrc.gov.au/research-policy/ethics/ethical-guidelines-research-aboriginal-and-torres-strait-islander-peoples

12. National Health and Medical Research Council (NHMRC). Keeping research on track II: A companion document to Ethical conduct in research with Aboriginal and Torres Strait Islander Peoples and communities: Guidelines for researchers and stakeholders. Commonwealth of Australia 2018. Accessed 16 March 2022. https://www.nhmrc.gov.au/research-policy/ethics/ethical-guidelines-research-aboriginal-and-torres-strait-islander-peoples

13. National Health and Medical Research Council (NHMRC). Road Map 3: A strategic framework for improving Aboriginal and Torres Strait Islander health through research. 2018. Accessed 16 March 2022. https://www.nhmrc.gov.au/about-us/publications/road-map-3-strategic-framework#block-views-block-file-attachments-content-block-1

14. Australian Institute of Aboriginal and Torres Strait Islander Studies (AIATSIS). AIATSIS Code of Ethics for Aboriginal and Torres Strait Islander Research. 2020. Accessed 16 March 2022. http://aiatsis.gov.au/ethics

15. Jamieson LM, Paradies YC, Eades S, Chong A, Maple-Brown L, Morris P, et al. Ten principles relevant to health research among Indigenous Australian populations. Med J Aust. Jul 2 2012;197(1).16-8. doi:https://doi.org/10.5694/mja11.11642.

16. Harfield S, Pearson O, Morey K, Kite E, Canuto K, Glover K, et al. Assessing the quality of health research from an Indigenous perspective: the Aboriginal and Torres Strait Islander quality appraisal tool. BMC Med Res Methodol. Apr 10 2020;20(1).79. doi:10.1186/s12874-020-00959-3.

17. Huria T, Palmer SC, Pitama S, Beckert L, Lacey C, Ewen S, et al. Consolidated criteria for strengthening reporting of health research involving indigenous peoples: the CONSIDER statement. BMC Med Res Methodol. Aug 9 2019;19(1).173. doi:10.1186/s12874-019-0815-8.

18. The Wardliparingga Aboriginal Research Unit of the South Australian Health and Medical Research Institute. National Safety and Quality Health Service Standards user guide for Aboriginal and Torres Strait Islander health. Australian Commission on Safety and Quality in Health Care, 2017. Accessed 16 March 2022. https://www.safetyandquality.gov.au/sites/default/files/migrated/National-Safety-and-Quality-Health-Service-Standards-User-Guide-for-Aboriginal-and-Torres-Strait-Islander-Health.pdf

19. Cancer Australia. National Aboriginal and Torres Strait Islander Cancer Framework. Australian Government, 2015. Accessed 16 March 2022. https://www.canceraustralia.gov.au/publications-and-resources/cancer-australia-publications/national-aboriginal-and-torres-strait-islander-cancer-framework

20. Cancer Australia. Optimal care pathway for Aboriginal and Torres Strait Islander people with cancer. Australian Government Accessed 16 March 2022. https://www.canceraustralia.gov.au/sites/default/files/publications/optimal-care-pathway-aboriginal-and-torres-strait-islander-people-cancer/pdf/optimal-care-pathway-for-aboriginal-and-torres-strait-islander-people-with-cancer.pdf

21. Fogarty W, Bulloch H, McDonnell S, Davis M. Deficit Discourse and Indigenous Health: How narrative framings of Aboriginal and Torres Strait Islander people are reproduced in policy,. 2018. The Lowitja Institute Melbourne. Accessed 16 March 2022. https://www.lowitja.org.au/page/services/resources/Cultural-and-social-determinants/racism/Deficit-Discourse-and-Indigenous-Health

22. Fogarty W, Lovell M, Langenberg J, Heron M-J. Deficit Discourse and Strengths-based Approaches: Changing the Narrative of Aboriginal and Torres Strait Islander Health and Wellbeing. 2018. The Lowitja Institute Melbourne. Accessed 16 March 2022. https://www.lowitja.org.au/page/services/resources/Cultural-and-social-determinants/racism/deficit-discourse-strengths-based

23. Cunningham J, Garvey G. Are there systematic barriers to participation in cancer treatment trials by Aboriginal and Torres Strait Islander cancer patients in Australia? Aust N Z J Public Health. Feb 2021;45(1).39-45. doi:10.1111/1753-6405.13059.

24. Stanaway F, Cumming RG, Blyth F. Exclusions from clinical trials in Australia based on proficiency in English. Med J Aust. Jul 3 2017;207(1).36. doi:10.5694/mja16.01012.

25. Ford JG, Howerton MW, Lai GY, Gary TL, Bolen S, Gibbons MC, et al. Barriers to recruiting underrepresented populations to cancer clinical trials: a systematic review. Cancer. Jan 15 2008;112(2).228-42. doi:10.1002/cncr.23157.

26. Glover M, Kira A, Johnston V, Walker N, Thomas D, Chang AB, et al. A systematic review of barriers and facilitators to participation in randomized controlled trials by Indigenous people from New Zealand, Australia, Canada and the United States. Glob Health Promot. Mar 2015;22(1).21-31. doi:10.1177/1757975914528961.

27. McFarlane SJ, Occa A, Peng W, Awonuga O, Morgan SE. Community-Based Participatory Research (CBPR) to Enhance Participation of Racial/Ethnic Minorities in Clinical Trials: A 10-Year Systematic Review. Health Commun. Aug 22 2021:1-18. doi:10.1080/10410236.2021.1943978.

28. Wilkins CH, Schindler SE, Morris JC. Addressing Health Disparities Among Minority Populations: Why Clinical Trial Recruitment Is Not Enough. JAMA Neurol. Sep 1 2020;77(9).1063-1064. doi:10.1001/jamaneurol.2020.1614.

29. Regnante JM, Richie NA, Fashoyin-Aje L, Vichnin M, Ford M, Roy UB, et al. US Cancer Centers of Excellence Strategies for Increased Inclusion of Racial and Ethnic Minorities in Clinical Trials. Journal of Oncology Practice. 2019;15(4). doi:https://doi.org/10.1200/JOP.18.00638.

30. Vuong I, Wright J, Nolan MB, Eggen A, Bailey E, Strickland R, et al. Overcoming Barriers: Evidence-Based Strategies to Increase Enrollment of Underrepresented Populations in Cancer Therapeutic Clinical Trials-a Narrative Review. J Cancer Educ. Oct 2020;35(5).841-849.

31. Australian Commission on Safety and Quality in Health Care (ACSQHC). National Clinical Trials Governance Framework - Guide for implementation. ACSQHC 2020. Accessed 16 March 2022. https://www.safetyandquality.gov.au/sites/default/files/2020-02/national_clinical_trials_governance_framework_and_user_guide_-draft_for_pilot_2020.pdf

32. Department of Health. The National Teletrials Compendium. Australian Government. Accessed 17 Feb 2022. https://www.health.gov.au/resources/collections/the-national-teletrials-compendium.

33. Clinical Trials Project Reference Group. National Principles for Teletrials in Australia 2020 Accessed 16 March 2022. https://www.health.gov.au/sites/default/files/documents/2021/03/national-principles-for-teletrials-in-australia.pdf

34. Clinical Trials Project Reference Group. National Standard Operating Procedures for Clinical Trials, including Teletrials, in Australia. 2020. Accessed 16 March 2022. https://www.health.gov.au/resources/publications/national-standard-operating-procedures-for-clinical-trials

35. Tuhiwai Smith L. Decolonizing Methodologies: Research and Indigenous Peoples. Third edition ed. Zed Books; 2021.

36. Thomas DP, Bainbridge R, Tsey K. Changing discourses in Aboriginal and Torres Strait Islander health research, 1914-2014. Med J Aust. Jul 7 2014;201(1 Suppl).S15-8. doi:https://doi.org/10.5694/mja14.00114.

37. McKay RR, Gold T, Zarif JC, Chowdhury-Paulino IM, Friedant A, Gerke T, et al. Tackling Diversity in Prostate Cancer Clinical Trials: A Report From the Diversity Working Group of the IRONMAN Registry. JCO Global Oncol 7. 2021;7:495-505. doi:https://doi.org/10.1200/GO.20.00571.

38. Cui Z, Truesdale KP, Robinson TN, Pemberton V, French SA, Escarfuller J, et al. Recruitment strategies for predominantly low-income, multi-racial/ethnic children and parents to 3-year community-based intervention trials: Childhood Obesity Prevention and Treatment Research (COPTR) Consortium. Trials. May 28 2019;20(1).296. doi:10.1186/s13063-019-3418-0.

39. Cunningham-Erves J, Deakings J, Mayo-Gamble T, Kelly-Taylor K, Miller ST. Factors influencing parental trust in medical researchers for child and adolescent patients' clinical trial participation. Psychol Health Med. Jul 2019;24(6).691-702. doi:10.1080/13548506.2019.1566623.

40. Lackland DT, Sims-Robinson C, Jones Buie JN, Voeks JH. Impact of COVID-19 on Clinical Research and Inclusion of Diverse Populations. Ethn Dis. Summer 2020;30(3).429-432. doi:10.18865/ed.30.3.429.

41. Ortega RF, Yancy CW, Mehran R, Batchelor W. Overcoming Lack of Diversity in Cardiovascular Clinical Trials: A New Challenge and Strategies for Success. Circulation. Nov 19 2019;140(21).1690-1692. doi:10.1161/circulationaha.119.041728.

42. Rink E, Knight K, Ellis C, McCormick A, FireMoon P, Held S, et al. Using Community-Based Participatory Research to Design, Conduct, and Evaluate Randomized Controlled Trials with American Indian Communities. Prev Chronic Dis. Nov 12 2020;17:E143. doi:10.5888/pcd17.200099.

43. Russo C, Stout L, House T, Santana VM. Barriers and facilitators of clinical trial enrollment in a network of community-based pediatric oncology clinics. Pediatr Blood Cancer. Apr 2020;67(4).e28023. doi:https://doi.org/10.1002/pbc.28023.

44. Strait A, Castillo F, Choden S, Li J, Whitaker E, Falasinnu T, et al. Demographic Characteristics of Participants in Rheumatoid Arthritis Randomized Clinical Trials: A Systematic Review. JAMA Netw Open. Nov 1 2019;2(11).e1914745. doi:10.1001/jamanetworkopen.2019.14745.

45. Willis A, Isaacs T, Khunti K. Improving diversity in research and trial participation: the challenges of language. Comment. Lancet Public Health. Jul 2021;6(7).e445-e446. doi:10.1016/s2468-2667(21)00100-6.

46. Olver I, Gunn KM, Chong A, Knott V, Spronk K, Cominos N, et al. Communicating cancer and its treatment to Australian Aboriginal and Torres Strait Islander patients with cancer: a qualitative study. Support Care Cancer. Jul 24 2021. doi:10.1007/s00520-021-06430-3.

47. Andrasik MP, Broder GB, Wallace SE, Chaturvedi R, Michael NL, Bock S, et al. Increasing Black, Indigenous and People of Color participation in clinical trials through community engagement and recruitment goal establishment. PLoS One. 2021;16(10).e0258858. doi:10.1371/journal.pone.0258858.

48. Warren RC, Forrow L, Hodge DA, Sr., Truog RD. Trustworthiness before Trust - Covid-19 Vaccine Trials and the Black Community. N Engl J Med. Nov 26 2020;383(22).e121. doi:10.1056/NEJMp2030033.

49. Napoles A, Cook E, Ginossar T, Knight KD, Ford ME. Applying a Conceptual Framework to Maximize the Participation of Diverse Populations in Cancer Clinical Trials. Adv Cancer Res. 2017;133:77-94. doi:10.1016/bs.acr.2016.08.004.

50. Doll KM. Minority enrollment on clinical trials enhances scientific rigor but requires structural changes and commitment. Gynecologic Oncology. 2020;157:301-302. doi:https://doi.org/10.1016/j.ijcard.2020.03.035.

51. Horowitz CR, Sabin T, Ramos M, Richardson LD, Hauser D, Robinson M, et al. Successful recruitment and retention of diverse participants in a genomics clinical trial: a good invitation to a great party. Genet Med. Oct 2019;21(10).2364-2370. doi:10.1038/s41436-019-0498-x.

52. Bass SB, D'Avanzo P, Alhajji M, Ventriglia N, Trainor A, Maurer L, et al. Exploring the Engagement of Racial and Ethnic Minorities in HIV Treatment and Vaccine Clinical Trials: A Scoping Review of Literature and Implications for Future Research. AIDS Patient Care STDS. Sep 2020;34(9).399-416. doi:10.1089/apc.2020.0008.

53. Rottas M, Thadeio P, Simons R, Houck R, Gruben D, Keller D, et al. Demographic diversity of participants in Pfizer sponsored clinical trials in the United States. Contemp Clin Trials. Jul 2021;106:106421. doi:10.1016/j.cct.2021.106421.

54. Shaw JL, Semmens E, Okihiro M, Lewis JL, Hirschfeld M, VanWagoner TM, et al. Best Practices for Conducting Clinical Trials With Indigenous Children in the United States. Am J Public Health. Sep 2021;111(9).1645-1653. doi:10.2105/AJPH.2021.306372.

55. Robler SK, Inglis SM, Gallo JJ, Parnell HE, Ivanoff P, Ryan S, et al. Hearing Norton Sound: community involvement in the design of a mixed methods community randomized trial in 15 Alaska Native communities. Res Involv Engagem. Nov-3 6(1).67. doi:https://researchinvolvement.biomedcentral.com/articles/10.1186/s40900-020-00235-0.

56. Rivers DA, Pal T, Vadaparampil ST, Adams LA, Dash-Pitts L, Quinn GP. A community-academic partnership to explore informational needs of African American women as a primer for cancer clinical trial recruitment. Ethn Health. Aug 24(6).679-693. doi:10.1080/13557858.2017.1367762.

57. Maar MA, Beaudin V, Yeates K, Boesch L, Liu P, Madjedi K, et al. Wise Practices for Cultural Safety in Electronic Health Research and Clinical Trials With Indigenous People: Secondary Analysis of a Randomized Clinical Trial. J Med Internet Res. Nov 4 2019;21(11).e14203. doi:10.2196/14203.

58. Masood Y, Bower P, Waheed MW, Brown G, Waheed W. Synthesis of researcher reported strategies to recruit adults of ethnic minorities to clinical trials in the United Kingdom: A systematic review. Contemp Clin Trials. Mar 2019;78:1-10. doi:10.1016/j.cct.2019.01.004.

59. Aristizabal P. Diverse populations and enrollment in pediatric cancer clinical trials: Challenges and opportunities. Pediatr Blood Cancer. Nov 2020;67(11).e28296. doi:10.1002/pbc.28296.

60. Niranjan SJ, Durant RW, Wenzel JA, Cook ED, Fouad MN, Vickers SM, et al. Training Needs of Clinical and Research Professionals to Optimize Minority Recruitment and Retention in Cancer Clinical Trials. J Cancer Educ. Feb 2019;34(1).26-34. doi:10.1007/s13187-017-1261-0.

61. Niranjan SJ, Martin MY, Fouad MN, Vickers SM, Wenzel JA, Cook ED, et al. Bias and stereotyping among research and clinical professionals: Perspectives on minority recruitment for oncology clinical trials. Cancer. Jan 1 2020;126(9).1958-1968. doi:10.1002/cncr.32755.

62. Niranjan SJ, Wenzel JA, Martin MY, Fouad MN, Vickers SM, Konety BR, et al. Perceived Institutional Barriers Among Clinical and Research Professionals: Minority Participation in Oncology Clinical Trials. JCO oncology practice. 2021-5 2021;17(5).e666-e675. doi:10.1200/OP.20.00970.

63. Tahhan AS, Vaduganathan M, Greene SJ, Alrohaibani A, Raad M, Gafeer M, et al. Enrollment of Older Patients, Women, and Racial/Ethnic Minority Groups in Contemporary Acute Coronary Syndrome Clinical Trials: A Systematic Review. JAMA Cardiol. Jun 1 2020;5(6).714-722. doi:10.1001/jamacardio.2020.0359.

64. Duke DLM, Prictor M, Ekinci E, Hachem M, Burchill LJ. Culturally Adaptive Governance-Building a New Framework for Equity in Aboriginal and Torres Strait Islander Health Research: Theoretical Basis, Ethics, Attributes and Evaluation. Int J Environ Res Public Health. Jul 27 2021;18(15). doi:10.3390/ijerph18157943.

65. Flash GM Study https://blogs.unimelb.edu.au/flashgmstudy/.

66. Clark LT, Watkins L, Piña IL, Elmer M, Akinboboye O, Gorham M, et al. Increasing Diversity in Clinical Trials: Overcoming Critical Barriers. Curr Probl Cardiol. May 2019;44(5).148-172. doi:10.1016/j.cpcardiol.2018.11.002.

67. Nazha B, Mishra M, Pentz R, Owonikoko TK. Enrollment of Racial Minorities in Clinical Trials: Old Problem Assumes New Urgency in the Age of Immunotherapy. American Society of Clinical Oncology. 2019. doi:https://doi.org/10.1200/EDBK100021.

68. Stephens D, Peterson R, Singer M, Johnson J, Rushing SC, Kelley A. Recruiting and Engaging American Indian and Alaska Native Teens and Young Adults in a SMS Help-Seeking Intervention: Lessons Learned from the BRAVE Study. Int J Environ Res Public Health. Dec 16 2020;17(24). doi:10.3390/ijerph17249437.

69. Trant AA, Walz L, Allen W, DeJesus J, Hatzis C, Silber A. Increasing accrual of minority patients in breast cancer clinical trials. Breast Cancer Res Treat. Nov 2020;184(2).499-505. doi:10.1007/s10549-020-05873-2.

70. Patel SN, Staples JN, Garcia C, Chatfield L, Ferriss JS, Duska L. Are ethnic and racial minority women less likely to participate in clinical trials? Gynecol Oncol. May 2020;157(2).323-328. doi:10.1016/j.ygyno.2020.01.040.

71. Slade AL, Retzer A, Ahmed K, Kyte D, Keeley T, Armes J, et al. Systematic review of the use of translated patient-reported outcome measures in cancer trials. Trials. Apr 26 2021;22(1).306. doi:10.1186/s13063-021-05255-z.

72. Amorrortu RP, Arevalo M, Vernon SW, Mainous AG, 3rd, Diaz V, McKee MD, et al. Recruitment of racial and ethnic minorities to clinical trials conducted within specialty clinics: an intervention mapping approach. Trials. Feb 17 2018;19(1).115. doi:10.1186/s13063-018-2507-9.

73. Cunningham-Erves J, Barajas C, Mayo-Gamble TL, McAfee CR, Hull PC, Sanderson M, et al. Formative research to design a culturally-appropriate cancer clinical trial education program to increase participation of African American and Latino communities. BMC Public Health. Jun 3 2020;20(1).840. doi:10.1186/s12889-020-08939-4.

74. Doroshow JH, Prindiville S, McCaskill-Stevens W, Mooney M, Loehrer PJ. COVID-19, Social Justice, and Clinical Cancer Research. J Natl Cancer Inst. Oct 1 2021;113(10).1281-1284. doi:10.1093/jnci/djaa162.

75. Wong R, Amano T, Lin SY, Zhou Y, Morrow-Howell N. Strategies for the Recruitment and Retention of Racial/Ethnic Minorities in Alzheimer Disease and Dementia Clinical Research. Curr Alzheimer Res. 2019;16(5).458-471. doi:10.2174/1567205016666190321161901.

76. Kidd J, Raphael D, Cassim S, Black S, Blundell R, Egan R. Health service provider responses to indigenous peoples with cancer: An integrative review. Eur J Cancer Care (Engl). Mar 2019;28(2).e12975. doi:10.1111/ecc.12975.

77. Ramirez AG, Choi BY, Munoz E, Perez A, Gallion KJ, Moreno PI, et al. Assessing the effect of patient navigator assistance for psychosocial support services on health-related quality of life in a randomized clinical trial in Latino breast, prostate, and colorectal cancer survivors. Cancer. Mar 1 2020;126(5).1112-1123. doi:10.1002/cncr.32626.

78. Nickell A, Stewart SL, Burke NJ, Guerra C, Cohen E, Lawlor C, et al. Engaging limited English proficient and ethnically diverse low-income women in health research: A randomized trial of a patient navigator intervention. Patient Educ Couns. Jul 2019;102(7).1313-1323. doi:10.1016/j.pec.2019.02.013.

79. Cartmell KB, Bonilha HS, Simpson KN, Ford ME, Bryant DC, Alberg AJ. Patient barriers to cancer clinical trial participation and navigator activities to assist. Adv Cancer Res. 2020;146:139-166. doi:10.1016/bs.acr.2020.01.008.

80. Te Karu L, Dalbeth N, Stamp LK. Inequities in people with gout: a focus on Maori (Indigenous People) of Aotearoa New Zealand. Ther Adv Musculoskelet Dis. 2021;13:1759720X211028007. doi:10.1177/1759720X211028007.

81. Snijder M, Wagemakers A, Calabria B, Byrne B, O'Neill J, Bamblett R, et al. 'We walked side by side through the whole thing': A mixed-methods study of key elements of community-based participatory research partnerships between rural Aboriginal communities and researchers. Aust J Rural Health. Aug 2020;28(4).338-350. doi:https://doi.org/10.1111/ajr.12655.

82. Haynes E, Marawili M, Marika BM, Mitchell AG, Phillips J, Bessarab D, et al. Community-based participatory action research on rheumatic heart disease in an Australian Aboriginal homeland: Evaluation of the 'On track watch' project. Eval Program Plann. Jun 2019;74:38-53. doi:10.1016/j.evalprogplan.2019.02.010.

83. Education Network to Advance Cancer Clinical Trials (ENACCT), Community-Campus Partnerships for Health (CCPH). Communities as Partners in Cancer Clinical Trials: Changing Research, Practice and Policy. 2008. Education Network to Advance Cancer Clinical Trials (ENACCT) and Community-Campus Partnerships for Health (CCPH). Silver Spring.

84. Seifer SD, Michaels M, Collins S. Applying Community-Based Participatory Research Principles and Approaches in Clinical Trials: Forging a New Model for Cancer Clinical Research. Progress in Community Health Partnerships: Research, Education, and Action; The Johns Hopkins University Press. 2010;4.1.

85. Eng C, Chen EY, Rogers J, Lewis M, Strosberg J, Thota R, et al. Moving Beyond the Momentum: Innovative Approaches to Clinical Trial Implementation. JCO Oncol Pract. 2021;17:607-614. doi:https://ascopubs.org/doi/full/10.1200/OP.20.00701.

86. Patel MI, Lopez AM, Blackstock W, Reeder-Hayes K, Moushey A, Phillips J, et al. Cancer Disparities and Health Equity: A Policy Statement From the American Society of Clinical Oncology. J Clin Oncol. 2020;38:3439-3448. doi:10.1200/JCO.20.

87. Wilkins CH, Mapes BM, Jerome RN, Villalta-Gil V, Pulley JM, Harris PA. Understanding What Information Is Valued By Research Participants, And Why. Health Aff (Millwood). Mar 2019;38(3).399-407. doi:10.1377/hlthaff.2018.05046.

88. Langford AT, Hawley ST, Stableford S, Studts JL, Byrne MM. Development of a Plain Language Decision Support Tool for Cancer Clinical Trials: Blending Health Literacy, Academic Research, and Minority Patient Perspectives. J Cancer Educ. Jun 2020;35(3).454-461. doi:10.1007/s13187-019-1482-5.

89. Langford A, Studts JL, Byrne MM. Improving knowledge and decision readiness to participate in cancer clinical trials: Effects of a plain language decision aid for minority cancer survivors. Patient Educ Couns. Feb 2021;104(2).422-426. doi:10.1016/j.pec.2020.07.005.

90. Victorian Aboriginal Community Controlled Health Organisation (VACCHO). Victorian Aboriginal Research Accord Project (VARAP). Accessed 7 March 2022. https://www.vaccho.org.au/research-resources/varap/.

91. COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN). Accessed 7 Mar 2022. https://www.cosmin.nl/.

92. Butler TL, Anderson K, Garvey G, Cunningham J, Ratcliffe J, Tong A, et al. Aboriginal and Torres Strait Islander people's domains of wellbeing: A comprehensive literature review. Soc Sci Med. Jul 2019;233:138-157. doi:https://doi.org/10.1016/j.socscimed.2019.06.004.

93. Howard K, Anderson K, Cunningham J, Cass A, Ratcliffe J, Whop LJ, et al. What Matters 2 Adults: a study protocol to develop a new preference-based wellbeing measure with Aboriginal and Torres Strait Islander adults (WM2Adults). BMC Public Health. Nov 17 2020;20(1).1739. doi:https://doi.org/10.1186/s12889-020-09821-z.

94. Garvey G, Beesley VL, Janda M, Jacka C, Green AC, O'Rourke P, et al. The development of a supportive care needs assessment tool for Indigenous people with cancer. BMC Cancer. 2012;12(300). doi:http://www.biomedcentral.com/1471-2407/12/300.

95. Garvey G, Thewes B, He VFY, Davis E, Girgis A, Valery PC, et al. Indigenous cancer patient and staff attitudes towards unmet needs screening using the SCNAT-IP. journal article. Supportive Care in Cancer. 2016;24(1).215-223. doi:https://link.springer.com/article/10.1007/s00520-015-2770-1

96. Le Grande M, Ski CF, Thompson DR, Scuffham P, Kularatna S, Jackson AC, et al. Social and emotional wellbeing assessment instruments for use with Indigenous Australians: A critical review. Soc Sci Med. Aug 2017;187:164-173. doi:http://dx.doi.org/10.1016/j.socscimed.2017.06.046.

97. Micklem JM. Self-reported health-related quality-of-life issues for Aboriginal and Torres Strait Islander patients with experience of cancer in Australia: a review of literature. Int J Evid Based Healthc. Dec 2015;13(4).233-53. doi:10.1097/xeb.0000000000000051.

98. Garvey G, Cunningham J, Yf He V, Janda M, Baade P, Sabesan S, et al. Health-related quality of life among Indigenous Australians diagnosed with cancer. Qual Life Res. 2016;25(8).1999-2008. doi:https://link.springer.com/article/10.1007%2Fs11136-016-1233-6.

99. Bureau of Health Information. The Insights Series – Aboriginal people's experiences of hospital care. 2021. BHI Sydney (NSW). Accessed 16 March 2022. https://www.bhi.nsw.gov.au/BHI_reports/Insights_Series/Aboriginal-peoples-experiences-of-hospital-care

100. Elvidge E, Paradies Y, Aldrich R, Holder C. Cultural safety in hospitals: validating an empirical measurement tool to capture the Aboriginal patient experience. Aust Health Rev. Apr 2020;44(2).205-211. doi:https://doi.org/10.1071/AH19227.

101. Department of Health. Review of the Australian New Zealand Clinical Trials Registry report (status). Australian Government. Accessed 22 December 2021. https://www1.health.gov.au/internet/main/publishing.nsf/Content/Clinical-Trials.

102. Queensland Clinical Trials Coordination Unit (QCTCU). Teletrials Pilot Analysis. 2019. Accessed 16 March 2022. https://www.health.qld.gov.au/__data/assets/pdf_file/0033/856950/TELETRIALS-PILOT-ANALYSIS-29-July-2019.pdf

103. Queensland Health. Queensland Teletrials Toolkit. Queensland Government. Accessed 16 March 2022. https://www.health.qld.gov.au/hiiro/html/teletrials.

104. Australian Commission on Safety and Quality in Health Care (ACSQHC). Clinical Trials Governance Framework Literature Review. 2018. Accessed 16 March 2022. https://www.safetyandquality.gov.au/sites/default/files/2020-02/national_clinical_trial_governance_framework_-_literature_review.pdf

105. Australian Commission on Safety and Quality in Health Care (ACSQHC). Mapping Exercise report: the Clinical Trials Governance Framework project. 2018. Accessed 16 March 2022. https://www.safetyandquality.gov.au/sites/default/files/2020-02/national_clinical_trials_governance_framework_-_mapping_exercise_report.pdf

106. Australian Commission on Safety and Quality in Health Care (ACSQHC). The Clinical Trials portal. User guide to the self-assessment and operational metrics tools. . 2020. Accessed 16 March 2022. https://clinicaltrials.safetyandquality.gov.au/user/login

107. National Institute on Minority Health and Health Disparities. Minority Health and Health Disparities Research Framework. 2018. Accessed 21 February 2022. https://www.nimhd.nih.gov/docs/research_framework/research-framework-slide.pdf

108. Chino F, Zafar SY. Financial Toxicity and Equitable Access to Clinical Trials. Invited article. American Society of Clinical Oncology. 2019. doi:DOI https://doi.org/10.1200/EDBK100019.

109. Nolan TS, Bell AM, Chan Y-N, Bryant AL, Bissram JS, Hirschey R. Use of Video Education Interventions to Increase Racial and Ethnic Diversity in Cancer Clinical Trials: A Systematic Review. Worldviews on Evidence-Based Nursing. 2021;18(5).302–309. doi: https://doi.org/10.1111/wvn.12539.

APPENDICES

APPENDIX 1: KEY DOCUMENTS: PRINCIPLES AND GUIDELINES (EXPANDED TABLE)

INSTITUTION, YEAR	DOCUMENT NAME	SUMMARY
RESEARCH ETHICS AND PRACTICE		
National Health and Medical Research Council (NHMRC) 2018a	Ethical conduct in research with Aboriginal and Torres Strait Islander Peoples and communities: Guidelines for researchers and stakeholders[11]	Six core values: spirit and integrity; cultural continuity; equity; reciprocity; respect; responsibility. Explains how the values are demonstrated and linked to the National Statement on Ethical Conduct in Human Research. Discusses related principles: consent, research agreements, cultural and intellectual property, and cultural competency. Connection to Country acknowledged: *Aboriginal lore and spirituality are intertwined with the land, the people and creation and this forms their cultural identity and sovereignty*.[11,p.26] Definition of health: *'"Aboriginal health" means not just the physical well-being of an individual but refers to the social, emotional and cultural well-being of the whole community. It is a whole of life view and includes the cyclical concept of life-death-life'.*[11,p.26]
NHMRC 2018b	Keeping research on track II[12]	Companion document to above Guidelines. Describes how the values and ethics can be implemented during the 8 identified steps along the research journey: '*building relationships; developing the research idea; developing the project and seeking agreement; data collection; analysing the data and making sense of the findings; report writing; sharing and translating the results into action; and learning from experience'*.[12,p.iii] Also identifies and discusses a number of rights that Aboriginal and Torres Strait Islander people have in relation to research.
NHMRC 2018c	Road Map 3[13]	Strategic framework to guide NHMRC's efforts to improve outcomes for Aboriginal and Torres Strait Islander people. Three key areas: workforce development; community engagement; and identified research priorities. Highest research priorities; 1) the social and cultural determinants of health and health services effectiveness; 2) conditions responsible for a high burden of disease and/or a large difference in quality of life; and 3) conditions that are (almost) exclusive to Aboriginal and Torres Strait Islander people, and research relating to personalised medicine/health care.

The Australian Institute of Aboriginal and Torres Strait Islander Studies (AIATSIS) 2020	Code of Ethics[14]	The new Code emphasises four principles which underpin appropriate research with Aboriginal and Torres Strait Islander people: Indigenous self-determination; Indigenous leadership; Impact and Value; and Sustainability and Accountability.
Jamieson et al. 2010	Ten principles regarding health research among Indigenous Australian populations[15] (5 essential, 5 desirable)	The authors recommended to consider these principles from the initial design phase. Essential principles: *1. Addressing a priority health issue as determined by the community 2. Conducting research within a mutually respectful partnership framework 3. Capacity building is a key focus of the research partnership, with sufficient budget to support this 4. Flexibility in study implementation while maintaining scientific rigour ("community-based approach is key to sustainability and acceptability") 5. Respecting communities' past and present experience of research.*[15,p.16-17] Desirable principles: *6. Recognising the diversity of Indigenous Australian populations 7. Ensuring extended timelines do not jeopardise projects 8. Preparing for Indigenous leadership turnover 9. Supporting community ownership 10. Developing systems to facilitate partnership management in multicentre studies*.[15,p.17]
Huria et al. 2019	CONSIDER statement: CONSolIDated critERtia for strengthening the reporting of health research involving Indigenous Peoples[17]	International collaborative effort that aims to strengthen research praxis and advance Indigenous health outcomes. The CONSIDER statement provides a checklist for the reporting of health research involving Indigenous peoples, and includes items related to governance, prioritization, relationships, methodologies, participation, capacity, analysis and interpretation and dissemination.
HEALTH SERVICES		
The Wardliparingga Aboriginal Research Unit of the South Australian Health and Medical Research Institute, 2017	National Safety and Quality Health Service (NSQHS) Standards User Guide for Aboriginal and Torres Strait Islander Health[18]	The NSQHS Standards require health services to improve health care provision for Aboriginal and Torres Strait Islander people; the User Guide is designed to support health services to meet the standards. Action 5.8 stipulates that all health service organisations must '*establish processes to accurately identify and record Aboriginal and Torres Strait Islander status*'.[18,p.3]
Commonwealth of Australia, 2016	Cultural Respect Framework for Aboriginal and	Aims to ensure accessible, responsive and safe health services for Aboriginal and Torres Strait Islander people through embedding cultural respect

	Torres Strait Islander Health, 2016-2026[3]	principles in health systems. Outlines six domains that underpin culturally respectful health service delivery. 1. Whole-of-organisation approach and commitment; 2. Communication; 3. Workforce development and training; 4. Consumer participation and engagement; 5. Stakeholder partnerships and collaboration; 6. Data, planning, research and evaluation.
The Australian Health Practitioner Regulation Agency (The National Registration and Accreditation Scheme), 2020	Aboriginal and Torres Strait Islander Health and Cultural Safety Strategy 2020-2025[4]	This strategy aims to eliminate racism from the health system. Through commitment and action by members of the national health practitioner registration system, the strategy aims to make cultural safety, as defined by Aboriginal and Torres Strait Islander people, 'the norm'.
Harfield et al 2020	Quality Appraisal Tool (QAT)[16]	The QAT is a 14-item checklist to guide the assessment of research quality from the perspectives of Aboriginal and Torres Strait Islander people: it aims to improve the quality and transparency of research with Aboriginal and Torres Strait Islander people. The QAT has been designed to assess the full breadth of research conducted with Aboriginal and Torres Strait Islander people, provides background, development and explanation of terms in a Companion document, and can be used in conjunction with established critical appraisal tools.
CANCER SPECIFIC		
Cancer Australia, 2015	National Aboriginal and Torres Strait Islander Cancer Framework[19]	The Framework established strategic direction to address disparities and improve cancer outcomes for Aboriginal and Torres Strait Islander people with cancer. Of the seven principles and corresponding priority areas for multilevel action, the following (abbreviated) are particularly relevant: ensure Aboriginal people receive optimal and culturally appropriate treatment, services, and supportive and palliative care; ensure families and carers are involved, informed, supported and enabled throughout; strengthen the capacity of cancer related services and systems to deliver good quality, integrated services that meet the needs of Aboriginal people through a) data systems that inform better outcomes and b) targeted and priority research to inform policy, health promotion, service provision and clinical practice.
Cancer Australia, 2018	Optimal Care Pathways (OCP) for Aboriginal and	This OCP is designed to complement the tumour-specific OCPs, focusing on aspects of the care pathway that need to be responsive to the needs of Aboriginal and Torres Strait Islander people with

	Torres Strait Islander people[20]	cancer. Contains detailed guidance for health practitioners and service planners on optimal care across the cancer continuum. Includes resource reference guide. Acknowledges health and connection to land, culture, community and identity and a whole-of-life view. Includes clinical trials.
Cancer Australia, 2020	A Guide to Implementing the Optimal Care Pathway for Aboriginal and Torres Strait Islander People with Cancer[2]	The Implementation Guide suggests activities to support OCP implementation at different levels: coordinated and consistent health system activities; activities as part of health service planning, review and reporting; guidance for individual health professional training and development. Overarching implementation activities: 1) Culturally competent workforce 2) Integrated planning and care delivery across services 3) Culturally appropriate care coordination and support. OCP implementation aims to support (amongst other aims) increased access and facilitation of participation in appropriate clinical trials by Aboriginal and Torres Strait Islander people. Consideration of clinical trials and provision of culturally appropriate clinical trial information is one of the 'Quick check' monitoring progress checks.

APPENDIX 2 METHODS 2019 – 2021 RAPID REVIEW

1. Peer reviewed literature: Australia, Indigenous people in other countries, underrepresented groups.
2. Cochrane database
3. Google scholar
4. Other

Inclusion and exclusion criteria

Articles were included if they reported strategies relevant to the aims of the ReViTALISE project, either in general or regarding specific aspects of clinical trials (e.g., PROM tools or promotional materials), or that covered overarching considerations (e.g., governance).

Articles were excluded for the following reasons: paediatrics unless focussed on CT recruitment in relevant population; diseases other than cancer unless review articles documenting strategies to increase enrolment of relevant population; studies only documenting low participation of relevant population (ie, not containing strategies); study protocols; wrong publication type; wrong outcome; wrong study design.

1. Peer reviewed literature

Three groups of searches of peer-reviewed literature were undertaken in Pubmed. The Primary Search related to Aboriginal and Torres Strait Islander Australians and cancer. Supplementary search A related to First Nations and

Indigenous people in other countries. Supplementary search B related to other underrepresented groups. Search strategies and results are detailed below. Limits applied were full text publications in English and a publication date between 2019 and Nov 2021.

Primary search

Aboriginal and Torres Strait Islander people in Australia and CT participation

	(a) Keywords (Title/Abstract)	(b) MESH Terms
1) Main population	Indigen* OR Aborigin* OR Torres Strai* OR First Nation* OR First People*	"Oceanic Ancestry Group"[mh]
2) Main focus	trial* OR randomi* control* trial* OR randomi* clinica* trial* OR clinical stud*	"Clinical Trials as Topic"[mh]
3) Secondary focus	participat* OR criteri* OR exclud* OR exclusion OR includ* OR inclusion OR barrier* OR improv* OR access* OR increas* OR enabl* OR recruit*	"Patient Selection"[mh] OR "Patient participation"[mh]

(1a OR 1b) AND (2a OR 2b) AND (3a OR 3b) = 259 (41 for full text review)

Supplementary A: First Nations and Indigenous people in other countries

	(a) Keywords (Title/Abstract)	(b) MESH Terms
1) Main population	Aborigin* OR Indigen* OR Maori OR Metis OR Eskimo OR Yupik OR Inuit* OR Inupiat* OR Tribe* OR Tribal OR First Nation* OR American Indian* OR Native America* OR Native People* OR Native Population*	"Oceanic Ancestry Group"[mh] OR "Indians, North American"[mh] OR "Inuits"[mh]
2) Main focus **(same as Primary Search)**	trial* OR randomi* control* trial* OR randomi* clinica* trial* OR clinical stud*	"Clinical Trials as Topic"[mh]
3) Secondary focus **(same as Primary Search)**	participat* OR criteri* OR exclud* OR exclusion OR includ* OR inclusion OR barrier* OR improv* OR access* OR increas* OR enabl* OR recruit*	"Patient Selection"[mh] OR "Patient participation"[mh]

(1a OR 1b) AND (2a OR 2b) AND (3a OR 3b) = 413 (21 for full text review)

Supplementary B: Other underrepresented groups

	(a) Keywords (Title/Abstract)	(b) MESH Terms
1) Main population	Underrepresented OR minorit* OR underserve* OR ethnic* OR CALD	"Ethnic Groups"[mh] OR "Vulnerable Populations"[mh] OR "Cultural Diversity"[mh] OR "Minority Groups"[mh]
2) Main focus **(same as Primary search)**	trial* OR randomi* control* trial* OR randomi* clinica* trial* OR clinical stud*	"Clinical Trials as Topic"[mh]
3) Secondary focus **(same as Primary Search)**	participat* OR criteri* OR exclud* OR exclusion OR includ* OR inclusion OR barrier* OR improv* OR access* OR increas* OR enabl* OR recruit*	"Patient Selection"[mh] OR "Patient participation"[mh]
4) Condition	cancer OR neoplas* OR malignan*	"Neoplasms"[mh]
5)	review	(adding "review, systematic"[mh] yielded no results)

(1a OR 1b) AND (2a OR 2b) AND (3a OR 3b) = 159 (10 for full text review)

2. Cochrane Library

A search of the Cochrane Library was conducted to identify relevant research. Keywords as tabled above were used to search titles, abstracts and keywords. MeSH descriptors [Oceanic Ancestry Group], [Neoplasms] and [Australia] were used, with the 'explode all trees' function. 0 additional articles

- Indigenous OR Aborigin* OR Torres (n=1 review; 0 relevant)
- Recruitment AND trial AND minority (n=16 reviews; 0 relevant)
- Participation AND trial AND minority (n= 84 reviews; 0 relevant)
- Recruitment AND trial AND ethnic (n= 5; 0 relevant)
- Participation AND trial AND ethnic (n= 29; 0 reviews)
- Recruitment AND trial AND Aboriginal (n=0 reviews)
- Participation AND trial AND Aboriginal (n=0 review)

- Recruitment AND trial AND Indigenous (n=0 reviews)
- Participation AND trial AND indigenous (n=0 reviews)
- Recruit AND trial AND improve (n=115; 0 relevant)
- Recruit AND trial AND increase (n=122 reviews; 0 additional relevant)

3. Google scholar

Several supplementary searches were undertaken using Google Scholar. For each search, the first 10 pages of results were screened using the title and, where necessary, the abstract. If new eligible articles were identified on pages 9 or 10, then screening was to continue until there were two consecutive pages with no new eligible articles identified. In practice, it was not necessary to go beyond the first 10 pages for any search. Exclusion criteria were more relaxed than for the searches reported above. For example, reviews that were about clinical trials in general (rather than cancer specific) could be included if they were focused on a relevant population group and explored enablers as well as barriers. Articles that reported on programs and initiatives related to increasing trial participation or otherwise shed light on a specific relevant aspect were also considered for inclusion. The search terms used and results are shown below.

Primary:

• (Aboriginal OR Torres Strait OR Indigenous) AND (trial OR clinical study) AND (participation OR participate OR exclude OR exclusion OR include OR inclusion OR barrier OR criteria OR improve OR access OR increase OR

enable OR recruit). (50 results: 1 relevant, not previously identified: Duke 2021)

• Participation in clinical trials Indigenous (2 relevant, not previously identified: Te Karu 2021; McFarlane 2021)

• Participation in clinical trials Aboriginal (1 relevant, not previously identified: Wong 2020)

• Participation in clinical trials Torres Strait Islander (0 potentially relevant)

4. Other mechanisms

a) A hand search of reference lists of included publications during full text review resulted in the inclusion of 1 additional article (Cunningham-Erves 2020).

b) An additional search was undertaken to add depth to the area of Community Based Participatory Research, which resulted in the inclusion of two additional articles (Haynes, 2019; Snijder, 2020).

APPENDIX 3 CLINICAL TRIALS: POLICY, GUIDELINES, FRAMEWORK DOCUMENTS

APPENDIX 3.1 RECENT AUSTRALIAN DEVELOPMENTS AND IMPLICATIONS FOR THE REVITALISE PROJECT

DOCUMENT, YEAR	SUMMARY	IMPLICATIONS FOR THE REVITALISE PROJECT
ANZCTR Aspex Consulting report (CTR review) 2018[101]	Under consideration by Australian Government.	Unknown at this stage.
Queensland Health Teletrials Pilot Analysis Report July 2019[102]	Following development of teletrials quality assurance framework, the framework was tested in a commercially sponsored clinical trial for a breast cancer drug, in the Qld public hospital system. The pilot informed SOPs in Qld Health. The pilot involved 8 satellite staff and 11 regional patients who would otherwise not have been able to participate in a CT. First patient recruited in Oct 2018. Key findings include (amongst others): industry support the national implementation of unified teletrials model; a clinical champion is required to drive policy implementation within health systems; positive patient and staff (primary and satellite) feedback; significant cross jurisdictional consultation necessary; cluster model enabled upskilling of regional sites; regular meetings b/w CT, institution management and Research Governance Office (RGO) staff required. Developed 'Queensland Teletrials Toolkit' (see below).	Unknown whether any Aboriginal people were recruited. Note strategies used, as teletrials may be an important option for the ReViTALISE project.
Queensland Teletrials Toolkit[103] (*Links to National Teletrials Compendium*)	Contains guidance for sponsors and sites (steps required to set up and manage a teletrial, HREC / site authorisation documents required and key steps of process) Evaluation of a clinical trial as a teletrial; Evaluation of a site as a satellite site; Primary site RGO submission document; Satellite site RGO submission document; Notification to reviewing HREC of satellite site joining a teletrial.	May be a useful checklist if the ReViTALISE project uses teletrials, to assess how each process addresses inclusion of Aboriginal people.

National Teletrials Compendium:[32] • National Principles[33] • National Standard Operating Procedures[34]	The National Teletrials Compendium, developed to support a consistent national approach to teletrial implementation in Australia, is supported by all states and territories and includes two documents: • National Principles for Teletrials in Australia, Clinical Trials Project Reference Group, 2020. This document specifies consistency with COSA's Australasian Teletrial Model 2016, which refers to Indigenous populations briefly in the background section and regarding recruitment; and • National Standard Operating Procedures for Clinical Trials, including Teletrials, Clinical Trials Project Reference Group, 2020. Also available: Clinical Trial Research Agreement - Teletrials Subcontract.	General reference. No discussion of issues or strategies specific to Aboriginal and Torres Strait Islander people. Refers to National Statement (2018); Ch 4.7 focuses on research with and for Aboriginal and Torres Strait Islander peoples.
National Clinical Trials Governance Framework - Guide for implementation 2020 (ACSQHC, contracted by Australian Govt Dept of Health: first step towards accrediting health services to undertake CTs)[31]	To support the delivery of high-quality clinical trial services, the Australian Commission on Safety and Quality in Health Care has developed the National Clinical Trials Governance Framework on behalf of all jurisdictions. The framework contains principles and strategies to guide CT services in Australia. The pilot implementation of the Framework was conducted from Sep 2020–Mar 2021 via a voluntary approach and a targeted approach. The targeted approach consisted of 14 pilot sites: Alfred Health, Canberra Hosp, Orange Health Service, Perth Children's Hosp, Ramsay Health Care (14 services), Royal Adelaide and QE Hospitals, RBWH, RDH, RHH, SVHN (Syd and Melb), Sydney PDH (RPAH), Royal Vis Eye and Ear Hosp, Townsville Hospital and Health Service, Victorian CT Research Support Service (Ballart, Barwon, Bendigo, Goulburn Valley, Northeast Health Wangaratta). Implementation is expected from January 2022. Consists of a Literature Review (see below) and Mapping Exercise (see below), guided by an expert Steering Committee. The Framework is based on two NSQHS Standards: 1 Clinical Governance Standard and 2 Partnering with Consumers Standard.	Items that directly relate to the aims of the ReViTALISE project are summarised in Table 2.2.
National Clinical Trials Governance Framework Literature Review 2018 [104]	Methods: January 2007 – 'present' (?Jan 2018); English; academic and grey literature. Commentary on CT governance and evaluation of CT governance frameworks at hospital and/or funding health agency level. PRISMA. n=66. Includes NZ, UK, South Korea, Canada, USA, European Union, Nordic region. Current approaches to CT governance in Australia, Canada, UK, South Korea.	Nothing specifically for Aboriginal people

	Table 10 p94 contains Australian reports and reviews into clinical trials and medical health research until 2017. Key findings: Successful national approaches are coordinated by a government-supported entity and underpinned by guiding polices, legislation and infrastructure. Key components of successful approaches (UK, South Korea) to CT governance: • A national strategic plan including guiding principles for the implementation of a governance framework, realistic objectives and measurable outcomes • A national legislation and policy framework • A national or central coordinating agency • A national or central IT platform • A national and local site-capability framework • National independent accreditation to assess local-level providers to confirm they have implemented the nationally harmonised approach to CT governance.	
National Clinical Trials Governance Framework Mapping exercise report 2018[105]	Purpose: build on literature review findings to identify existing policies and processes relating to the governance of CT in Australia and provide insights into private and public sector work aimed at improving local CT operating environments. Sections: 1) Background and methodology for mapping exercise. 2) Overview of national and jurisdictional regulation, legislation and guidance materials relating to the conduct of CTs. 3) CT process and overarching themes + overview of infrastructure investment and the context and scope of improvement activities. 4) Jurisdictional overview of current legislation, policies and improvement initiatives. The Mapping Exercise draws on the literature review and key informant semi-structured interviews. Feedback was sought on current challenges associated with the conduct of clinical trials and capturing activities currently underway nationally or within jurisdictions to streamline clinical trials operations. Stakeholder perceptions on the development of a national Clinical Trials Governance Framework were also	Limited direct implications. Re HREC processes: called for a consistent approach to the review of proposals for research involving Aboriginal and Torres Strait Islander people, rather than the current ad hoc approach. Case study LHD strategic plan aimed to develop pathways for approval and oversight for Aboriginal research.

	discussed. Interviews were conducted with staff from: Australian Institute of Aboriginal and Torres Strait Islander Studies; and the Aboriginal Health and Medical Research Council. Australian reports and guiding documents are in Appendix 2 of the Framework Mapping exercise report.	
The Clinical Trials portal and User guide to the self-assessment and operational metrics tools. 2020[106]	The Commission has developed the Clinical Trial portal to support the pilot and implementation of the Governance Framework. Self-assessment and operational metrics tools are within the Portal. The National Clinical Trials Governance Framework provides the first step toward the accreditation of health services for the conduct of clinical trials. A self-assessment tool has been developed to assist health services to identify gaps in their systems, to plan and to track their progress in meeting actions provided in the Governance Framework. The operational metrics tool enables the workforce within trial units, clinical departments, hospitals and health networks to collect and review their clinical trial service operations through a series of automated reports. These reports may assist health service organisations with strategic planning to deliver clinical trial services. The operational report items are aligned to the National Aggregate Statistics (NAS). A user guide has been developed to assist with the navigation and use of the self-assessment and operational metrics tools including the registration process.	Unknown
Duke et al. 2021[64] Culturally Adaptive Governance Framework (CAGF)	Culturally Adaptive Governance - Building a New Framework for Equity in Aboriginal and Torres Strait Islander Health Research: Theoretical Basis, Ethics, Attributes and Evaluation. New approach for mainstream research project governance: identifies the realities of power, acknowledges the complexities of culture and emerging health technologies, and foregrounds the principle of equity for mainstream Indigenous health research. The CAGF is currently being implemented in a national Indigenous multicentre trial, the FlashGM Study (evaluating the use of continuous blood glucose monitors to improve diabetes care and treatment for Indigenous Australians). See text 'Governance of clinical trials' for more information.	Promotes purposeful collaboration between Indigenous knowledge systems and Western Scientific traditions. Possible collaboration with pilot sites in regional Victoria.

APPENDIX 3.2 EXTRACTION OF RELEVANT ITEMS FROM THE NATIONAL CLINICAL TRIALS GOVERNANCE FRAMEWORK (CTGF) USER GUIDE

CATEGORY	CONTENT	IMPLICATION FOR THIS WORK: KEY TASKS, STRATEGIES, OR SUPPORTING EVIDENCE TO SUPPORT ACTIONS
Core governance principle for CT services: Equity (p17)	Health service organisations observe cultural safety, competence and respect in providing clinical trial services to meet the needs and priorities of Aboriginal and Torres Strait Islander people in delivering CT services. Resource appropriately to allow participation in all available trials.	Guiding principle
Organisational leadership: management and executive leadership Action 1.4 p25	'The health service organisation implements and monitors strategies to meet the organisation's safety and quality priorities for Aboriginal and Torres Strait Islander people.'	Strategies: undertaking trials that meet the priorities of Aboriginal people; improve access to trials by employing ALOs; setting workforce participation targets of Aboriginal people across all levels in the CT workforce; provision of cultural mentors for non-Indigenous CT staff; collaboration with ACCHOs, adopting a holistic model of health and wellbeing in the design, planning and implementation of CT services, amongst other strategies regarding information, communication, review and reporting. Key tasks are outlined. Supporting evidence to facilitate progress monitoring includes documenting community engagement or workforce training, and incorporation of priorities into CT services documentation.
Risk Management: Diversity and high-risk groups. Action 1.15 p45	Health service organisation or trial site: a. Identifies the diversity of the consumers using its services b. Identifies groups of patients using its services who are at higher risk of harm	Key tasks: Identify clinical and administrative data systems that indicate patient diversity using the organisation's health services and the formats, languages and tools to be used to communicate and recruit patient to clinical trials; Develop strategies to identify high risk patients who maybe potential trial participants and implement mechanisms to provide safety and quality protections for these patients participating in a clinical trial.

	c. Incorporates information on the diversity of its consumers and higher-risk groups into the planning and delivery of care	Supporting evidence examples: Demographic data for the health service organisation and community that are used for strategic planning purposes; CT network meetings and consumer representation committees reflect local diversity of patient population; consumer CT participant information available in formats and languages that reflect population.
Safe environment for the delivery of care Action 1.33 p55	The health service organisation demonstrates a welcoming environment that recognises the importance of the cultural beliefs and practices of Aboriginal and Torres Strait Islander people.	Key tasks: health service organisation reviews factors that create a welcoming environment for Aboriginal and Torres Strait Islander people to participate in CTs. Strategies: in collaboration with local Aboriginal and Torres Strait Islander people, review design, use and availability of information in language; seek feedback on signs, symbols and displays that could be used to promote CT in a culturally safe way. Evidence: committee/meeting records; availability of Aboriginal support officer specifically to support Aboriginal and Torres Strait Islander people's participation in CTs; information (in language) about role of support officer and services available; consumer survey responses.
Partnering with consumers: Health literacy Action 2.8 p68	Communication that supports effective partnerships. The health service organisation uses communication mechanisms that are tailored to the diversity of the consumers who use its services and, where relevant, the diversity of the local community.	Strategies: health service organisations can work to develop a framework that integrates cultural competency into its communication mechanisms; Identify diversity of the community; Review current communication mechanisms; consider cultural competency training if Aboriginal and Torres Strait Islander people regularly use the service (*Note; consider whether patients are not using the service <u>because</u> it's not culturally safe*). Key tasks: health service organisation provides communication material in general and specifically in relation to clinical trials that meets the needs of their diverse consumer and community population, and ensure that accredited interpreter services are available to consumers who require them; a variety of mechanisms to meet the communication needs of the diverse consumer and community population are also used to improve participant recruitment and to support the retention of participants on a clinical trial. Examples of supporting evidence: Demographic profile or demographic survey for the health service organisation that identifies the diversity of the community it serves; Feedback from consumers from culturally or linguistically diverse backgrounds during the development or review of information packages or resources.

Roles and functions of identified positions. Appendix 1	Consideration should be given for cultural safety, competence and respect in providing clinical trial services that meet the needs and priorities for Aboriginal and Torres Strait Islander people.	Additionally, the functions of the principal investigator include: Engaging with Aboriginal and Torres Strait Islander peoples and respecting their legal rights and local laws, customs and protocols as they relate to clinical trials.

APPENDIX 3.3 INTERNATIONAL FRAMEWORK / POLICY DOCUMENTS

TITLE	SUMMARY	IMPLICATIONS FOR THE REVITALISE PROJECT
National Institute on Minority Health and Health Disparities (NIMHD) Research Framework[107] USA	The Research Framework aims to promote the health of minority populations, and the understanding and reduction of health disparities. It reflects the complex and multifaceted nature of minority health and health disparities. The Framework consists of domains (biological, behavioural, physical/built environment, sociocultural environment, healthcare system) and levels of influence within the domains (individual, interpersonal, community, societal). It provides a classification structure to facilitate analysis of research progress, gaps and opportunities. Adaptations for different US populations have been published e.g., 'Adapted to reflect historic and socio-cultural influences for American Indian and Alaska Native Nations' includes specific items relevant to this community; 'implicit bias' at the intersection of the *healthcare system* domain and the *interpersonal* level of influence and 'historical trauma' at the intersection of the *sociocultural environment* and *individual* level of influence. Other items are spirituality, collective resilience, non-biomedical constructions of illness, traditional healing resources, boarding school education, alternate financing and structure of healthcare, tribal sovereignty, major federal Indian policies. The determinants can be readily operationalized, measured, and analyzed in ways 'analogous to their conceptual counterparts for other populations'.	Use the framework to assess research design, implementation, monitoring and reporting processes. Possibly set up a working group with majority membership of Aboriginal people to adapt to the (regional) Australian setting.
Patel et al. American Society of Clinical Oncology (ASCO) Cancer Disparities and Health Equity: Policy statement[86]	This policy statement addresses cancer disparities and health equity, rather than clinical trials specifically, however many strategies have direct relevance to the ReViTALISE project. ASCO has been working on diversification of CTs since ~2015, with policy documents and recommendations on older adults (2015), broadening eligibility criteria (2017), recommendations to FDA aimed at reducing barriers (2018), and addressing financial barriers to CT participation (2018). ASCO acknowledges that the COVID-19 pandemic has highlighted the consequences of a failure to provide accessible, equitable care to all and is currently working on a strategic plan to address and help implement the recommendations. ASCO recommendations for promoting health equity (*abbreviated*):	Multiple relevant strategies: stratified recruitment strategies; multisector partnerships; targeted awareness strategies; patient navigations and engagement of community health workers; research team diversity; promotion of culturally safe care; examine and address institutional discrimination; support and model open dialogue; work towards inclusive

	Ensure equitable access to high-quality care: Support and promote policies, systems, environments, and practices to address persistent barriers to equitable receipt of high-quality cancer care; Protect and promote health care system and payment reforms that improve health equity; Advocate against proposed policy changes that could result in reduced care and worse treatment outcomes for patients with cancer, survivors, and their families; Support and expand alternative payment models and programs to ensure equitable receipt of high-quality cancer care; Facilitate and support stakeholder collaborations to promote equitable receipt of essential cancer care services. **Ensure equitable access to research:** Promote policies, systems, environments, and practices that improve equitable participation in all research, including clinical trials, population science, health services research, and CBPR; Understand and address ongoing barriers and promote facilitators to equitable research participation; Promote use of stratified recruitment strategies to ensure adequate representation of key groups at risk of disparate toxicity or mortality outcomes for the disease or treatment of interest, e.g., socioeconomic status, race/ethnicity, and location of residence; Require routine collection and public reporting of research data on variables known to influence cancer outcomes e.g. race / ethnicity, SES; Facilitate and encourage multisector partnerships among e.g., community organizations and academic institutions, to improve inclusion into research studies; Promote and encourage sustained economic and infrastructure support to help reduce multilevel barriers to equitable participation in research. Encourage collaborations and programs to improve equitable participation in research e.g. patient navigation, community health workers, and partnerships with advocacy organizations. **Address structural barriers:** Promote policies, systems, environments, and practices to improve and sustain cancer workforce diversity including researchers; Promote and encourage culturally and linguistically appropriate, respectful, and high-quality cancer care within all health care systems; Partner with local communities and local legislatures to support the implementation of activities and application of research findings known to improve health equity; Encourage organizations and institutions to internally examine and appropriately address institutional discrimination; Support and equip providers to address disparate health outcomes resulting from institutional discrimination through providing education and activities that can inform practice and research; Support open dialogue among stakeholders, patients, and organizations to discuss discrimination and subsequent health outcomes and promote activities	and respectful workplaces; wide dissemination of approach; patient-centred recruitment messaging; broaden eligibility criteria; address financial barriers and promote access to participation; strong data management to facilitate monitoring of key outcomes.

	that support inclusion and respectful workplace environments; Strengthen ASCO support for educational activities and forums regarding institutional discrimination. **Increase awareness and action:** Promote policies, practices and multisector collaborations to increase awareness of and solutions that can address health inequities; Develop and disseminate appropriate literacy materials for providers, patients, caregivers and advocacy groups; Promote health equity through the use of multiple dissemination approaches as proposed by representatives from different sectors or stakeholder groups. Other strategies: informed consent methods that are accessible to a range of linguistic and cultural backgrounds (e.g. patient-centred recruitment messaging); research and infrastructure funding to achieve these goals; quality data management infrastructure to support research activities, broaden inclusion criteria of CTs and other research, address financial barriers to participation, and promote access to research in underrepresented areas. Workforce disparities require attention: disparities result in '*additional downstream effects that can have a chilling effect on research into health equity' (*p3444*)*. National Cancer Institute's Cancer Center Support Grants now includes requirements regarding catchment area (e.g. CT recruitment populations), community outreach and engagement – advocates for better funding and to enable lasting relationships.	

APPENDIX 4 CANCER: CLINICAL TRIALS OR CLINICAL RESEARCH WITH UNDERSERVED GROUPS

CATEGORIES: REVIEWS; PATIENT NAVIGATOR PROGRAMS (RCTS, EVALUATION); COMMENT AND STRATEGY DEVELOPMENT; TOOL DEVELOPMENT; QUALITATIVE RESEARCH; OTHER.

AUTHOR, YEAR,	STUDY TYPE	DESCRIPTION	SHORT SUMMARY	FINDINGS
REVIEW OR SUMMARY ARTICLES				
Chino, 2019, USA[108]	Review – invited article	Financial Toxicity and Equitable Access to Clinical Trials (US focussed but detail about addressing direct and indirect CT cost issues)	Increased costs present a specific obstacle to enrollment in a clinical trial. Nonmedical costs of trial participation (including travel, lodging, and other hidden expenses) may drive decision-making for some vulnerable patient groups. American Society of Clinical Oncology (ASCO) has prioritized efforts to improve clinical trial enrollment for those facing financial toxicity.	**Known costs** of clinical trial participation: Standard care: Drugs, studies, tests, and treatment that would be given regardless of participation in a clinical trial (typically paid for by insurance for insured patients) Study drugs or devices: Investigational use only (typically paid for by the study fund/sponsor) Special studies/tests (laboratories and imaging): Investigational laboratory draws and imaging studies (typically paid for by the study fund /sponsor) Complications: Additional costs owing to unexpected treatment side effects, including copays for medications for symptoms, hospitalizations, or other medical care needed (typically paid for by insurance for insured patients). "**Hidden costs**" of clinical trial participation (more frequent clinical visits and travel to trial sites.) Travel: Gas, vehicle wear and tear, tolls, parking, airfare, lodging Food: Eating out while away from home (for both patient and family members) Child/eldercare: Hiring sitters or paying for daycare or day programs Employment: Lost wages for patient and/or spouse Insurance: Higher copays and costs if out of network; costs for "standard care" and treatment of complications that insurance companies may ultimately deny because of participation in clinical trial (grandfathered plan or Medicaid). Improving rural access, stabilizing consistent insurance payments, and normalizing noncoercive financial support for participants are all avenues that may decrease disparities in clinical trial enrollment and create more equitable outcomes for all. Cites papers with increased CT participation of (1) rural patients and (2) those with lower incomes due to (1) increased resources and support and (2) graded reimbursement of travel and lodging expenses. Also suggests improving patient education and engagement (increase awareness and decrease misconceptions of CT via interactive video, mass media, social media) as key to eliminating disparities in access to CTs and cancer assistance foundations (cites patient navigator). Advocates for cost transparency to reduce financial toxicity and improve shared decision making.
Cunningham and Garvey, 2020, Aust[23]	Ca CT, Aboriginal people, Australia	Are there systematic barriers to participation in cancer treatment trials by Aboriginal and Torres Strait	Analysis of online documents from the Australia and New Zealand CTs Registry for cancer treatment trials (Phase 3, 4 or Not Applicable) with at least one Australian site, registered in 2014–2018.	Among 365 eligible trials, most (89%) had sites only in major cities/inner regional areas, but 39% of Aboriginal and Torres Strait Islander Australians live outside these areas. Seven cancer types accounted for 58% of cancers among Aboriginal and Torres Strait Islander people, but only 46% of trials addressed these cancers. Most trials specified exclusions relating to comorbidities/health status. A substantial minority of trials (38%) explicitly referred to investigator opinion/judgment as a relevant determinant of patient eligibility. **Conclusion**: Aboriginal and Torres Strait Islander patients appear to have a reduced opportunity to participate in trials because of where they live, their type of cancer and their general health status, as well as for less transparent reasons relating to investigator

		Islander cancer patients in Australia?		judgment. **Implications for public health**: Greater transparency and scrutiny of barriers to trial participation for Aboriginal and Torres Strait Islander Australians are needed to ensure equitable access.
Kidd, 2019, NZ[76]	Integrative review: cancer	Health service provider responses to Indigenous peoples with cancer: An integrative review	Assessed: 1) reporting of ethnicity in CTs; 2) were translated and culturally appropriate measures used to capture PRO data; 3) barriers/facilitators to using appropriate PROMs with ethnically diverse groups. Systematic review. 8 of the 14 studies were multicentre, multi-national trials.	Nine studies (7 USA; 1NZ; 1Aust [Mooi Whop telehealth 2012]). Patient navigator programs n=4, all American Indian (Walking Forward). Telehealth n=2 (1 USA, 1 Aust). Other n=3 (symptom management toolkit; Cancer survivors support network, NZ paper overview of prog/interventions prov by Maori health providers). Inclusion of cultural aspects notable. The Walking Forward project has shown to provide financial assistance, reduce treatment interruptions and **improve the incidence of CT participation among AI.** (also showed that AI cancer patients expressed higher satisfaction levels with health care after cancer treatment while receiving PN services.)
Nazha, 2019, USA[67]	Review	Enrollment of Racial Minorities in CTs: Old Problem Assumes New Urgency in the Age of Immunotherapy.	The expectation and practical application is that this review along with others will drive policy decisions to promote minority enrollment in CTs as a deliberate strategy that guides CT design. We will provide a summary of strategies proposed to exert maximal impact on this intractable problem ranging from individual-level intervention for patients and investigators, structural problems related to study design and conduct, and larger societal level intervention in the form of community engagement and policy enunciation.	Changes at every level are needed. Individual level: promote awareness - targeted social media ads, enhanced visibility at practice locations that serve minority patients. Incentive vs inducement. Overcome financial barriers (ASCO Health Disparities Committee has detailed policy statement including recommendations to overcome financial barriers - transparent process to estimate out-of-pocket expenses and cover these costs). Provider barriers: culturally appropriate tools. Physical proximity and culture competence (ref Wash DC 2012-14). Address diversity gap in biomed workforce. Structural barriers: reduce rigidity of eligibility criteria. At cancer centre level, regional partnerships b/w large academic centres and satellite sites in underserved communities. Develop framework for community based minority recruitment. Build biobanks across minority comms to enable genomic testing - response to immunotherapy. National level: regulatory interventions and policy enactments. Enforcement of diverse recruitment. National Black Church Initiative. FDA.
Nolan, 2021, USA[109]	Systematic review	Use of Video Education Interventions to Increase Racial and Ethnic Diversity in Cancer CTs: A Systematic Review	This systematic review examined the use of video education interventions to impact BIPOC cancer survivor participation in CTs.	Seven selected articles described six distinct interventions. Although the six interventions reduced barriers to participation in CTs, their findings varied on Black and Hispanic survivors' readiness to enroll and participate in trials. Four themes: (a) cultural sensitivity is needed in video development and delivery; (b) video content should be aimed to educate and change attitudes about CTs; (c) video interventions are feasible and acceptable; and (d) video interventions affect outcomes on intention or actual enrollment. LINKING EVIDENCE TO ACTION: Video interventions are well-received by BIPOC survivors and may improve representation in CTs. Yet, video interventions are underutilized. More studies are needed to establish best practices for video interventions aimed at diversifying CT participation as widening cancer disparities and rapidly changing cancer care continue to emerge.
Slade, 2021, UK[71]	Systematic review - translated PROMs in Cancer CT	Systematic review of the use of translated patient-reported outcome measures (PROMs) in cancer trials	Assessed: 1) reporting of ethnicity in CTs; 2) were translated and culturally appropriate measures used to capture PRO data; 3) barriers/facilitators to using appropriate PROMs with ethnically diverse groups. Systematic review. 8 of the 14 studies were multicentre, multi-national trials.	1) Most studies did not report ethnicity data; 14/84 (17%) reported any type of ethnic group profile data. 2). No studies reported using translated / culturally appropriate PROMs in the design, despite 7 studies used PROMs that have been translated. 3) 44 interviews with broad range of international stakeholders. Themes: (1) **recruitment** (lack of resources for recruitment and inclusive recruitment strategies were described as flaws in the trial design and a barrier to recruitment.); (2) **development of research questions and study design** (Extent to which translated / culturally appropriate PROMs were considered during trial design process and included in protocol depended on prominence of the PRO within the study and whether targeted recruitment of specific groups was compatible with study design. It was also noted that fluency in English is often used as an eligibility criterion for PRO components. Participants described using English as the default language and this was considered standard practice in many studies, rendering the use of translated and culturally validated measures unnecessary. Concerns were voiced about balancing the need for inclusivity without additionally burdening the investigator. Research questions formulated with consideration of the target population promotes the use of study design and PRO strategy that is appropriate and reflects the priorities of the groups.); and (3) **implementing translated and culturally validated PROMs** (difficulty of ensuring translated and culturally validated PROMs were available and the time-consuming, expensive, labour-intensive nature of their use. **Facilitators** of inclusive PRO research: clear recruitment aims at the beginning of the design process and monitored throughout the study in real time to ensure a representative sample; making use of existing translated/validated instruments; piloting PROMs with the target community groups; adopting an "enrichment" strategy to promote recruitment; and recruitment in diverse localities. Participants described the key

				role of key research institutions and ethics committees could request details pertaining to diverse recruitment and diversity targets could be linked to funding.
Vuong, 2020, USA[30]	Narrative review	Aim: to summarize the current evidence for effective approaches to increase enrollment of underrepresented minorities in cancer therapeutic CTs. Peer reviewed articles published: 2008- 30 March 2018.	Cancer clinical decision-making is based on research studies where the majority of research participants are white males, despite the disproportionate cancer burden in racial and ethnic minority groups. Multiple reviews detailing barriers to enrollment for these populations in cancer CTs, but a notable lack of research on possible strategies to overcome them. Evidence of variability in effectiveness of specific therapies or medications across racial/ethnic groups. Barriers: lack of CT awareness; cost of participation; lack of culturally relevant CT education; medical distrust; decreased opportunities for participation e.g. exclusion from CTs based on comorbidities; lack of knowledge /understanding; language; fear the experiment will be prioritised over patient's health; fear unknown side effects; general distrust of medical system; SES barriers - travel, time/sick leave for clinic visits, lack of health insurance, distance from trial centres, lack of social support.	n=15 studies - only studies addressing enrolment of minority populations eligible. Ten studies used more than one strategy (community relationships + education delivered by trained culturally / racially congruent people. Studies using a single intervention strategy (n=5) had less effective outcomes. Summary of current evidence for effective approaches to increase enrollment of underrepresented minorities in cancer therapeutic CTs: (1) cultural and linguistic adaptations of marketing materials (n=11) (most commonly used and most effective; (2) the use of patient navigators (n=3) (increased retention, fewer treatment interruptions and higher enrolment [1 did not show higher enrolment]); (3) building ongoing community partnerships (n=1). The majority of studies reviewed employ multiple improvement strategies simultaneously. Identifying effective approaches to increase enrollment of underrepresented populations in cancer CTs is a critical step in reducing persistent disparities in cancer incidence and mortality among racial and ethnic populations. Detail re each strategy in Appendix table.
PATIENT NAVIGATOR PROGRAMS – RCTS AND EVALUATION				
Cartmell 2020, USA[79]	Evaluation	Evaluated intervention - 'lay' navigators provided patient education and support to help them overcome barriers to trial participation and related clinical care.	(**not focussed on minority groups** – included to demonstrate challenges) 40 patients receiving patient navigation services to address low participation in CTs. Identified barriers faced by patients using a barrier checklist. Determined whether barriers could be overcome.	Most common barriers faced by navigated patients: fear (n=9); issues communicating with medical personnel (n=9); insurance issues (n=8); transport difficulties (n=6); perceptions about providers and treatment (n=4). Most common activities undertaken by navigators: making referrals and contacts on behalf of patients (e.g., support services, family, clinicians; n=25). Navigators made arrangement for transport, financial, medication and equipment services (n=11) and proactively navigated patients (n=8). Barriers not overcome for >=2 patients included insurance issues, lack of temporary housing resources for patients in treatment and assistance with household bills. Wide array of patient barriers to CT participation and navigator assistance documented here supports CT navigator role in facilitating quality care.
Nickell, 2019, USA[78]	RCT (in CBPR)	Engaging limited English proficient and ethnically diverse low-income women in health research: A randomized trial of a patient navigator intervention	Evaluate community-based navigator intervention to increase breast cancer patients' and survivors' access to research participation opportunity information. Prospective RCT in context of CBPR. Primary outcome: health research info-seeking behaviour. Secondary outcomes: health research knowledge; willingness to participate in health research; health empowerment. Qualitative interviews n=11.	No significant difference between intervention / control groups' health seeking behaviour. Responses indicated willingness to participate, but competing priorities limited participant's motivation to seek enrollment information. Community-based navigators are a trusted link between health research and underserved communities. Systematic barriers, such as English-only research staff and materials, the high literacy level of verbal and written communication about research, and the failure to invite low-income and minority patients and survivors to participate, continue to restrict participation in research. .
Ramirez, 2020, USA[77]	RCT	Assessing the effect of patient navigator (PN) assistance for psychosocial support services on health-related quality of life (HRQOL) in a randomized CT in	Latinos experience higher prostate, breast, colorectal cancer mortality rates and lower HRQOL compared with other ethnic/racial groups. PN and lay community health workers are effective in increasing cancer screening and early-stage diagnosis among Latinos. Little is known about the effect of PN on HRQOL among Latino cancer survivors. Methods: Latinos previously diagnosed with	PN-LCNS demonstrated a significant improvement in HRQOL in comparison with PN only for colorectal cancer survivors but not for breast and prostate cancer survivors. The breast cancer finding was consistent with previous research demonstrating that Latina breast cancer survivors report greater unmet supportive care needs and lower HRQOL and self-efficacy after completing primary treatment. Authors concluded that further research is required to determine how PN programs should be adapted to address HRQOL concerns among Latina breast cancer survivors. Enhanced PN improves HRQOL among Latino colorectal cancer survivors. Future research should identify the best strategies for engaging Latino survivors in PN programs.

		Latino breast, prostate, and colorectal cancer survivors	breast, prostate, or colorectal cancer (n = 288) were randomized to either 1) or 2): 1) Patient Navigator LIVESTRONG Cancer Navigation Services (PN-LCNS) survivor care program; participation in phone-based program which included promotion of services on referral onwards to specific services if appropriate e.g. emotional support, information about cancer type and treatment options, addressing financial and insurance concerns including applying for benefits, matching people to clinical trials, providing education about fertility information. Tools including a guidebook, journal and care plan were offered, some language congruent. 2) PN only (limited access to PN services – maximum of 6 participant-initiated phone calls to PN to seek information). HRQOL measured: Functional Assessment of Cancer Therapy– General (FACT-G) and cancer-specific Functional Assessment of Cancer Therapy symptom burden subscales.	
Patient navigation (PN) is also part of the following articles (further details elsewhere in the tables) - Patel 2020 USA[70]. Prospective survey. Recommended PN from different racial/ethnic minority groups. - Vuong 2020 USA[30]. Narrative review. Use of PN found to be an effective approach to increase enrolment of underrepresented minorities in cancer CT. - Amorrortu 2018 USA[72]. Intervention mapping. PN was one of four intervention modules to modify recruitment behaviours of investigators/coordinators to increase diversity in CTs. - Kidd 2019 NZ[76]. Review. Walking Forward (USA project) - improved incidence of CT participation among American Indian people. Higher satisfaction with care after cancer treatment aided by PN.				
COMMENT AND STRATEGY DEVELOPMENT				
Doll, 2020, USA[50]	Comment	Minority enrollment on CTs enhances scientific rigor but requires structural changes and commitment. Only broad strategies.	Mistrust, time constraints, financial needs, and uncertainty regarding side effects are concerns that have been identified among Black Americans, Asian Americans, Latinx communities, and Pacific Islanders. Shared concerns that go far beyond lack of information about CTs. In gynecologic oncology and cancer generally, minority enrollment has dropped, rather than improved over the past 15 years. Must be evaluated from a systems perspective, in addition to individual interventions.	Among these 4 racial/ethnic groups, consistently reported facilitators include: culturally congruent study design; benefits to participation including appropriate compensation and/or access to care; and altruism - expressed as a desire to help their families and communities. These are shared facilitators that will be expressed differently by each community, and interpreted differently by geographic region, or primary language, or type of disease. Thus, community engagement and patient-oriented design of CTs, regardless of the study area, is required to meaningfully address minority enrollment disparity. This specificity is needed to generate actionable information for health equity.
McKay, 2021, USA[37]	Report: strategy development	Tackling Diversity in Prostate Cancer CTs: A Report From the Diversity Working Group (DWG) of the IRONMAN Registry	DWG of the IRONMAN registry has developed informed strategies for site selection, recruitment, engagement and retention, and trial design and eligibility criteria to ensure broad inclusion and needs awareness of minority participants. (IRONMAN: global registry of men with advanced prostate cancer). In concert with systematic strategies to tackle the complex levels of disparate care, our ultimate goal is to expand minority engagement in clinical research and bridge the disparities gap in prostate cancer care. The IRONMAN registry can serve as a model	Site selection: Participation of sites capturing larger minority populations, including international sites, with capacity for additional support for underresourced sites through the Prostate Cancer CTs Consortium centralized clinical research organization; Facilitate partnerships between large academic centers and satellite sites in underserved communities; (specific international cooperation); develop LMIC Working Group to address unmet needs unique to participating international sites with differing CT operations and infrastructure support. Participant recruitment: Development of culturally appropriate recruitment materials (ie, patient brochure) Site engagement and retention: Monthly study calls that address current status, barriers, and solutions for minority recruitment; Outreach to investigators though targeted personalized communications, general emails, newsletter updates, and investigators meetings (three/year). Data quality: Working group for Clinical Research Coordinators and PROMs to ensure clinical data and patient-

			for disparity-focused research. Systematic efforts necessary to revamp the existing CTs construct to promote representation of minority groups in clinical research.	reported data are completely captured; Regular data monitoring and quality control to ensure complete data entry and PROMs completion Study design and eligibility: Broad eligibility criteria with simplified study design with embedded flexibility; Ensuring translated informed consents forms and PROMs questionnaires in different languages; Reasonable allowances for modified eligibility criteria or data capture methods to suit local cultural or medical practices.
Regnante, 2019, USA[29]	Strategies used to increase enrol by REMG	US Cancer Centers of Excellence Strategies for Increased Inclusion of Racial and Ethnic Minorities in CTs	Aimed to identify notable practices used by leading US cancer centers that facilitate REMG participation in cancer trials. N=8. In-depth interviews. Strategies for increased REMG accrual to cancer trials were reported across five broad themes: commitment and center leadership, investigator training and mentoring, community engagement, patient engagement, and operational practices. Specific notable practices included increased engagement of health care professionals, the presence of formal processes for obtaining REMG patient/caregiver input on research projects, and engagement of community groups to drive REMG participation. Centers also reported an increase in the allocation of resources to improving health disparities and increased dedication of research staff to REMG engagement.	Specific strategies used by multiple institutions to enhance community outreach and engagement included: • Cultural competence training for staff that includes information about motivators, challenges, and barriers to research participation among REMGs • Community advisory boards composed of diverse stakeholders to guide the development, feasibility, and implementation of research studies • Lay community representatives—ambassadors—from REMG communities to cultivate community talent and tap into their expertise and networks to reach potential participants • Transparency in sharing research findings, (e.g. via concise, plain language summaries) to help participants understand their contributions to science and their community. Using these strategies was reported as a means to enhance recruitment efforts and to strengthen community partnerships, often described as trusted brokers, with patients and care partners. Although community education and outreach can increase a community's understanding of research, leaders noted that the actual invitation to participate in a specific study must remain in the hands of an investigator or study coordinator involved in the study—and for an intervention treatment study, the physician caring for the patient. Centers achieved sustainable high recruitment of REMGs by excelling in: 1. Strategic engagement with providers, as they are the most important influence on whether the patient is recruited and participates in CTs 2. Community leader engagement as a core center function which results in trust and engagement with REMGs and their care partners 3. Seeking dedicated input into cancer clinical research programs, such as feasibility of implementation, from REMG patients and caregivers. 4. Establishing clear, cross–cancer center leadership commitment to quality and hiring practices to ensure that the composition of research staff represents the population served, allied with a corresponding development and training culture. CWG (Community Working Group) industry members' organizations report that they are actively working to establish practices in support or recruitment and retention of REMGs in cancer CTs. These include: 1. Proactive identification of new trial sites during selection process to understand approach and capabilities, asking active investigator sites to recruit a diverse patient cohort and provide recruitment strategy 2. Careful consideration of protocol inclusions and exclusions, such as non–clinically relevant criteria that disproportionately affect REMGs 3. Discussion of prospective support/logistics measures for patients so that patients understand what is available to them in the recruiting stage 4. During investigator meetings, provide a rationale for the inclusion of REMGs and provide sites that are culturally sensitive and health literate recruitment materials for use by research staff 5. Active engagement by industry-supported patient engagement programs of representative populations of patients and care partners for insights into protocol and feasibility designs 6. Working with patient organizations to share and educate membership about the availability of specific clinical studies.
TOOL DEVELOPMENT				

Langford, 2020, USA[88]	Tool development	Development of a Plain Language Decision Support Tool for Cancer CTs: Blending Health Literacy, Academic Research, and Minority Patient Perspectives	Development of a plain language, web-based decision support tool (CHOICES DST) in English and Spanish to support decision-making about CCTs among Blacks and Hispanics. The final version was well received and understood by Black and Hispanic participants, and adheres to mandates for plain language communication. This research provides preliminary data that CHOICES DST holds promise for improving knowledge of CCTs and potentially improving informed decision-making about participation in trials.	Patient engagement included following steps: (1) information collection to guide the development of the DST, (2) content development of the DST based on data from diverse sources, and (3) usability testing of the DST. As DSTs and other interventions become more widely used, particularly with minority populations, there is a need for careful tool development, including attention to plain language principles and attentive intervention design. These efforts are particularly timely for interventions designed to improve knowledge and decision-making about enrolling in CCTs. The CHOICES DST goes beyond education and knowledge enhancement to incorporate values and empowerment components as recommended by IPDAS .
Langford, 2021, USA[89]	Tool evaluation	Improving knowledge and decision readiness to participate in cancer CTs: Effects of a plain language decision aid for minority cancer survivors	To evaluate the impact of a web-based, plain language decision aid (CHOICES DA) on minority cancer survivors' knowledge of cancer CTs (CCTs), readiness for making decisions about CT participation, and willingness to participate in a CT. n=64.Black and Hispanic cancer survivors. single arm intervention study, participants completed self-report assessments of CCT knowledge, decision readiness regarding CT participation, and willingness to participate at three time points.	Reviewing the CHOICES DA was associated with significantly improved knowledge and decision readiness to participate in a CCT immediately and at 2-week follow-up. Practical Implications: These findings suggest that CHOICES DA may support informed decision making about CCT participation within an acute, yet clinically relevant window of time for minority cancer patients who are substantially under-represented in cancer research.
QUALITATIVE STUDIES				
Cunningham-Erves, 2020, USA[73]	Qualitative; formative research	Describes the formative research process used to design a culturally appropriate cancer CT education program for African American and Latino communities.	Three engagement approaches: including community-based organization (CBO) leaders as research team members; conducting focus groups and cognitive interviews with community members as reviewers /consultants; and interacting with two community advisory groups.	Focus group themes were: 1) Community Perspectives on Overall Presentation; 2) Community Opinions and Questions on the Content of the Presentation; 3) Culturally Specific Issues to Participation in Cancer Clinical Trials; 4) Barriers to Clinical Trial Participation; and 5) Perspectives of Community Health Educators. Feedback was documented during reviews by scientific experts and community members with suggestions to ensure cultural appropriateness using peripheral, evidential, linguistic, sociocultural strategies, and constituent-involving. The final program consisted of two versions (English and Spanish) of a culturally appropriate slide presentation with speaker notes and videos representing community member and researcher testimonials. Conclusions: Incorporating multiple community engagement approaches into formative research processes can facilitate the inclusion of multiple community perspectives and enhance the cultural appropriateness of the programs designed to promote cancer clinical trial participation among African Americans and Latinos.
Niranjan, 2019, USA[60]	Qualitative	Assessed perspectives of cancer center clinical and research personnel on their training and education needs toward minority recruitment for cancer CTs.	Qualitative interviews (n=91) conducted at five U.S. cancer centers among four stakeholder groups: cancer center leaders, principal investigators, referring clinicians, and research staff. Qualitative analyses focused on response data related to training for minority recruitment for cancer CTs.	Four prominent themes: (1) Research personnel are not currently being trained to focus on recruitment and retention of minority populations; (2) Training for minority recruitment and retention provides for a specific focus on factors influencing minority research participation; (3) Training on cultural awareness may help to bridge cultural gaps between potential minority participants and research professionals; (4) Views differ regarding importance of research personnel training designed to focus on minority population recruitment. There is a lack of systematic training for minority recruitment. Many stakeholders acknowledged benefits of minority recruitment training and welcomed training that focuses on increasing cultural awareness to increase participation of minorities in cancer CTs.
Niranjan, Martin, et al, 2020, USA[61]	Qualitative	Bias and stereotyping among research and clinical professionals: Perspectives on minority recruitment for oncology CTs.	91 qualitative interviews at 5 US cancer centers among 4 stakeholder groups: 1) cancer center leaders; 2) principal investigators; 3) referring clinicians; and 4) research staff. Content analysis approach to generate themes.	Five prominent themes: 1) recruitment interactions with potential minority participants were perceived to be challenging; 2) potential minority participants were not perceived to be ideal study candidates; 3) a combination of clinic-level barriers and negative perceptions of minority study participants led to providers withholding CT opportunities from potential minority participants; 4) when CT recruitment practices were tailored to minority patients, addressing research misconceptions to build trust was a common strategy; 5) for some respondents, race was perceived as irrelevant when screening and recruiting potential minority participants for CTs. Not only did some respondents view racial and ethnic minorities as less promising participants, some respondents

				reported withholding trial opportunities from minorities based on these perceptions. Some providers endorsed using tailored recruitment strategies whereas others eschewed race as a factor in trial recruitment. The presence of bias and stereotyping among clinical and research professionals recruiting for cancer CTs should be considered when designing interventions to increase minority enrollment.
Niranjan Wenzel, …2021, USA[62]	Qualitative	Perceived Institutional Barriers Among Clinical and Research Professionals: Minority Participation in Oncology CTs	We assessed perspectives of cancer center professional stakeholders on the institutional factors that can potentially influence racial and ethnic minority recruitment for cancer CTs. Ninety-one qualitative interviews were conducted at five US cancer centers among four stakeholder groups: cancer center leaders, principal investigators, referring clinicians, and research staff. Qualitative analyses examined response data focused on institutional factors related to minority recruitment for cancer CTs.	Four prominent themes emerged regarding institutional barriers among clinical and research professionals. (1) There are no existing programs currently being used to recruit or retain minorities to CTs. (2) Institutional efforts are needed to increase trial participation and are not specific to potential minority participants. (3) Access to cancer CTs and navigation within an Academic Medical Center need to be simplified to better facilitate recruitment of minority patients. (4) Community outreach by cancer centers will increase clinical research awareness in the community. To increase participation among minority populations, medical centers must address mutable institutional barriers such as setting specific minority recruitment goals for cancer CTs, ensuring that cancer CTs are accessible, especially to minority patients, and supporting sustained community outreach programs to increase clinical research awareness.
Olver et al. 2021, Australia[46]	Qualitative: Cancer and communication	Communicating cancer and its treatment to Australian Aboriginal and Torres Strait Islander patients with cancer: a qualitative study	Through qualitative interviews with health professionals, investigate successful strategies of health workers who support and regularly communicate with Aboriginal and Torres Strait Islander people about cancer and its treatment. The study aimed to identify practical tools and approaches that could form the basis of professional education for clinicians and, in turn, improve patient experiences and outcomes for Aboriginal and Torres Strait Islander people with cancer.	23 health professionals, interviewed by phone or face-to-face. Six themes emerged. (1) Create a safe environment, engender trust and build rapport. This involves considering the physical environment and allowing time in interviews to establish a relationship. (2) Employ specific communication strategies to explain cancer, treatment and its side effects through language choices and employing visual aids such as drawings, metaphors and relatable analogies. (3) Obtain support from Aboriginal and Torres Strait Islander staff and patient escorts who can assist in communication. (4) Consider culture which involves collective decision making, strong connection to country and community, with cultural obligations and a unique understanding of cancer. (5) Anticipate the contextual complexities of conflicts between Western medicine and Aboriginal culture, practitioner bias and difficulty maintaining contact with patients. (6) Develop personal qualities of good communicators, including being patient-centred, showing respect, patience, empathy and honesty
Rivers, 2019, USA[56]	Qualitative	Explore information needs of African American women re cancer CT (CCT) via FGDs.	Identify 'message considerations' for educational information, as a primer for CCT recruitment. Results - general fear re CCTs - historic research abuses, lack of information re CCT, lack of cultural relevance of the education and outreach materials for AA communities.	Recruitment of AAs to CCTs may be enhanced by educational and outreach approaches that increase awareness of CCTs as well as involvement of the AA community in developing such interventions. The material under consideration acknowledged past research abuses which was also discussed by participants, though the conclusion was indeterminant, with only one favourable comment about acknowledging this. Conclusion: Interventions should include the perspectives of AA women, as key stakeholders and decision-makers for their family and provide research information in a multimedia format that will facilitate family discussion and decision-making regarding CCTs.
OTHER METHODS				
Patel, 2020, USA[70]	Prospective survey study	Are ethnic and racial minority women less likely to participate in CTs? Assess whether race is associated with willingness to participate in gynecologic oncology CTs in a rural Southern academic medicine setting. Secondary aim: determine if willingness to participate impacted	Following education, White women and those with more education were significantly more willing to participate in CTs than their minority and less educated counterparts. Conclusions. Willingness to participate improved among all sub-categories following an educational intervention. The increase in willingness was less robust among racial and ethnic minorities, suggesting that different tools are needed for recruitment of minorities to gynaecologic oncology CTs. Educational intervention quite minimal: 'Answering “YES” for Q3 was taken as willingness to participate, and they would then move on to complete the other two validated surveys. If “NO” or “DO NOT KNOW” was answered for Q3, then participants proceeded to answer the additional Qs4–7. Education on CTs is built into Qs4, 5, 6. Final Q7	Willingness to participate improved among all sub-categories following an educational intervention. The increase in willingness was less robust among racial and ethnic minorities, suggesting that different tools are needed for recruitment of minorities to gynecologic oncology clinical trials. Future efforts should focus on developing tools specific to ethnic and racial minority groups, in multiple languages, and using peer navigators from different ethnic and racial minority groups. Several recent articles have discussed the difficulties inherent in understanding all the factors that contribute to racial disparity in cancer care. For example, understanding race as a social construct, and recognizing the contributions of biologic difference, social determinants of health and systemic barriers as factors underlying disparity when designing future research, is critical to increasing minority enrollment and participation in clinical research. Being able to elucidate patient perceptions of RCTs and willingness to participate will allow for greater recruitment of underrepresented patients. Having better representation in CTs will allow for greater external generalizability of future trials and could help promote more personalized management and treatment for individuals with gynaecologic cancers, and ultimately bridge the gap in cancer health disparities. As it stands, low recruitment and engagement of ethnic and racial minorities in CTs is unfortunately negatively impacting trial enrollment in the exact population that could most benefit from the scientific knowledge gained through their participation.

		by educational intervention.	asks if participants are willing to participate in CT, after going through the educational questions.'	
Trant, 2020, USA[69]	Mixed methods	Increasing accrual of minority patients in breast cancer CTs	The Oncology Welcomes New Haven into Trials (OWN IT) initiative at Yale Cancer Center used a multi-tiered approach to improve breast cancer minority CT accrual through community focus groups, ongoing community outreach, institutional executive council representation, grand rounds presentation, and didactic lectures with healthcare providers. Eligibility criteria of breast cancer trials at Smilow Cancer Center were reviewed. An anonymous, 5-min survey was conducted at regular visits with Smilow Breast Center patients to gauge awareness of and access to CTs. The percentage of black and Hispanic patients who participated in CTs at Smilow Cancer Hospital rose from 12.7% in 2016 to 16.4% in 2018; far higher than the national average which was 8.6% in 2016. The OWN IT Initiative incorporated both community outreach as well as institutional initiatives. As these components were completed simultaneously, it is difficult to say which was responsible for the increase in accrual as these results were likely multifactorial. Multi-tiered approach was important.	First step: use existing institutional platforms to start discussions about diversity in CTs to develop a comprehensive plan (e.g. grand rounds). These discussions with other providers working with varied patient populations in different practice settings would provide a rapid broad assessment of the institutional catchment area's populations and would potentially allow for better targeted community-based interventions later on. There was no significant difference in the rates at which patients declined to participate in CTs based on race or ethnicity. Invitation rates for CTs were not significantly different based on race or ethnicity either; this indicates that staff were not preferentially inviting one group to participate in CTs over another. There was a large knowledge gap regarding CTs in black and Hispanic patients compared to white and Asian patients. This disparity in knowledge about CTs is likely due to long-standing structural racism, which prevents people of color from obtaining the same education and access to healthcare as their white counterparts. Health literacy, internet access, or access to centres offering CTs may affect access. To address this, institutions should provide listings of their actively enrolling CTs both online and in clinical care settings; these listings should provide brief simple descriptions about the studies at an eighth-grade reading level or lower. Community-based practitioners should be made aware of CT offerings to establish good referral networks. Additionally, community outreach at local churches, schools, and recreation centers should be done regularly to teach black and Hispanic communities about all of the potential options.
PAEDIATRICS				
Russo, 2020, USA[43]	Qualitative study	Interviews with oncologists and CT enrollment by race/ethnicity. Barriers and facilitators of CT enrollment of underrepresented populations in a network of community-based pediatric oncology clinics	Nine qualitative interviews with paediatric haematologists/oncologists. Examined variation in CT enrolment according to racial/ethnic demographic. The major barriers to CT enrollment for pediatric cancer minority participants included language discordance, travel difficulties, and complex trial designs. In contrast, the major facilitators included building trust with participants and their parents, and education on the merits of clinical research studies. We did not observe any disparities in CT enrollment among the racial and ethnic minority participants of the CTs conducted across our network of pediatric oncology clinics.	Not hugely robust: did not find racial/ethnic enrolment disparities but significant number refused to state ethnicity - see below. Identifying barriers and facilitators may improve CT enrollment for underrepresented participant groups. Major facilitators of CT enrollment were (1) participants and parents having general awareness and appreciation of scientific investigation; and (2) the importance of building a trusting relationship (Table 2). Education is a process and is best accomplished in stages over time. All interviewees stated that it was critically important to ensure that families recognize the benefits of clinical research. Importance of discussing CT research with family members and family advocates. Trust in the provider was cited as a key element from the providers' perspective of parent decisions to enroll children in CTs. This is not remarkable, as patient trust in health care providers is known to affect adherence to medical care. Alternatively, distrust is a common reason for participants who refuse enrollment in clinical research trials. Our finding that a significant number of participants refused to state either their race or ethnicity may be an indicator of such distrust. Indeed, a notable disparity in those participants who refused to identify both race or ethnicity and declining participation in CTs was evident. Specifically, the rate of CT enrollment was significantly lower for the group of participants who refused to state their race and ethnicity than it was for the total group and those who identified their race and ethnicity groups.

Aristizabal 2020, USA[59]	Comment	Paediatric Ca CT - trial enrollment for diverse populations. Barriers, opportunities.	Outlines barriers to enrollment: structural, clinical, physician level (physician preference - unconscious bias), patient level. Positive relationship between CT enrollment and improvement in survival outcomes. Interventions to improve minority enrollment have focussed on adults. National level regulatory interventions and policy enactments driven by advocacy groups will be required. With the evolving changes in racial/ethnic distribution of children in the United States, assessing the health needs to equitably serve racial/ethnic minority patients will both remove a social justice impediment and will improve the generalizability of discoveries and treatments to mitigate disparities in clinical outcomes.	Strategies need to address structural barriers (study design and content, informed consent processes), physician and patient level. Clinical level: reduce rigidity of inclusion/exclusion criteria. Regional partnerships between large academic cancer centres and satellite sites in underserved communities (also described by Russo). Investigate role of telehealth. Partnerships between institutions and training of cancer scientists from diverse backgrounds. Culturally appropriate tools and training, including in patient-provider communications and use of interpreters. Promote awareness of CTs. Address socioeconomic barriers e.g. provide food/transport.

APPENDIX 5 OTHER CONDITIONS: CLINICAL TRIALS / CLINICAL RESEARCH WITH UNDERSERVED GROUPS

CATEGORIES: COMMENT; SYSTEMATIC REVIEWS AND REVIEWS; STUDIES OUTLINING STRATEGIES; RCTS; PAEDIATRICS

AUTHOR, YEAR	CONDITION	STUDY TYPE	DESCRIPTION	SHORT SUMMARY	FINDINGS
COMMENT					
Ortega, 2019, USA[41]	CVD and CTs	Comment	Cardiovascular disease (CVD) Sets out importance of heterogeneity of CTs, Regulatory conundrum, Strategies for success, The path forward. Target greater inclusion as 'a new top-level research priority.' Strategies outlined, very USA focussed.	Untenable clinical model that the decision-making process for 50% of our patient population is based on empiricism and/or extrapolation of results obtained in patient populations they do not reflect. Addressing gaps in the evidence base is a social imperative, a clinical necessity and important business consideration. Describes US regulatory 'conundrum. 'While race-only or sex-only recruitment works if a unique hypothesis is being tested, it does not otherwise represent a reasonable standard of clinical trial design. However, these kinds of enriched cohort studies, especially when conducted in the US, may generate important safety and efficacy data in groups who are otherwise poorly represented in international RCTs.' Another approach is to seek race/ethnicity/sex/age specific data from existing databases that aggregate information from multiple trials or registries. 'Electronic health records and large digital data warehouses also hold promise, but new methods will be needed to analyze such large nonrandomized datasets with an expected high degree of missing data. Any of these new research methods will require careful evaluation and determination if these nontraditional study models are to constitute an adequate level of evidence, particularly for clinical practice guidelines.'	Path forward (requires rigorous testing): • Consideration of economic incentives (or penalties) by the FDA (or payers) that would enable greater inclusion of diverse patients in clinical trials. • Commitment by industry and the clinical science community to revisit the design of trials, selection of investigators and sites, and geographic balance of US and non-US subjects. • Engagement with peer investigators outside of the United States to target more race/ethnicity diversity and gender balance in clinical trial recruitment. • Exploration of enhanced cohort recruitment in phase IV or postapproval studies to address important safety and implementation questions. • Recruitment and training of more diverse coordinator and investigator research teams. • Incorporation of novel information technology strategies, including use of electronic health data, social media, gamification, and other digital health technologies as unique steps to expand the pool of potential research subjects. • Revision of the informed consent process, assuring that language matches literacy levels and that consent is culturally sensitive. • Education at the societal level to advance the overall “research IQ” of the populace, thus overcoming a legacy of mistrust of the research enterprise and reducing barriers to participation in clinical trials.

Willis, 2021, UK[45]	CT and language	Comment	Importance of language - identifies gaps in knowledge re best practice guidance for inclusive trial recruitment.	Engaging a substantial proportion of such groups to make the recruited sample more representative of the target population is unlikely to be easy or cheap. Simply translating a document into a heritage language is unlikely to be an effective solution for this complex challenge. Such an approach is impervious to working with communities to facilitate sustained understanding and enhance trust.' There are gaps in current knowledge of the most effective methods to inform best practice guidance aimed at more inclusive recruitment to clinical trials centring on language.	Pragmatic approaches are needed to ensure that research is open to a broader participant base, without undue participant exclusion decisions being made due to the non-clinical criterion of language barriers and with additional resources available to support the inclusion of ethnic (including linguistic) minorities. Once an intervention or therapy has shown efficacy at a population level, targeted approaches, where there is greater scope for tailoring of interventions, could be successful.
SYSTEMATIC REVIEWS AND REVIEWS					
McFarlane, 2021[27]	CBPR	Systematic review	Community-Based Participatory Research (CBPR) to Enhance Participation of Racial/Ethnic Minorities in Clinical Trials: A 10-Year Systematic Review	Objective: update 2012 systematic review on empirical research, with a particular focus on elements of CBPR methods used to improve the rate of accrual of members of racial and ethnic minority communities for CTs.	104 articles. 80 (76.9%) were RCTs. 14 (13.5%) used randomised design with delayed intervention. Cluster randomisation: by recruitment sites (n=38); by community (n=20); by school (n=9). Majority of studies recruited members of a single minority ethnic population. Findings: large increase in number of CBPR studies and studies related to racial/ethnic representation in research. >85% of studies using CBPR methods saw statistically positive outcomes. Elements associated with positive outcomes: community partner participation in 1) study advisory committee, 2) data collection 3) development of interventions 4) participant recruitment. Researchers need to be more transparent about the extent of community participation and more thoroughly and accurately describe nature of the partnership with members of minority communities to build on the literature re community-engaged methods.
Tahhan, 2020[63]	RCTs ACS patients	Systematic review	Characterize the representation of older patients, women, and racial/ ethnic minorities in Acute Coronary Syndrome (ACS) randomized trials. Limited strategies - mostly reporting underrepresentation.	Older patients and women are underrepresented in contemporary ACS trials compared with epidemiologic studies. Over time, there has been modest improvement in the representation of older patients but not women patients. Compares trial participants with epidemiologic studies of those with ACS.	More than three-quarters of trials (n=99, 21.5%) did not report race/ethnicity data, with available data suggesting a modest increase in the enrollment of nonwhite patients owing to the enrollment of Asian (? due to industry sponsored trials with global sites) and Hispanic patients. Enrollment of black patients remained low over time. Although there have been efforts to improve the representative enrollment of racial/ethnic minority groups, future work may focus on the black population, which continues to be underrepresented. Moreover, **future trials should be required by journals and editors to include detailed information on race/ ethnicity in publications and on trial registration websites**, such as ClinicalTrials.gov, even if the numbers are underpowered to show differential outcomes or treatment effects. Innovations in trial design and conduct (such as the use of existing registries as the basis for patient enrollment) and implementation of patient-centered trial designs (such as pragmatic, bayesian, and adaptive trials) can improve enrollment of underrepresented minorities.
Te Karu, 2021, NZ[80]	Gout	Review	Inequities in people with gout: a focus on Maori (Indigenous People) of Aotearoa New Zealand.	Gout, but contains framework for evaluating CBPR for Indigenous people – refs Oetzel framework (cultural centredness, community engagement, systems thinking, integrated knowledge translation).	Not strategies, but may be useful for monitoring evaluation of revitalise project. Addresses Western medicine worldview vs Indigenous people. Acknowledges problems with CT recruitment but not strategies.

Clark, 2019[66]	CVD - diversity in CT	Literature review	Barriers and strategies re diversity in CTs. Part of addressing need to increase CT diversity in an effective, sustainable and scalable manner - challenge for pharmaceutical industry, academic institutions and clinical research.	Overall goal: develop potentially sustainable solutions that would benefit all key stakeholders and lead to making diversity in clinical trials a standard part of the clinical research model 1. In-depth literature review. 2. Gap analysis. 3. Expert interviews 4. In-depth review and analysis based on steps 1-3. 5. Stimuli (with respective barriers and potential solutions) development with stakeholders. Reviewed for consistency with health literacy. 6. Pilot IIR interviews.(Individual Instant Response) 7. Field testing IIR interviews. 8. In-person patient session.	Identified key themes from solutions that resonated with stakeholders using a transtheoretical model of behavior change and created a communications message map to support a multistakeholder approach for overcoming critical participant barriers. Five critical **patient barriers**: mistrust, lack of comfort with process, lack of info, time and resource constraints, lack of awareness. **Investigator/coordinator barriers**: how patient concerns or perceptions will affect recruitment (comorbidities, trial too burdensome), (patient non-adherent or will not enrol if asked), concern that patient will not return to the physician's clinic if referred to study, no incentives for referring physicians to become involved in CTs, time constraints related to measurement-intensive studies. Community outreach research barriers overlapped with patient barriers. **Solutions**: <55yrs interested in flexible/extended hours and cell phone apps to mitigate time and resource constraints. >55yrs interested in covering transportation costs, altruistic reasons for participating in clinical trials, and directly addressing historic events which may lead to concerns about CT participation. From Investigator/physicians/coordinators, AA patients more likely to be reluctant to take part in CTs (mistrust, lower education, SES). Hispanic/Asian pts; mistrust prevalent in community. Higher education and understanding of CTs correlate with greater willingness CT participation. Patients with higher education value altruistic reasons more than less education. Lower SES unfamiliar and skeptical of CTs and more likely to be focussed on own health.
Masood, 2019, UK[58]	CT and ethnic minorities	Systematic review	Systematic review of published RCTs exclusively targeting ethnic minorities, to identify strategies for recruiting ethnic minorities to clinical trials in the UK.	Twenty-one included RCT's identified various strategies to recruit ethnic communities to clinical trials; does not report on effectiveness of strategies used - none of the reported trials evaluated the efficacy of recruitment strategies on trial outcomes. Suggests researchers report this info separately and that guidelines be developed for CT recruitment of ethnic minorities. (p7 refers to report of 64% of recruiting studies excluded participants unable to communicate in English).	Describes strategies under 3 themes: adaptation of screening and outcome measures; culturally specific recruitment training; and recruitment processes. Engagement w community and family (working with religious leaders, collaborating with ethnic community organisations, self referrals and assistance from family/carers); recruitment sites; study invitation process (multilingual invitations); patient information materials and follow-up arrangements (translation of patient info sheets, tape-recorded participant info in language, choice of interview location, follow-up arrangements e.g. home recruitment visits with phone follow-up); researcher and participant communication (linguistic matching - bilingual staff, gender matching); awareness of cultural practices and norms e.g. food, consideration of cultural festivals in planning recruitment etc, transport assistance. The review highlighted that researchers employed limited strategies to enhance the recruitment level. The full extent of the use of strategies was not described well in the publications. There is a need for wider training and support for the trialist to enhance and build up recruitment skills to facilitate the recruitment of ethnic minorities to clinical trials.
Wong, 2019[75]	Alzheimer's disease	Systematic review	Synthesize current evidence on strategies to recruit and retain racial/ethnic minorities in Alzheimer disease and dementia clinical research.	19 included studies. 14 implemented recruitment strategies, 5 implemented recruitment and retention strategies. All studies weak quality. Four major themes were identified for the recruitment strategies: community outreach (94.7%), advertisement (57.9%), collaboration with health care providers (42.1%), and referral (21.1%). Three major themes were identified for the retention strategies: follow-up communication (15.8%), maintain community relationship (15.8%), and convenience (10.5%).	Our findings highlight several promising recruitment and retention strategies that investigators should prioritize when allocating limited resources, however, additional well-designed studies are needed. By recruiting and retaining more racial/ethnic minorities in Alzheimer disease and dementia research, investigators may better understand the heterogeneity of disease progression among marginalized groups. Contains search strategy. Most effective strategies: community outreach and collaboration with health care providers. Highest recruitment rates were reported in studies that utilized community outreach through direct contact with participants, however, the range of recruitment rates was wider within the community outreach theme compared to the other recruitment themes. Although all included studies implemented multiple retention strategies simultaneously, our review also found that follow-up communication and maintaining community relationships were both common retention strategies across studies with the highest retention rates.
STUDIES OUTLINING STRATEGIES					

Rink, 2020[42]	Multiple	Implementation evaluation: CBPR RCT	(no pdf, article avl online) Using Community-Based Participatory Research to Design, Conduct, and Evaluate Randomized Controlled Trials with American Indian Communities. Examine how Tribal Nations and researchers collaborated to design, implement and evaluate CBPR RCTs.	Case studies: Sexual/Repro Health; chronic illness support (?social); childhood obesity prev and healthy lifestyle promotion. 'Successful strategies outlined; Long-standing community-researcher relationships were critical to development, implementation, and evaluation of RCTs, although what constituted success in the 3 CBPR RCTs was diverse and dependent on the context of each trial. Respect for the importance of diverse knowledge systems that account for both Indigenous knowledge and colonial science also contributed to the success of the RCTs.	IMPLICATIONS FOR PUBLIC HEALTH: Tribal-academic partnerships using CBPR RCTs must include 1) establishing trusted CBPR partnerships and receiving tribal approval before embarking on RCTs with Tribal Nations; 2) balancing tribal community interests and desires with the colonial scientific rigor of RCTs; and 3) using outcomes that include tribal community concepts of success as well as outcomes found in standard colonial scientific research practices to measure the success of the CBPR RCTs. **Long standing partnerships**: • 5- to 20-year partnerships • Open dialogue on the most appropriate RCT to meet tribal interests • Strength of partnership to withstand the test of time and changes in tribal leadership and personnel • Co-learning and sharing between tribal members and researchers • Capacity to find solutions to meet tribal needs and the rigor of RCT designs **Diverse concepts of success**: • Substantial community engagement before the design and implementation of an RCT can increase its success • Hiring tribal members to work on implementation and data collection enhances the success of the RCT • RCT research participants' sharing of information is in accordance with tribal cultural philosophies of inclusiveness • Identify an RCT design that ensures all eligible tribal members have the opportunity to participate in the intervention **Respect for diverse knowledge systems**: • Understanding and integrating traditional Indigenous knowledge systems and ways Indigenous people view the world with knowledge based on a colonial worldview • Marrying CBPR principles and practices with Indigenous cultural beliefs and practices and the rigors of RCT standards and requirements • Layering of traditional knowledge and colonial science knowledge with contemporary culture on reservations, which is neither traditional nor modern • Tribal ethical approval as crucial component of tribal sovereignty and Tribes rights to make decisions about what kind of research and how research is conducted on their lands and with their peoples.
Rottas, 2021[53]	CTs Pfizer	Analysis CT diversity	Demographic diversity of participants in Pfizer sponsored clinical trials in the United States	Mostly documenting minority enrolment in Pfizer CTs. Several broad strategies presented section 4.5.	Enhancing representation in CTs requires commitment and sustained investment from pharmaceutical companies and the broader research and medical communities, healthcare providers, and regulators. Include selection of investigative sites and recruitment approaches that are **informed by** community, medical, and patient advocacy partners. It requires **early input** into clinical development planning **from patients and investigators with diverse backgrounds** to help gain insights on additional approaches to increase diverse clinical trial participation. It requires implementing **clinical trial education and awareness campaigns**. It will be important that we partner with our investigative sites toward a shared goal of enhancing diverse participation in clinical trials by growing and fostering community engagement. Finally, by **reducing participant burden** and **introducing flexibility in trial design and conduct**, we aim to improve diversity across our clinical trials.
Stephens, 2020[68]	Mental health	RCT	Lessons re recruiting and engaging American Indian and Alaskan Native teens and young adults to assess capacity of two intervention arms.	Intervention arms; text messages to improve mental health, help-seeking, promote cultural pride or 8 weeks STEM text messages designed to affirm Native voices in STEM. Recruited via We R Native's social media channels (Facebook [FB], text message, Instagram [Ig]). Additional recruitment: listservs associated with tribes, tribal health organizations, Indian education and human service organizations that serve AI/AN teens and young adults. Data from FB and Ig used to explore participant retention and message engagement.	Results indicate that social media channels like Facebook and Instagram can be used to recruit AI/AN teens and young adults. Retention in this study was high, with 87% of participants completing both the BRAVE and STEM intervention arms. Lessons learned from this process may help teen and young adult-serving organizations, prevention programs, policy makers, researchers, and educators as they support the next generation of AI/AN change makers.

Cunningham-Erves, 2019[39]	Paediatric - Parent trust in med research	Cross-sectional study	Identify psychosocial and modifying factors influencing parental trust in medical researchers to improve child / adolescent CT participation, and health outcomes.	Multiple ordinary linear (OLS) regression was conducted to determine: (1) psychosocial and modifying factors associated with parental trust; and (2) perceived advantages and disadvantages associated with parental trust.	Parent's race (White) (β = .343, p < .001), higher education level (β = .409, p < .001), higher perceived advantages of adolescent clinical trials (β = .142, p < .001), and lower perceived disadvantages of adolescent clinical trials (β = -.337, p = .001) were the most significant predictors of higher levels of parental trust in medical researchers. Parents who were African American and had lower education levels expressed lower levels of trust in medical researchers. Education on the benefits of clinical trials could reduce parents' apprehension towards their child's participation in clinical trials. Results support the development of a CT education program for parents to improve their trust in medical researchers.
Horowitz, 2019[51]	Translational genomics research	Descriptive - strategies	Aimed to determine the impact of stakeholder-engaged strategies on recruitment and retention of AA adult patients into a clinical trial testing them for renal risk variants nearly exclusive to AAs.	Our academic-clinical-community team developed ten key strategies that recognize AAs' barriers and facilitators for participation. Using electronic health records (EHRs), we identified potentially eligible patients. Recruiters reached out through letters, phone calls, and at medical visits.	Of 5481 AA patients reached, 51% were ineligible, 37% enrolled, 4% declined, 7% were undecided when enrollment finished. We retained 93% at 3-month and 88% at 12-month follow-up. Those enrolled are more likely female, seen at community sites, and reached through active strategies, than those who declined. Those retained are more likely female, health-literate, and older. While many patients have low income, low clinician trust, and perceive racism in health care, none of these attributes correlate with retention. **10 strategies**; 1. Stakeholder engagement. 2.Formative work (interview patients to inform protocol). 3. Clinician buy-in. 4 Study materials and stipends (respectful not coercive). 5. recruiter training and oversight. 6.efficient patient identification in variety of settings. 7.Flexible, targeted outreach and scheduling. 8.Study branding. 9.Relationship centred recruitment/ retention. 10.Collect data for impact of strategies. **CONCLUSION**: With robust stakeholder engagement, recruiters from patients' communities, and active approaches, we successfully recruited and retained AA patients into a genomic CT.
Amororrtu, 2018[72]	CT - specialty	Intervention mapping	Systematic framework, Intervention Mapping (IM), to develop an intervention to modify recruitment behaviors of coordinators and specialist investigators. Goal: increasing diversity in trials conducted within specialty clinics.	IM framework was used to ensure that the intervention components were guided by health behavior theories and evidence. The IM steps consisted of (1) conducting a needs assessment, (2) identification of determinants and objectives, (3) selection of theory-informed methods and practical applications, (4) development and creation of program components, (5) development of an adoption and implementation plan, and (6) creation of an evaluation plan.	The intervention included five educational modules, one in-person and four web-based, plus technical assistance calls to coordinators. Modules addressed the intervention rationale, development of clinic-specific plans to obtain minority-serving physician referrals, physician-centered and patient-centered communication, and patient navigation. The evaluation, a randomized trial, was recently completed in 50 specialty clinics and is under analysis. Conclusions: Using IM we developed a recruitment intervention that focused on building relationships with minority serving physicians to encourage minority patient referrals. IM enhanced our understanding of factors that may influence minority recruitment and helped us integrate strategies from multiple disciplines that were relevant for our audience.
Wilkins et al. 2019, USA[87]	Research, return of value	Survey, framework development	Understanding What Information Is Valued By Research Participants, And Why – 'Return of value'	Rather than 'return of *results'*, this article advocates for the term *value* — referring to the perceived worth, usefulness, or benefit of the information. Aligns with an emerging focus on patients' values in health care decision making.	We intentionally recruited a sample with a range of racial/ethnic, educational, and geographic diversity to include groups often underrepresented in research. Findings: participants across all demographic characteristics highly valued receiving information from research studies and were more likely to trust researchers and to volunteer if research information were returned. Results of pharmacogenomics studies and genetic risk of disease had the highest value. However, respondents highly valued information beyond research results, including information on "clinical trials near me" and "how researchers are using my information". Receiving information beyond clinically actionable results was more highly valued than monetary compensation by all ages, races/ethnicities, educational levels, genders and income levels. If implemented broadly, the return of valued information could improve trust in research and increase people's willingness to volunteer for studies. People will have different preferences: need appropriate policies and practices. Policies should promote access to relevant and easy-to-understand information for all demographic categories, especially people who are socially disadvantaged. May include information from the research process, how we use the data, how they have contributed, what it means.
RCTs					

Maar, 2019, Canada[57]	Hypertension	RCT - practices	Identifies culturally safe research practices for RCTs in Indigenous communities: 'wise practices for RCTs in Indigenous communities'.	Secondary analysis of qualitative data in existing large dataset (Diagnosing Hypertension-Engaging Action and Management in Getting Lower Blood Pressure in Indigenous Peoples and Low- and Middle- Income Countries (DREAM-GLOBAL); hypertension mngmnt in Indigenous people and low-mid income countries). Thematically analysed survey/qual interview/FGD in 6 Indigenous Canadian communities during evaluation of DREAM-GLOBAL. 34 interviews, 12 FGD, n=142.	Successful eHealth research in collaboration with Indigenous communities requires a focus on cultural safety that includes: (1) building a respectful relationship; (2) maintaining a respectful relationship; (3) good communication and support for the local team during the RCT; (4) commitment to co-designing the innovation; (5) supporting task shifting with the local team; and (6) reflecting on our mistakes and lessons learned or areas for improvement that support learning and cultural safety.
PAEDIATRICS					
Cui, 2019[38]	Childhood obesity	Survey	Recruitment staff and investigators from four comm based childhood obesity RCTs (2xprevention, 2xRx) which recruited low-income racial/ethnic minorities. Asked for top three recruitment strategies and barriers regarding recruitment of low-income racial/ethnic minorities.	Four trials (each 3 yrs) which enrolled low income / racial minority pts. Research unit completed systematic lit r/v and categorisation of documented recruitment strategies: 1.Planning; 2.recruitment staffing; 3.community outreach and participant ID; 4.eligibility screening; 5.consent and assent; 6. measurement, incentives and eligibility; 7. Enrolment, randomisation. Based on these stages, survey was developed which was completed by trial group staff re what strategies they had used to recruit this population. Survey included open ended questions re top 3 strategies and barriers. One survey from each of 4 trial groups.	Recruitment strategies reported included: (1) careful planning, (2) working with trusting community partners, (3) hiring recruitment staff who were culturally sensitive, personality appropriate, and willing to work flexible hours, (4) contacting potential participants actively and repeatedly, (5) recruiting at times and locations convenient for participants, (6) providing incentives to participants to complete baseline measures, (7) using a tracking database, (8) evaluating whether participants understand the activities and expectations of the study, and (9) assessing participants' motivation for participating. Working with community partners, hiring culturally sensitive staff, and contacting potential participants repeatedly were cited by two trials among their top three strategies. For the top three recruitment barriers, the 3-year commitment to the trial was cited by two trials. Table 2 presents top 3 strategies and barriers - several were study specific (eg 'accelerometer' wear time requirements, 3 year commitment, eligibility requirements). Comprehensive strategies that include 1) community partnership support, 2) culturally sensitive, personality appropriate recruitment staff who will work flexible hours, and 3) repeated contacts with potential participants, can result in successful recruitment of low-income racial/ethnic minority families into obesity prevention and treatment trials.
Robler, 2020[55]	Childhood hearing loss	RCT Mixed methods community	Community engagement and participation in research design to address loss to follow-up from school hearing programs.	Community engagement and participation in research design occurred through focus groups and through the integration of stakeholders into the study team. Representation was cross-sectoral, involving individuals from multiple levels of the school and health system, as well as community members from each of the 15 communities. Feedback (Apr-Aug 2017) informed final design of the randomized trial. Began enrollment of children Oct2017, concluded Mar2019.	Results; Stakeholder involvement and community participation shaped the design of specific trial elements. The engagement and participation resulted in changes to the research question (e.g. identified appropriate processes to measure), comparators (requested intervention screening process prioritise affordability and ease of use), outcomes and measures (developed measures to address sensitivity of survey, determined primary outcome measurements), telemedicine protocols (which telemedicine workflows to be completed by community health aid/practitioner [CHA/P], processes for scheduling CHA/P availability), and recruitment and retention (designed and led social media and other communication to communities, in-person communication and enrolment with schools, essential recruitment leadership, holding community events, realtime feedback on recruitment, event site advice). Community involvement was strengthened by the use of multiple modalities of involvement and inclusion of lead stakeholders on the study team. This study highlights the effectiveness of multifaceted stakeholder involvement and participation in the design of health research conducted within Alaska Native communities. It offers an example of involvement and reporting that could be mirrored in future research in order to protect and further the interests of the participating community.
Shaw, 2021[54]	CTs with paeds	Guidelines, case studies	Best Practices for Conducting Clinical Trials with Indigenous Children in the United States	Literature review and author's experience. Indigenous children must be included in CTs to reduce health disparities and improve health outcomes in these populations. Environmental Influences on Child Health Outcomes Institutional Development Award States Pediatric Clinical Trials Network (ECHO ISPCTN, 2016) creates a unique and timely opportunity to increase Indigenous children's participation in CTs.	3 best practices for conducting pediatric trials with Indigenous communities: (1) early and sustained community engagement, (2) building Indigenous research capacity, and (3) supporting community ownership and oversight of Research. Effective engagement requires equity, trust, shared interests, and mutual benefit among partners over time. Capacity building should prioritize developing Indigenous researchers. Supporting community oversight and ownership of research means that investigators should plan for datasharing agreements, return or destruction of data, and multiple regulatory approvals.

APPENDIX 6 COVID-19 ARTICLES, ALL USA

AUTHOR, YEAR	STUDY TYPE	DESCRIPTION	SHORT SUMMARY	FINDINGS
Andrasik, 2021[47]	Descriptive; COVID vaccine trials	Describes methods used for successful enrollment of Black, Indigenous and People of Color (BIPOC) participants in the US govt-funded COVID-19 vaccine efficacy trials and analyze the related demographic and enrollment data to inform future efforts on inclusive participation	Increasing BIPOC participation in CTs through community engagement and recruitment goals. Four CTs (Moderna, Novavax, AZ, J&J). Four part community engagement strategy: use of CBPR approaches to meaningfully involve communities throughout research process; stakeholder engagement and building trust; a faith initiative; communications and community influencers. Tracked enrolments in COVID-19 Prevention Network (CoVPN). Set targets and instructed sites to slow, then stop enrollment of white participants, in order to facilitate BIPOC enrolments.	Enrollment of White participants ranged from 44% (Moderna) to 56% (AZ), and the enrollment of BIPOC communities closely mirrored their composition in the larger US population. 'Trials opening later (Novavax 5 mths later) benefitted considerably from strengthened community engagement efforts (especially partnering with tribal leaders to address data sovereignty and ownership, resulting in increased participation among Indigenous peoples), and greater and more diverse volunteer registry records (*volunteer database*). Despite robust fiscal resources and a longstanding collaborative and collective effort, enrollment of White persons outpaced that of BIPOC communities. With appropriate resources, commitment and community engagement expertise, the equitable enrollment of BIPOC individuals can be achieved. To ensure this goal, intentional efforts are needed, including an emphasis on diversity of enrollment in clinical trials, establishment of enrollment goals, ongoing robust community engagement, conducting population-specific trials, and research to inform best practices.' 'Without established recruitment goals that reflect the slower yet steady pace of BIPOC enrollment, the allocated enrollment slots were quickly filled, effectively blocking BIPOC persons' opportunities for participation. Rather than directing sites to slow or halt White enrollment, which presents its own operational challenges, future vaccine clinical trial efforts must include clear established goals for BIPOC enrollment from the outset of study accrual, reserving space in the trial to ensure equitable inclusion.' Population-specific trials and setting of recruitment goals according to established frameworks were also proposed to ensure the inclusion of under-represented populations in research that could be beneficial. Prolonged and directed engagement with communities aided inclusive enrolment in these trials; the authors saw ongoing commitment to such partnerships as potentially helping research and research institutions to be viewed by communities as trustworthy.
Doroshow, 2021[74]	Comment	COVID-19, Social Justice, and Clinical Cancer Research	Barriers to inclusion of underserved populations in cancer CTs: rigid eligibility criteria; frequent and expensive 'standard of care' tests; procedures that exclude those with multiple comorbidities; transport issues; inadequate insurance. Barriers worse for industry vs NCI-sponsored investigations. COVID has further heightened SES disparities. Black people experiencing disproportionate employment and health insurance loss - limits feasibility of frequent healthcare visits.	Rapid adaptability demonstrated via COVID - electronic informed consent, clinical care transferred to local providers to reduce travel requirements, shipping oral agents to local sites, decreasing impact of minimal protocol deviations on assessment of CT site performance, remotely auditing CT documents and accepting validity of telehealth CT assessments. Demonstrates feasibility of major changes to the conduct of cancer CTs and capacity to do this promptly. 'The "new normal" must facilitate simpler, faster, flexible, and less expensive trials that seamlessly integrate with the needs of daily clinical practice. 'Enhance patient access (bring cancer CT to the patient. Telemedicine, permit those with chronic comorbidities, support and train clinical research teams that currently lack necessary infrastructure to enrol underserved patient pops); Improved operational efficiency (e-data collection methods, including remote auditing, monitoring EHRs, harmonizing e-clinical data); transforming statistical designs; Minimising the review process (enable rapid evaluation of CT docs); Rethinking strategic research infrastructure (diminish the person-hours required for study development and conduct to decrease time to completion); simplifying regulatory framework (USA); minimising non-essential tests; promoting use of electronic consent.

Eng, 2021[85]	Comment	Moving Beyond the Momentum: Innovative Approaches to Clinical Trial Implementation	Cites need for diversity in CTs. Proposes adaptations resultant from the pandemic as standard practice to improve access to CT. Many are consistent with strategies to increase participation of under-represented populations.	Recommends changes necessitated by COVID-19 pandemic: * trials to develop standardised treatment order sets that are adaptable to different technology platforms (communication of specific research plans, eliminate individual builds at each site, enhancing uniformity of care, workflow, patient safety, reduced activation time); * CT participants should be offered the option of virtual visits, defined in the protocol (review of current symptoms and medication changes, confirm adherence to prescribed medications, will require significant IT support, App supported by sponsor would improve communication, real-time documentation, reduce travel, patient and carer burden; care with implementation as this could further increase disparity); * 'Next generation sequencing (NGS) platforms are widely used to guide treatment. Resources should be shared between NGS vendors, providers, and patients to help identify clinical trials and enhance enrollment.'; * remote clinical trial education and prescreening (Partnership b/w advocacy groups, trial sponsors, and research teams using innovative strategies can expand CT awareness / availability for patients with cancer and expedite accrual to studies) * modifications of trials with oral agents (Trials of oral cancer therapies could make greater use of telemedicine, framework for direct patient shipping of experimental therapeutics needed); * Capture of adverse events and PROs (Apps for improved symptom management, expedited adverse event reporting patient-generated health data (PGHD) and improved compliance); * Regulatory (site initiation visits and monitoring conducted remotely - standard practice).
Lackland, 2020[40]	Comment	Perspective: Impact of COVID-19 on Clinical Research and Inclusion of Diverse Populations	Articulates potential of COVID to exacerbate disparities in RCT participation of diverse populations. May impact vaccine trial generalisability. Seeks to draw attention to unresolved lack of inclusion of diverse populations in RCTs. COVID-19 has resulted in an excess burden for underrepresented minority groups, with higher infection rates, hospitalisation and mortality. Disparities are further complicated by comorbidities (higher prevalence in minority populations) and SES factors. COVID treatment and vaccines are dependent on expediting RCTs and must include all groups. This requires specific strategies.	Reasons underlying RCT low participation by minority groups: **System** (clinical researchers have opportunity to communicate critical importance of inclusion - address negative perceptions of RCTs, build trust. Distinguish between 'physical distancing' and 'social distancing' - social interactions important for minorities. Identify centres that are more accessible to minority populations e.g., regional medical centres. Use COVID trials as opportunity to develop continuing med education and distance learning tools - build competencies in community based health workforce. COVID provides opportunity for innovative strategies that enhance community engagement while respecting restricted social interactions.). **Individual;** awareness of CTs (major barrier - covid may be mechanism to enhance knowledge and awareness of RCTs. **Strategies to address**: Highlight role of RCT participation by minority groups (scientific enhancement and external validity) to engage community and build trust; perception of CT infrastructure (address negative experiences from the past - provide assurances re future positive participation), attitude and experience, perception of patient's ethnicity, eligibility (modify inclusion and external criteria to enhance participation), trust (major detriment to RCT validity. focussed strategies required, to build and sustain trust. Acknowledge past, recognise personal bias and systematic inequalities, address barriers through effective policies and procedures), access (may be compounded by COVID. Design innovative access strategies - telehealth /telecommunications).
Warren, 2020[48]	Comment	Trustworthiness before Trust - Covid-19 Vaccine Trials and the Black Community	Recent data: Black people make up 13% of the US population, account for 21% deaths from Covid-19 but only 3% vaccine trials enrollees. Threatens validity / generalizability of trial results. Particular concern in vaccine trials; differences in lifetime environmental exposures can result in differences in immunologic responses that could affect both safety and efficacy. Barriers: trust - **it is not the job of Black people to fix structural racism**. Cannot just ask Black people to be more trusting. Clinicians, investigators and pharmaceutical companies must produce convincing evidence that they are trustworthy. Overcome the extensive historical evidence to the contrary.	Four proposals: 1. Trial sponsors and regulatory agencies can ensure that the informed-consent process is exemplary, including ensuring that all relevant aspects of the design and conduct of the clinical trials are maximally transparent. 2. Follow recent NAS guidelines of ensuring priority access to vaccines for people considered to be the most disadvantaged or worst off. 3. Vaccine safety and efficacy must be convincing to general public as well as audiences who are socioeconomically, culturally and educationally diverse and who have had distinct historical experiences with the health system. 4. Earn and deserve trust by ensuring trial participants receive appropriate medical care if they are injured - black people are disproportionately likely to be uninsured. Pharmaceutical companies could establish a fund to guarantee health care coverage and death benefits as compensation for serious vaccine injuries/deaths. The success of vaccines in Black and other communities will depend on whether they trust the vaccines are safe and effective, and if the organisations are trustworthy. Earn trust: proposed collaboratively designed Operation Build Trustworthiness that matches the seriousness and scope of Operation Warp Speed. Needs to be firmly grounded in grassroots involvement of individuals and organizations with solid, well-earned reputations for trustworthiness in Black and other minority communities, including respected elected representatives, trusted local / national faith leaders, community advocates, and others. Active, ongoing, and fully bidirectional collaboration, learning, and communication will be essential.