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A Systematic Review of Self-Reported Ethical Practices in Publications of Cluster Randomised Trials Conducted in Aboriginal and Torres Strait Islander Settings

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Cover Photo

This desert rose flourishes in the garden of Ms Kathy Watson, co-founder of Broome Regional Aboriginal Medical Services (BRAMS) and one of the first Aboriginal Health Workers in the Kimberley.

Cover Artwork: 'Seeing Country' by Nyaparu Laurel

Nyapuru Laurel was a Walmajarri artist and educator from the Kadjina Community (part of Millijidee Station) in the Kimberley region of Western Australia on the edge of the Great Sandy Desert. Along with her sisters, brothers and mothers, Nyapuru advocated to set up the remote Wulungarra Community School and, through her work, contributed to the passing on of knowledge of the land, law and culture to future generations. She passed away in August 2015. Extracts from 'Seeing Country' are located throughout the document.

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Acknowledgements

We acknowledge Aboriginal and Torres Strait Islander leaders past, present and emerging in Australia, and respect the continuing relationship of all Indigenous peoples to the land and waters in Australia and Canada. We acknowledge that Aboriginal and Torres Strait Islander peoples in Australia never ceded their sovereignty or country to European colonisers. We also acknowledge that the benefits now enjoyed by some as a result of European colonisation in both countries have been at the expense of incalculable suffering to others.

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Acronyms

ACCHO: Aboriginal community-controlled health organization
ACCHS: Aboriginal community-controlled health service
AMS: Aboriginal Medical Service
AIATSIS: Australian Institute for Aboriginal and Torres Strait Islander Studies
ANZCTR: Australian and New Zealand Clinical Trials Register
ARC: Australian Research Council
CEO: Chief Executive Officer
CRT: Cluster randomized trial
GPHC: Government-managed primary health care service
HREC: Human Research Ethics Committee
MGPs: mainstream general practices (private businesses)
MR: Main results publication
N: number
NHMRC: National Health and Medical Research Council
ORIC: Office of the Registrar of Indigenous Corporations
PBC: Prescribed Body Corporate
PL: Parallel CRT
PR: prospectively registered with ANZCTR
RCT: Randomised controlled trial
RR: retrospectively registered with ANZCTR
SP: Study protocol publication
SW: Stepped wedge CRT
TO: Traditional Owners
UNDA: University of Notre Dame Australia
XO = Cross-over CRT

FOREWORD

Randomization in health and medical research of entire social units to experimental arms as occurs in 'cluster' randomized trials (CRTs) presents researchers, ethics committees, participants and evidence users with ethical issues quite unlike those of conventional randomized control trials (RCT) in which the individual is randomized and their right to give free, prior and informed consent is readily protected. By contrast, units of randomisation, intervention and outcome measurement are different in CRTs. Clearly determining who are research participants and establishing whose consent is required - not only for recruitment and intervention but also data collection - are correspondingly difficult.

Aboriginal and Torres Strait Islander peoples in Australia reside in, react to and resist ongoing colonisation and daily manifestations of health inequity due to their continuing marginalization, denial of rights and dispossession. Australian ethical research guidelines informed by Aboriginal and Torres Strait Islander perspectives assist researchers to negotiate within these structural conditions, ensuring that the rights of Aboriginal and Torres Strait Islander research participants are not compromised. Yet none of these guidelines currently contains explicit guidance for ethical conduct of CRTs in which entire communities or essential services upon which Aboriginal and Torres Strait Islander peoples rely are randomized as occurs in the CRT design.

This timely systematic review has produced a unique overview of ethical practices self-reported in publications of CRTs conducted in Aboriginal and Torres Strait Islander settings published since 2008. Social units such as schools or local primary health care serving Aboriginal and Torres Strait Islander peoples and even entire communities have been randomized to intervention or control arms in experimental trials. This systematic review also documents how researchers justified their use of the CRT design, the process of obtaining cluster permission, intervention targets and concomitant consent, and approaches to primary outcome measurement and consent for data collection.

Published by the Nulungu Research Institute, this review presents a methodically produced snapshot of self-described ethical practices as at December 2020 as a baseline with which independent Aboriginal and Torres Strait Islander human research ethics committees can develop CRT-specific guidance for their contexts. Randomisation to experimentation of clusters of Aboriginal and Torres Strait Islander peoples or services upon which they rely as occurs in CRTs behoves careful consideration.

Ms Vicki O'Donnell
Chair, WA Aboriginal Health Ethics Committee
Aboriginal Health Council of Western Australia
September 2021

EXECUTIVE SUMMARY

Cluster randomised trials (CRTs) present unique ethical complexities for research ethics committees, participants, researchers and evidence users. In this design, whole social units ('clusters') such as hospitals, schools or entire communities are randomised to interventions. In addition, units of randomisation, intervention and outcome measurement differ within the one study. As a consequence, clearly determining research participants and establishing whose consent is required not only for randomisation and interventions but also data collection are correspondingly difficult.

This systematic review describes self-reported ethical practices in research conducted in Australia in which social units comprising Aboriginal and Torres Strait Islander people, their communities or services upon which they rely were randomised as whole clusters to trial interventions. To undertake this systematic review, we developed a study protocol and registered it prospectively on a public database (PROSPERO protocol CRD42018106463). Applying this protocol meant we could methodically identify all CRTs conducted in Aboriginal and Torres Strait Islander settings in Australia by finding their peer-reviewed study protocols or articles with main results reporting primary outcomes.

We identified 18 eligible CRTs published from January 2008 to December 2020. In six CRTs (33%), researchers had randomised entire Aboriginal and Torres Strait Islander communities. Other cluster types included schools, stores and health services. Depending on study design, community-based health services randomised as clusters included mainstream practices, government-managed clinics, Aboriginal and Torres Strait Islander community-controlled health services or combinations of these. Cluster level permission was documented for ten CRTs (55%) although gatekeeper authority to give this permission was not always explained in detail. Cluster eligibility to participate in the CRT was based exclusively on prior relationships in six CRTs (33%). Material incentives from researchers to clusters or financial payments to people within clusters ranged from none to substantial. Three CRTs (17%) had obtained consent waivers for individual informed consent. Grounds for waivers were not always explained, including whether they covered intervention participation only, access to individual data without consent, or both. Of ten CRTs (10%) requiring access to routinely collected individual data for primary outcome measurement, one (10%) obtained individual written consent. Approaches to cultural safety and data sovereignty varied. For 11 (61%), independent Aboriginal and Torres Strait Islander ethics committee approval was obtained. Among the 18 CRTs, seven (39%) were stepped-wedge CRTs in which all clusters had been exposed by the end of the trial to an untested intervention. Only five (39%) of the 13 CRTs with published main results produced statistically significant impact on health outcomes.

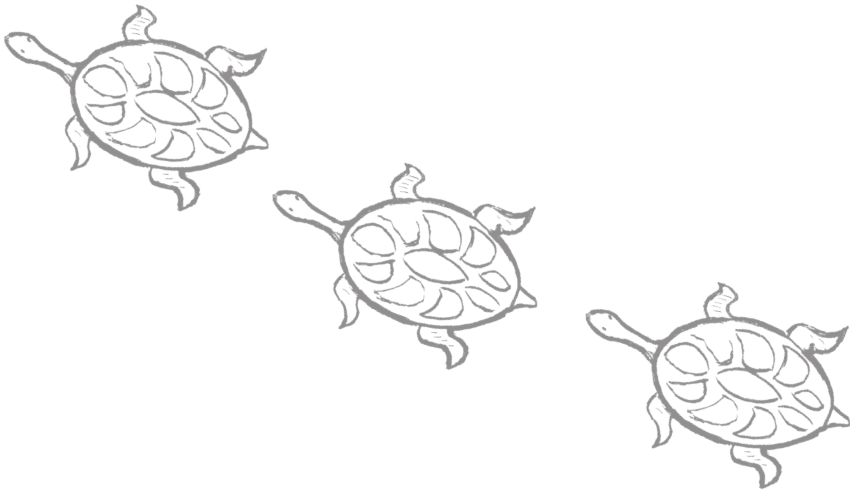
This systematic review of 18 CRTs from 2008 to the present day reveals considerable variation in self-reported ethical practices for key features in CRT design. This variation invites specific effort in conjunction with independent human research ethics committees to strengthen conceptualisation and conduct of trials in which large social units comprising Aboriginal and Torres Strait Islander peoples or services they receive are randomised as clusters with potential for both benefit and harm.

INTRODUCTION

Key features of cluster randomised trials (CRTs)

For more than a century, health and medical research has used the conventional randomised controlled trial design (RCT) as the foundation for testing the efficacy and harms of individual clinical treatments. As is widely recognised, RCTs

> … are structured around the individual patient: the patient is recruited and allocated independently to either intervention or control arm, administered the allocated intervention and observed prospectively. This design is optimal in the sense that the number of independent allocation units is the same as the number of observations to be analyzed (Taljaard & Grimshaw 2014:1)



This design is familiar and straightforward in terms of its methodological architecture and secures meaningful consent because randomization, intervention and data collection implicate only the individual, and it is the individual who is asked to participate and sign consent.

By contrast, cluster randomized trials (CRTs) differ profoundly from individual RCTs because their defining feature is randomization of entire 'social units' rather than individuals are assigned randomly to trial arms. These social units are known as 'clusters' and, depending on the research, might be hospitals, schools, workplaces, child care centres or social services for example. Interventions to which these clusters are randomised might target every individual in the cluster, only a subset of individuals or, if the cluster is an organization or service, staff intermediaries who work in the cluster structure. CRTs have been used in diverse health settings for research and evaluation purposes such as projects to evaluate different models of health services delivery, health promotion campaigns or interventions designed to increase the uptake of evidence-based methods in medical practice for example. It is entirely possible that individuals in CRTs may be unaware of a randomized experiment underway that might affect their outcomes or their cluster's social dynamic, functioning or social capital.

There are three main CRT types. Of these, the most common is a parallel arm CRT in which clusters are randomized to either intervention or control groups. Here, control group clusters will not receive the intervention as part of the CRT. Occasionally, mechanisms might be in place following the demonstration of positive impact to deliver the intervention to those on hold as wait-list controls. In cross-over CRTs, clusters are exposed to two or more interventions being compared: for example, a 2x2 cross-over CRT will randomize half of the clusters to receive intervention A followed by intervention B, while the other half receive intervention B followed by intervention A. The third type is known as the stepped-wedge CRT (SW-CRT). In this type of CRT, the intervention is delivered to every cluster in a sequence of steps determined by randomization so that, by intention, all clusters eventually receive it (Campbell et al 2019).

RCTs compared with CRTs: key ethical differences

Human research ethics committees (HRECs) determine whether risks to people invited to participate in health research are minimized consistent with sound scientific design. Knowledge gained must outweigh risks (Weijer et al 2011). Three ethical principles are widely accepted and applied to make such determinations, namely respect for persons, beneficence and justice. As reviewed elsewhere

> the principle of respect for persons … requires that individual autonomy be acknowledged and that persons with diminished autonomy be protected; the principle of beneficence … requires that persons not only be protected from harm, but also that steps be taken to ensure their well-being; while the principle of justice …refers to the fair distribution of goods; in the context of research, it refers to the equitable distribution of the risks and potential benefits of research participation (Weijer 1999:503).

Additional principles for health and medical research proposals involving communities have also been proposed (Weijer & Emanuel 2000).

As described earlier, CRTs bring inherent risk for social units and the individuals within these social units. Assessment of benefits and harms in CRTs is not as straightforward as in RCTs (Taljaard & Grimshaw 2014). In an RCT, the state of equipoise and the rationale for inviting individuals to participate in a RCT can be readily communicated to each potential participant one by one in consent procedures. What participants can expect and their agency in an RCT including access to their health data is also clearly conveyed in participant information prior to consent. By contrast, the moral rights of social units in CRTs are less easily defined and harder to operationalise. Gauging true equipoise is more challenging (Hey et al 2018; Hemming et al 2018). Nonetheless,

> CRTs should be conducted in accord with appropriate scientific and ethical principles (Hemming et al 2018:664)

CRTs

raise distinct ethical challenges that may require more thought and time at the protocol development and research ethics application stages. The decision to adopt cluster rather than individual randomization should therefore not be made lightly (Taljaard & Grimshaw 2014:1)

Ethical obligations require a 'cluster gatekeeper' of whom researchers will gain permission for cluster participation in a CRT. However, the identities and authorities of such gatekeepers to act on behalf of the cluster in this way may be unclear or contestable. In CRTs, gatekeepers could be individuals, Chief Executive Officers (CEOs), boards or councils authorized through agreed means - such as elections or corporate appointments with delegations - to speak on behalf of their respective cluster and legitimately assert cluster interests.

In addition, multi-level interventions in various combinations can similarly make the identification of research participants unclear and mechanisms for intervention consent challenging. Researchers must obtain free, prior and informed consent from anyone exposed to the intervention and anyone with whom the researcher interacts for the purpose of collecting data or anyone whose identifiable information is obtained as part of research conduct unless a waiver of consent is sought and granted by an appropriately constituted research ethics committee. In CRTs however, interventions introduced by researchers might target the cluster as a whole, all individuals who make up the cluster or only a subgroup of individuals (Taljaard & Grimshaw 2014). If the cluster is an organization or service, staff might be targeted for interventions but with consequences for users of the organization or service.

IIn health research, outcome measurement in CRTs adds further complexity for ethical appraisal (Taljaard & Grimshaw 2014; Campbell et al 2019). Quantitative measures to analyse the primary outcome for which the CRT is designed might require data collection directly from individual participants using specific measures such as surveys or accessed via routinely collected clinical information as contained in a clinical record with or without the individual's knowledge.

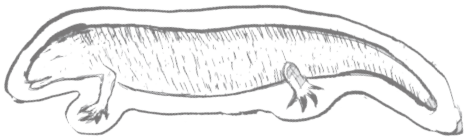
To summarise, the conventional RCT aligns allocation to randomisation, receipt of intervention and unit of observation and analysis to the same entity - the individual - in a relatively uncomplicated fashion. Informed consent is individualistic. In CRTs, it may not be immediately easy to discern from whom consent is required after randomization and whether for intervention, data collection or both (Weijer et al 2011). The foundation of international biomedical ethics is that every research ethics committee must minimize risks to potential research participants by considering the soundness of the proposed scientific design and ensure that knowledge gained will outweigh risks (CIOMS 2016).

'Ottawa Statement' on the ethical design and conduct of cluster randomized trials

In 2012, a collaborative international academic team published the 'Ottawa Statement on the Ethical Design and Conduct of Cluster Randomized Trials' (Weijer et al 2012). This Ottawa Statement includes 15 recommendations on ethical aspects of CRTs organized in seven domains including justification for choosing cluster randomization rather than individual randomisation, steps to identify research participants, obtaining gatekeeper permission for randomization of an entire cluster, evaluating mechanisms for informed individual consent for interventions, and assessing ethical requirements for data collection and individual consent for outcome measures. Contextualised grounds for granting waivers in CRTs are also described in the Ottawa Statement (Weijer et al 2012).

CRTs affecting Aboriginal and Torres Strait Islander peoples

Aboriginal and Torres Strait Islander leaders and scholars have long argued about the unique ethical issues inherent in research conducted in Australia, particularly when studies are led by or disproportionately advantage non-Indigenous research institutions or researchers (Wyatt 1991; Schnarch 2004; Thomas & Anderson 2006; Jamieson et al 2012; Bainbridge et al 2015). Throughout Australia, histories of colonization have left an indelible mark on Indigenous health (Anderson et al 2006; Paradies 2016). By acknowledging this wider



political context in Australia, research and its ethical conduct abuts the overarching powers of the 'settler state' in which Aboriginal and Torres Strait Islander peoples have been and continue to be systematically marginalized and disempowered (Ninomiya & Pollock 2017; Rigney 1999; McPhail-Bell et al 2018; Rix et al 2018; Benveniste & King 2018). In Australia, declaration of terra nullius by Governor Bourke in 1835 masked the truth that Aboriginal and Torres Strait Islander peoples never ceded their sovereignty or relationship to country and waters to the British crown. Prosperity and re-empowerment of Aboriginal and Torres Strait Islander communities requires strong culture, nation-rebuilding and relationship to land and waters defined in their own terms (Yu 1994; Arabena 2006; AIATSIS 2012; Pearson 2012; Dwyer 2012).

Aboriginal and Torres Strait Islander communities and organisations are complex socio-political environments, and priorities for research focus may vary between members and/or within organizational Boards. Deeper considerations of ethical research practice in these environments must account for the possibility of alterity within the community – of nonconforming, or unrepresented others: there are always 'groups with groups' (Sullivan 2020). As with any form of pseudo-representation, the use of gatekeepers in these contexts might represent a superficial or unreliable form of permission-giving for the entire cluster.

Randomisation of clusters of Aboriginal and Torres Strait Islander peoples or services upon which they rely to experimentation as undertaken in CRTs behoves careful ethical consideration. While Australian ethical research guidelines informed by Aboriginal and Torres Strait Islander perspectives exist (NAILSMA 2007; Lincoln et al 2017; Taafe 2008; Laycock et al 2011; NHMRC 2018; Fitzpatrick et al 2019; Lovett et al 2019; AIATSIS 2020; AHMRC 2020), none to date contains explicit guidance for ethical conduct of CRTs. Although the only international guidance for CRTs, the Ottawa Statement was developed without the explicit participation of First Nations Canadians, Aboriginal and Torres Strait Islander peoples, Maori or other Indigenous representatives.

In this context, our multidisciplinary team of six research collaborators came together to summarise self-reported ethical practices as described in research publications for CRTs conducted in Australian Aboriginal and Torres Strait Islander settings. This systematic review was conducted with the specific aims of ascertaining the types of clusters randomized in these CRTs and documenting ethical practices with respect to design justification, cluster permission, intervention levels and consent, and approaches to primary outcome measurement. Despite their ethical complexity, such a snapshot has not before been produced.

METHODS

We developed and then registered our protocol for this systematic review prospectively with the PROSPERO register (CRD42018106463) where details about our adherence to Cochrane and PRISMA requirements are provided (Ward et al 2018).

To determine eligibility for inclusion in our systematic review, we applied the definition of a CRT as presented in the Ottawa Statement as follows:

> A study design that randomizes to different study arms groups or clusters of individuals (such as households, primary care practices, hospital wards, classrooms, neighbourhoods or communities), rather than independent individuals. Another distinguishing feature of CRTs is that the units of allocation, intervention, observation, and analysis may be different within a single study. CRTs may also be referred to as group randomized, place randomized, or community intervention trials (Weijer et al 2012:S3).

Study methods of potential Australian CRTs needed to describe and randomly allocate social units of Aboriginal and/or Torres Strait Islander people or organisations directly serving them for inclusion in our systematic review. Our time period was pre-specified from 2008 to 2020 to provide 12 years of research output including a reasonable period to assess uptake in Australia of the Ottawa Statement published in 2012.

To generate the largest possible pool of potential Australian CRTs, we adapted previous search strategies (Taljaard et al 2010; Siebenhofer et al 2016). We

searched five electronic databases for eligible studies, namely: MEDLINE (Medicine / Nursing / Dentistry / Preclinical Science), PREMEDLINE, Embase (Biomedical/ Pharmaceutical / Health Policy / Nursing), PsycINFO (Psychology / Education/ Behaviour) and EMCARE (Nursing / Allied Health). Precision was enhanced by including cluster design-related term using the Boolean operator AND (Taljaard et al 2010). Box 1 presents our search strategy for MEDLINE. For other databases, we modified if necessary. To address the variation in spelling of 'randomized' or 'randomised', our search strategy used the $ sign to encompass both. Two authors independently examined titles, abstracts and full text for retrieved citations. Only CRTs with peer-reviewed study protocols or main results publications were included in our final sample for detailed review. Studies using non-randomized assignment of clusters to interventions were excluded. Disagreements in eligibility were noted and resolved. We also searched the Australian New Zealand Clinical Trial Registry (ANZCTR). Any CRT with ANZCTR registration but without either published study protocol or main results article was noted for future reference but excluded from this review. For any CRT with a published study protocol, we continued to search monthly for main results until December 2020.

BOX 1 – Example of search strategy (Medline)

Database: MEDLINE(R) including Daily update <1996-current>
Search Strategy:

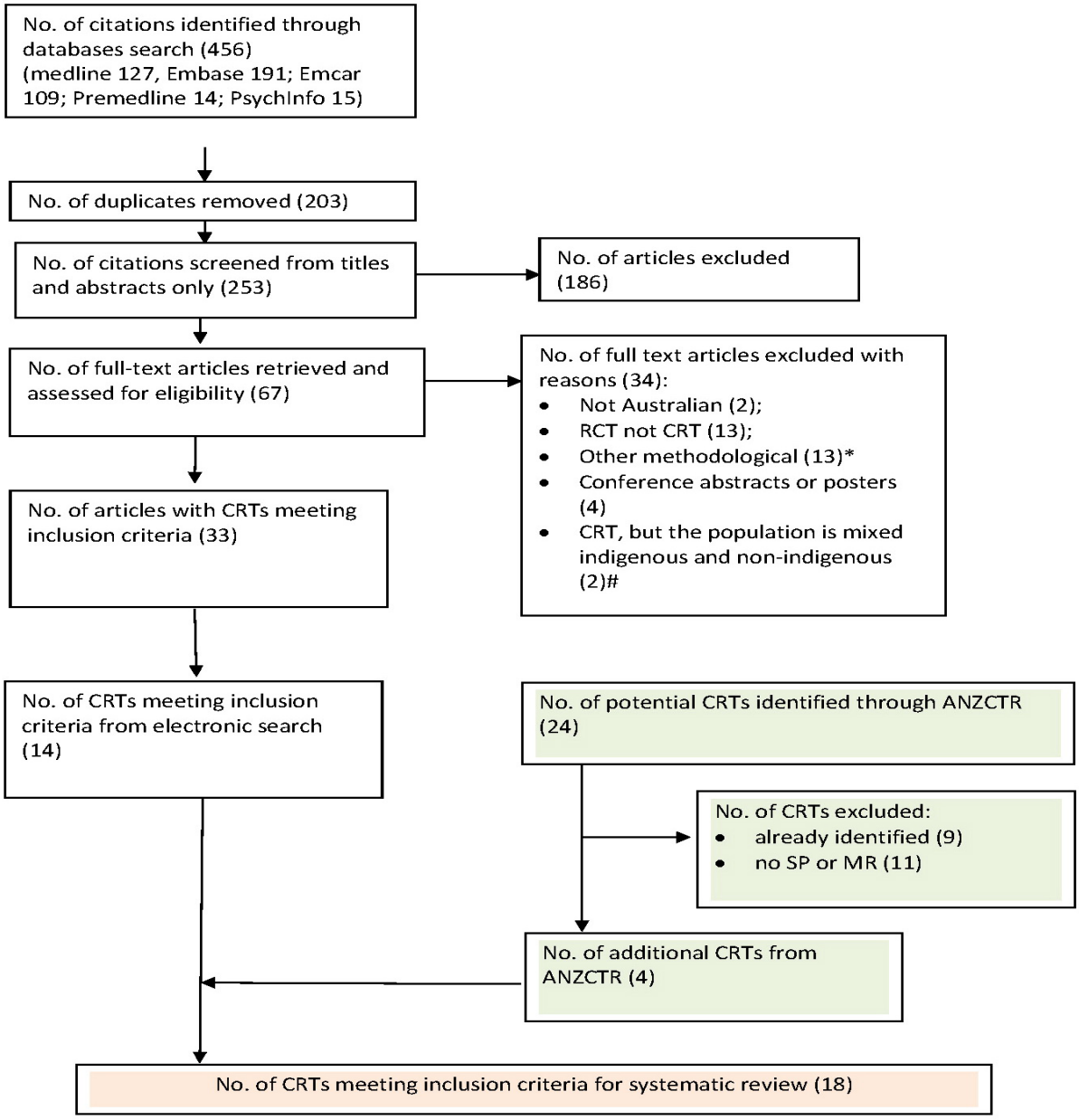
---

1 randomized controlled trial/ (410254)
2 animals/ (3896408)
3 humans/ (11450181)
4 2 not (2 and 3) (2487387)
5 1 not 4 (399299)
6 (cluster$ adj2 randomi$).tw. (9815)
7 ((communit$ adj2 intervention$) or (communit$ adj2 randomi$)).tw. (6413)
8 group$ randomi$.tw. (2771)
9 6 or 7 or 8 (18462)
10 intervention?.tw. (707732)
11 cluster analysis/ (59684)
12 health promotion/ (61847)
13 program evaluation/ (55871)
14 health education/ (32254)
15 10 or 11 or 12 or 13 or 14 (861112)
16 9 or 15 (864232)
17 5 and 16 (94672)
18 aboriginal$.ab. (5585)
19 indigenous.ab. (19986)
20 18 or 19 (24426)
21 17 and 20 (151)
22 limit 21 to (english language and yr="2008 -Current") (127)

"$" allows for truncation of words so that variations such as "randomisation", "randomization" are included;
"Adj" refers to the adjacency operator to accommodate terms such as "community-based randomized trial";
"pt" refers to publication type
"?" refers to optional wildcard character retrieving 1 or 0 characters;
"/" refers to MeSH
"tx" refers to text words in the title or abstract

To extract information from each publication, we adapted an earlier data template (Taljaard et al 2011). We used this adapted template to extract data consistently from every publication. For each CRT, we first referred to the study protocol to extract details about cluster design justification, cluster sampling and recruitment. We documented how researchers had defined their study 'clusters'. We then extracted details about cluster gatekeepers as described by the researchers, governance structures and the process of requesting and documenting gatekeeper permission. In Australia, Aboriginal and Torres Strait Islander governance differs by community according to factors such as history, resources, relationships and capacity (Hunt et al 2008). Therefore, we also noted any statement made by researchers about community governance, implications for cluster permission and details of those described as gatekeepers. Because units of randomization, experimentation, and outcome measures differ within the one CRT study, we carefully abstracted information about intervention levels and corresponding participant consent, incentives, consent for data collection for primary outcome measurement, and any relevant detail about data management and relationships already existing or developed during the CRT by researchers with Aboriginal and Torres Strait Islander peoples. Where there was no study protocol, we used the main results article to extract the above details. If both were available, we double-checked ethical practices reported in both, synthesizing both sources and noting any discrepancies.

FIGURE 1 PRISMA flow chart of yield from electronic bibliometric journal search

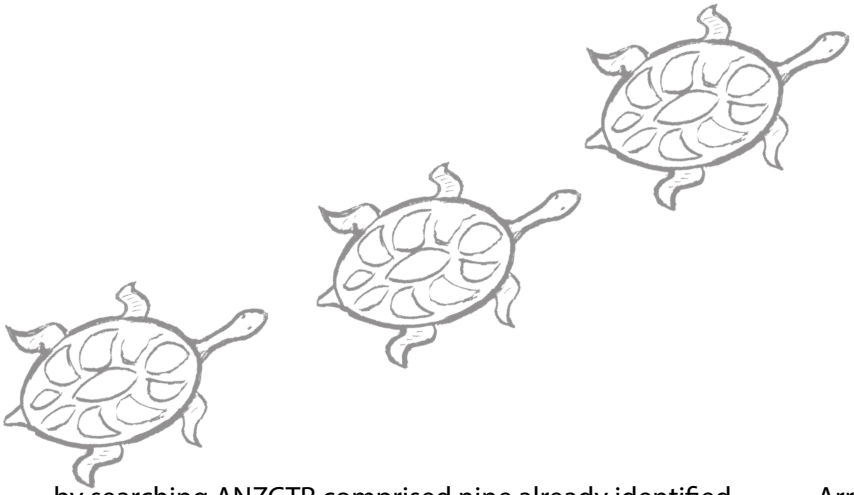


Because this was a systematic review of content in open access articles already in the public domain, institutional ethics committee approval was not required. As no external funding was obtained for this review, we were unable to contact study authors. This also precluded any further follow-up to identify Aboriginal and Torres Strait Islander authors unless included in the retrieved articles.

RESULTS

Sources of CRTs identified in this systematic review

From 456 citations, 14 CRTs with either study protocol or main results publications were obtained from the electronic search method (Figure 1). Those 24 CRTs found



by searching ANZCTR comprised nine already identified from the electronic literature search. Four registered CRTs had published peer-reviewed study protocols and/or main results articles. Adding these four from the ANZCTR search to our electronic search yield, we identified 18 distinct CRTs randomising clusters as below:

- Community-based primary care services meeting the health needs of Aboriginal and Torres Strait Islander peoples [CHS]: CHS1 (Schmidt et al 2012; McDermott et al 2015; Segal et al 2016); CHS2 (Peiris et al 2012; Peiris et al 2015); CHS3 (Guy et al 2013; Guy et al 2018); CHS4 (Bar-Zeev et al 2017; Gould et al 2019); CHS5 Liaw et al 2019); CHS6 (Harrison et al 2019) and CHS7 (Bradley et al 2020)

- Entire communities [EC]: EC1 (Slade et al 2011); EC2 (Ward et al 2013; Ward et al 2019); EC3 (Brimblecombe et al 2013; Brimblecombe et al 2017); EC4 (Ralph et al 2016; Ralph et al 2018); EC5 (Arrow et al 2018; Arrow et al 2020) and EC6 (Mullane et al 2019).

- Stores in remote communities [RS]: RS1 (Brimblecombe et al 2019; Brimblecombe et al 2020)

- Schools [SCL]: SCL1 (Kiran & Knights 2010) and SCL2 (Wagner et al 2017; Wagner et al 2020)

- Households [HLD]: HLD1 (Borg et al 2018)

- Hospitals [HPL]: HPL1 (McAulley et al 2016)

As shown in greater detail in Table 1, ten of these 18 CRTs had both published study protocol and main results article by December 2020; four had only a published study protocol and four had been reported in the peer-reviewed literature only as main results articles without prior study protocols. Each CRT has been assigned a unique label for reader convenience.

TABLE 1 Characteristics of 18 CRTs conducted in Australian Aboriginal and Torres Strait Islander settings

STUDY		SP year of publication	MR year of publication	DESIGN TYPE	LOCATIONS	N CLUSTERS	N HREC (N INDEPENDENT)	ANZCTR	FUNDING
Local health services (MGPs / ACCHOs / GPHC or combinations)									
CHS1	ACCHOs + GPHC	2012	2015	PL	Outer regional / remote / very remote	12	1 (0)	Yes PR	NHMRC; Queensland Government
CHS2	MGPs + ACCHOs	2012	2015	PL	Outer regional / inner regional / metropolitan	60	2 (1)	Yes PR	NHMRC; NSW Department of Health
CHS3	ACCHOs + GPHC	2013	2018	XO	Outer regional / remote / very remote	12	5 (2)	Yes RR	NHMRC
CHS4	ACCHOs only	2017	2019	SW	Metropolitan / outer regional	6	4 (2)	Yes RR	NHMRC; Cancer Institute; Hunter Cancer Research Alliance
CHS5	MGPs only	-	2019	PL	Metropolitan	53	4 (1)	Yes PR	NHMRC
CHS6	ACCHOs only	2019	-	PL	Metropolitan / inner regional / outer regional / remote / very remote	22	8 (3)	Yes RR	NHMRC
CHS7	ACCHOs only	2020	-	SW	Recruited from four states / no other information in SP	12	3 (2)	Yes PR	NHMRC
Entire Communities									
EC1		-	2011	PL	Remote / very remote	30	3 (0)	Yes RR	NHMRC
EC2		2013	2019	SW	Remote / very remote	24 #	6 (1)	Yes PR	NHMRC
EC3		2013	2017	SW	Remote / very remote	20	3 (0)	Yes RR	NHMRC; ARC; Heart Foundation
EC4		2016	2018	SW	Inner regional / outer regional / remote / very remote	10	2 (0)	Yes PR	NHMRC
EC5		2018	2020	PL	Remote / very remote	26	3 (1)	Yes PR	NHMRC; Dental Health Services WA
EC6		2019	-	SW	Remote / very remote	4	3 (1)	Yes PR	NHMRC; WA Health Future Health WA Initiative; Healthway
Stores in communities									
RS1		2019	2020	PL	Remote / very remote	20	2 (0)	Yes RR	NHMRC; Canadian Cancer Society
Schools (Mainstream only / Aboriginal only)									
SCL1	Mainstream	-	2010	PL	Outer regional	4	2 (0)	No	None specified
SCL2	Aboriginal only	2018	2020	PL	Very remote	8	3 (1)	Yes PR	NHMRC; Commonwealth of Australia; 100 Women
Households									
HLD1		-	2018	PL	All of Victoria	5534	1 (0)	Yes RR	Victorian Public Sector Innovation Fund, DPC, Victoria
Hospitals									
HPL1	Mainstream	2016	-	SW	WA	25	3 (1)	Yes PR	NHMRC

NOTE: # 24 clusters comprised either a single or several communities that share close cultural affinities and/or are geographically proximal. Within these clusters, there were 68 community-based health services both ACCHOs, government clinics and mainstream general practices in each cluster included).

TABLE 2 Reasons given by authors for choosing CRT design (more than one possible per CRT)

Reason	Parallel arm CRTs /Crossover CRTs (n=11)	SW-CRTs (n=7)
Intervention targets cluster-level systems, staff and individuals	4	4
Rapid translation of research findings	2	4
Avoids contamination	4	2
Cluster level activities augment individual-level activities	2	1
Participant motivation	1	2
Feasibility	1	1
Promotes partnerships	1	1
Every cluster receives the intervention		6
Efficiency through logistics / research burden		5
Reduces cost		2
Robust method / statistical method		2
Local resources required to contextualize intervention		1
Controls for confounding		1
TOTAL	15	32

Types and locations of clusters

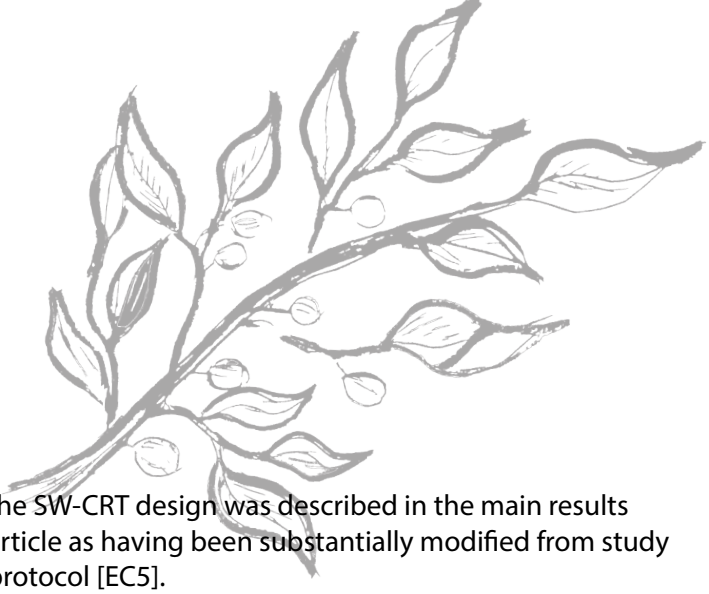
Across all of these 18 RCTs, we identified six distinct categories of clusters (Table 1). In seven CRTs (39%), researchers reported randomizing primary care organisations serving Aboriginal and Torres Strait Islander people (Table 1). Entire communities had been randomized as clusters in six CRTs (33%)(Table 1). Other clusters comprised birthing hospitals, schools, stores and households (Table 1). Across 18 CRTs, the median number of participating clusters per CRT was 20 (range 4–5,534)(Table 1). While two CRTs recruited only four clusters each, one had recruited and randomized every large Aboriginal community across a designated region of interest [EC6] while the other had recruited and randomised every school within a remote geographic footprint known to be at high risk of service failure [SCL2].

In terms of design, more than a third (n=7, 39%) were SW-CRTs. All (100%) had been approved by at least one HREC (number of HRECs per CRT ranged from 1 to 8; median 3). However, only 11 (61%) had been approved by independent Aboriginal and Torres Strait Islander ethics committee(s). NHMRC ethical guidelines for Aboriginal and Torres Strait Islander research (2018) were cited by four [CHS4, EC6, RS1 AND SCL2]. All but two CRTs (89%) were funded entirely or in part by the NHMRC (Table 1). Among the 12 CRTs published after release of the Ottawa Statement, only one had cited it [ECS2]. Cited in the study protocol, the Ottawa Statement was not used in reference to ethical practices but to state that the design allowed the intervention to be delivered to all clusters and would likely have a potential beneficial effect [ECS2].

Justification of cluster design

All CRTs gave at least one justification for the choice of a cluster randomized design (Table 2). While the strength of these assertions could not be independently assessed from publication details, the most common overall was the necessity to deliver the intervention at entire cluster-level. Four SW-CRTs explicitly stated that it was ethically preferable that all clusters received their intervention as part of their research offering [CHS4; CHS7; EC6; HPL1]. Three of these prospectively distinguished anticipated benefits as a reason not to withhold their intervention from any cluster [CHS7; EC6; HPL1]. Four SW-CRTs explicitly acknowledged their design choice was preferable to other study choices specifically on ethical grounds. One was affirmed as a preferred model with stakeholders [EC2].

Other details revealed additional insight into design choices. For one, [SCL2], the original design had been proposed as a SW-CRT but stakeholder feedback after earlier pilot testing rejected the SW-CRT design. Researchers pursued a parallel CRT. In another, [CHS4], researchers had conducted a SW-CRT design as reported. As participating clusters had found the SW-CRT confusing, all future research by this team would no longer deploy this design as intended. In another,



the SW-CRT design was described in the main results article as having been substantially modified from study protocol [EC5].

Cluster recruitment, permission and gatekeepers

Six (33%) CRTs used pre-existing relationships to define sampling frames. In other words, eligibility for cluster research participation had been predetermined through familiarity, partnerships or earlier collaborations [CHS4; CHS5; CHS7; EC3; EC5; RS1]. Five (28%) used demographic, epidemiological or service criteria with or without additional stakeholder consultation to identify and approach clusters [CHS5; EC1; EC2; EC4; EC5]. Reproducible cluster recruitment strategies including random selection from a sampling frame reduces CRT bias. Six (33%) CRTs reported a priori relationships that materially influenced their recruitment strategy [CHS4; CHS5; CHS7; EC3; EC5; RS1]. Demographic, epidemiological or service requirements were applied in five (28%) CRTs although subsequent additional stakeholder consultation may have diminished generaliseability [CHS5; EC1; EC2; EC4; EC5].

Cluster permission was reported for 11 CRTs (61%) although not always with clear information about the corporate governance of respective clusters or scope of permission (CHS2; CHS3; CHS5; CHS6; CHS7; EC1; EC2; EC3; EC4; RS1). Where obtained, cluster permission was documented in a variety of ways including research agreements, site participation agreements, partnership agreements and memoranda of understanding. It was uncommon for the specific details of permission in these documents to be stated or for the role held by the signatory on behalf of the cluster to be described. Community permission was conflated with service consent in three [EC2; EC3; EC4]. Specifically, researchers assumed service organizations could give cluster permission on behalf of the entire community without corroborating detail about the community's specific governance structures legitimizing this approach to gatekeeper permission. Further, one CRT described only meetings organized with the CEO of the respective remote community council but no specific description of cluster permission process [EC5].

Consent for study interventions and incentives

Table 3 summarises intervention levels and their combinations. Table 4 presents further details about consent for interventions. Obtaining consent to participate in interventions at professional level (usually staff as intermediaries in clusters) or from individuals exposed to interventions due to randomization was less common than obtaining cluster permission. Of 13 CRTs delivering interventions to professional-level intermediaries, only one reported obtaining their consent [CHS7]. For those 13 CRTs where individuals were targeted, individual consent for interventions was clearly obtained in four (31%)[CHS4; EC1; EC5; SCL2]. In one CRT, consent to participate was only obtained from individuals in clusters randomized to intervention leaving those in control clusters unaware [HPL1]. In another, individual consent for service delivery changes was obtained only for those being prescribed medication off-label as part of this change [EC6]. Eight CRTs (44%) offered some kind of financial reimbursement in recognition of costs for trial participation, material incentive or benefit [CHS2; CHS3; CHS4; CHS6; EC2; EC3; EC5; SCL2]. Two of these provided payments to services tied to clinical performance [CHS3; EC2]. Three (17%) CRTs described research employment opportunities for local community members [EC3; EC5; SCL2]. One (6%) CRT organized formal training [SCL2]. Seven of these eight CRTs (88%) had been reviewed by at least one independently constituted Aboriginal and Torres Strait Islander research ethics committee (Table 1).

TABLE 3 Levels of interventions

Cluster + Intermediaries + Individuals	6
Cluster + staff intermediaries	4
Intermediaries + Individuals	3
Cluster + Individuals	3
Cluster only	1
Individuals only	1

TABLE 4 Consent, intervention levels, primary outcome, measure, consent for data access and result for 18 CRTs in Aboriginal settings

STUDY	WRITTEN CLUSTER PERMISSION	WRITTEN CONSENT FOR INTERVENTION PARTICIPTATION BY INTERVENTION LEVEL*	PRIMARY OUTCOME	LEVEL OF DATA USED FOR PRIMARY OUTCOME	DATA TYPE	CONSENT TO ACCESS DATA	INDEPENDENT ABORIGINAL AND TORRES STRAIT ISLANDER ETHICS REVIEW	PRIMARY OUTCOME RESULT
Local health services								
CHS1	No	Staff: NO Individual: NO	Reduction in HbA1c measured at 18 months.	Individual	Routinely collected	*Individual patient consent procedure not described. Patients recruited for the program. No information about patient consent for intervention or data collection.* *CLASSIFICATION: NO INFORMATION. NO CONSENT.*	No	Non significant
CHS2	Yes – signed cluster agreement	Cluster: YES Staff: NO	Proportion of eligible patients receiving appropriate measures of their CVD risk.	Individual	Routinely collected	*No patient consent for data extraction from records. Patients of ACCHOS could opt-off but no details about process to do so.* *CLASSIFICATION: WAIVER GRANTED #*	Yes	Non significant^
CHS3	Yes – signed cluster agreement	Cluster: YES Staff: NO Individual: NO	Reduction in rates of repeat positive infections at three months among people with CT or NG infection in remote communities.	Individual	Routinely collected	*No patient consent for data extraction. No mention of waiver.* *CLASSIFICATION: NO CONSENT*	Yes	Non significant
CHS4	Not reported	Cluster: UNCLEAR Staff: NO Individual: YES	Recruitment rate (no threshold set)	Individual	Bespoke	*Patient consent for intervention explicit. Patient consent for data implicit. CLASSIFICATION: UNCLEAR. NO CONSENT*	Yes	No hypothesis
CHS5	Yes – format not reported	Cluster: YES Staff: NO	Rate of claims for MBS items 715, 721 and 723	Individual	Routinely collected	*No patient consent for billing data extraction. No mention of waiver.* *CLASSIFICATION: NO CONSENT*	Yes	Non-significant
CHS6	Yes – cluster agreement (MOU)	Cluster: YES Staff: NO	Rate of screening of clients attending the service by AUDIT-C	Individual	Routinely collected	*No patient consent for data extraction. No mention of waiver.* *CLASSIFICATION: NO CONSENT*	Yes	Not yet reported
CHS7	Yes – format not reported	Cluster: YES Staff: YES	Rates of documentation of dementia and cognitive impairment not dementia (CIND) and improved management	Individual	Routinely collected	*Patient consent for intervention explicit. Patient consent for record linkage.* *CLASSIFICATION: WRITTEN CONSENT*	Yes	Not yet reported
Entire Communities								
EC1	Yes – statement signed by community	Cluster: YES Individual: YES	Rate of new caries assessed by dental examination	Individual	Bespoke	*Parent/guardian consent for both intervention and data collection.* *CLASSIFICATION: WRITTEN CONSENT*	No	Significant reduction
EC2	No. Agreement with health services only	Staff: NO ^^ Individual: NO	Prevalence of chlamydia, gonorrhea or trichomonas in male and female Aboriginal residents 16-34 years	Individual	Routinely collected	*No patient consent for data collection.* *CLASSIFICATION: NO CONSENT*	Yes	Non significant
EC3	No – agreement with stores only	Cluster: YES Staff: NO	Store level average quantity of fruit and vegetables sold per capita	Store	Routinely collected	Cluster sales data *CLASSIFICATION: WRITTEN CONSENT*	No	Significant increase
EC4	No – agreement with health services only	Cluster: NO # Staff: NO # ^^ Individual: NO #	Proportion of people with ARF/RHD receiving ≥80% of scheduled penicillin injections over a minimum 12-month period.	Individual	Routinely collected	*No patient consent for data extraction. Ethics gave waiver.* *CLASSIFICATION: WAIVER GRANTED #*	No	Non significant
EC5	Not reported	Cluster: NO Staff: NO Individual: YES	Proportion of children with dental decay successfully managed	Individual	Bespoke	*Parent/guardian consent for both program and data collection.* *CLASSIFICATION: WRITTEN CONSENT*	Yes	Significant decrease
EC6	Yes – letter of support giving permission	Cluster: NO Staff: NO Individual: NO ex subset for those receiving off-label medication	50% reduction in the prevalence of impetigo in school-aged children (5-9 years) from baseline (visit 1, 2019) to maintenance (visit 9, 2021)	Individual	Bespoke	*Parent/guardian consent for intervention and data collection.* *CLASSIFICATION: WRITTEN CONSENT.*	Yes	Not yet reported
Stores in communities								
RS1	Yes – cluster agreement	Cluster: YES	Difference in free sugars (g/MJ) from baseline in intervention versus control stores derived from store sales data.	Store	Routinely collected	Cluster sales data *CLASSIFICATION: WRITTEN CONSENT*	No	Significant decrease
Schools								
SCL1	No	Staff: NO Individual: NO	Increase in physical activity and sense of cultural connectedness for Indigenous students	Individual	Bespoke	*Passive parental consent for intervention.* *CLASSIFICATION: PASSIVE. NO CONSENT.*	No	Non significant
SCL2	Yes – format not reported	Cluster: YES Staff: NO Individual: YES	Change in students' SESBI Intensity Scale scores	Individual	Bespoke	*Parent/guardian consent for intervention. Separate parent/guardian consent for data collection.* *CLASSIFICATION: WRITTEN CONSENT*	Yes	Non significant
Households								
HLD1	No	Cluster: NO # Individual: NO #	Proportion of households where all eligible children received the influenza immunization May-Aug 2017	Individual	Routinely collected	*No patient consent for data extraction. Waiver obtained.* *CLASSIFICATION: WAIVER GRANTED ##*	No	Significant increase (pamphlet only)
Hospitals								
HPL1	Not reported	Individual: NO	Reduced hospitalization rate in Aboriginal infants younger than three months.	Individual	Routinely collected	*No patient consent for data extraction for primary outcome.* *CLASSIFICATION: NO CONSENT*	Yes	Not yet reported

* Clusters can have up to three levels of intervention:
Cluster: Cluster level interventions and strategies implemented
Staff: Strategies delivered at professionals or intermediaries within the cluster eg teachers within a school that had been randomized as a cluster to intervention or staff in clinics within a community that had been randomized to intervention
Individual: Strategies at targeted or all individuals in a cluster randomized to intervention

^ ACCHOs permitting Aboriginal data access

Waiver obtained for data collection only and not intervention consent

Waiver could have covered intervention consent and data collection consent but details not provided

^^ Health service signed consent but staff did not

Primary outcome measurement, consent for data collection and safety monitoring

Table 4 also shows primary outcomes, their levels of data collection and consent. For two CRTs, the primary outcome had been measured from routine sales data and permission obtained from shop managers [EC3; RS1] (Table 4). For the remaining 16 CRTs (89%), primary outcome was measured at individual level (Table 4): six of these developed bespoke measures outside routine data capture while ten of these required access to routinely collected data at individual level for primary outcome measurement. One of these ten obtained individual written consent [CHS7]. Waivers were obtained from ethics committees for three CRTs [CHS2; EC4; HLD1]. For one of these however[CHS2], an 'opt out' option was offered for individual data level access but only for Aboriginal people seen in ACCHOs and no-one attending mainstream general practices. Contradicting the waiver, how this 'opt out' option was operationalized was not described. Two CRTs (11%) mentioned the existence of a Data Safety and Monitoring Board or similar to advise researchers [CHS7; EC6]. CHS4 explained why such was not needed. For 14 (78%), main results had been published (Table 4). One did not have a quantifiable null hypothesis [CHS4]. Five of the remaining 13 (39%) had produced statistically significant results [EC1; EC3; EC5; RS1; HLD1]. One of the four SW-CRTs with main results had produced a statistically significant primary outcome [EC3].

Aboriginal and Torres Strait Islander sovereignty and veto

In six CRTs (33%), strategies that aimed to support Aboriginal and Torres Strait Islander perspectives including data governance were clearly described for example an Indigenous Reference Group [EC1], a Stakeholder and Consumer Aboriginal Advisory Panel [CHS4] and an Aboriginal Advisory Group [EC5]. Terms of reference were outlined or implied. Elders were more commonly cited than Traditional Owners. CHS3 had written principles of data ownership and processes for public release of results. Two CRTs were self-described in study protocols as 'co-design' [CHS7; RS1]. All CRTs acknowledged extensive consultation prior to research commencement but not always sufficient for replication or improvement. Seeking feedback on drafted research materials from a state-wide Aboriginal peak group which was then incorporated where possible evoked later criticism [HLD1](Crooks et al 2019). Table 1 also presents the number of authors per CRT for protocol and/or main result publication. None of the study protocols or main result publications specified if any authors were Aboriginal or Torres Strait Islander.

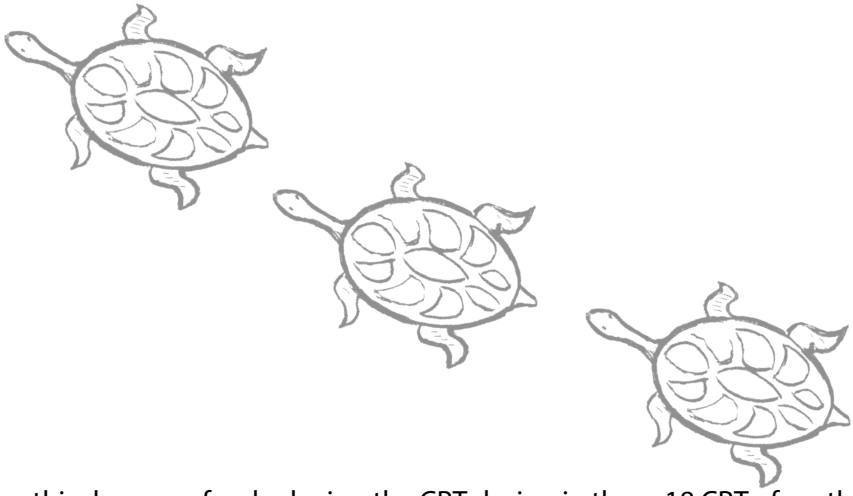
DISCUSSION

This systematic review identified 18 CRTs conducted in Australia and published since 2008. By employing a thorough search strategy comprising standardized searches of electronic databases combined with ANZCTR access, we conclude it is unlikely that we have missed any CRTs in which communities where Aboriginal and Torres Strait Islander peoples live or socially significant entities such as schools, stores or health services upon which they rely have been randomized to interventions. We extracted publicly available self-reported ethical practices from researchers' peer-reviewed study protocols, main results articles or, for ten CRTs, both. To our knowledge, this systematic review is the first to furnish such a timely overview.

What we learned

Ethical aspects of such CRTs are challenging to understand. As shown, the units of randomization, experimentation and observation may differ within a single trial. Hence, it is not straightforward (as in a conventional RCT) to determine who should be considered a 'research participant'. Equally important, CRTs involve groups of people who are organized as social units within the designated clusters. Their relationships are bound by these clusters. Further, neither the moral status of groups per se nor the rights of individuals within these groups when randomized in CRTs with or without their knowledge are well understood. Hence, Weijer et al (2011:5) have declared that CRTs '... only partly fit within the current paradigm of research ethics'. They continue to articulate unique ethical conundrums:

> First, … the answers to pivotal ethical questions, such as who may speak on behalf of a particular group and on what authority they may do so, are unclear. Second, in cluster trials the units of randomization, experimentation, and observation may differ, meaning, for instance, that the group that receives the experimental intervention may not be the same as the group from which data are collected (Weijer et al 2011:5).



To inform and encourage dialogue about these ethical dimensions as put into practice in CRTs, we highlight four grouped findings regarding (1) context and rationale (2) permission, consent and data (3) cultural authority over design and (4) additional ethical aspect of SW-CRTs. Overall, we note that all 18 CRTs had been reviewed by at least one human research ethics committee, an improvement over earlier international findings (Taljaard et al 2017; Siebenhofer et al 2018; Taljaard et al 2020; Al-Jaishi et al 2020; Prost et al 2015; Grayling et al 2017). However, less than two thirds had been reviewed by an independent Aboriginal and Torres Strait Islander HREC.

Context and rational

Reasons given for cluster randomization accorded with findings of other systematic reviews of CRTs conducted internationally (Taljaard et al 2011; Taljaard et al 2017; Siebenhofer et al 2018). We also found variation across these 18 CRTs in their sampling frames to identify and recruit eligible clusters and methods for obtaining cluster permission for interventions prior to randomization. Pre-existing relationships pre-determined the sampling frame for six CRTs (33%). Although well-established before initiating research implementation, their nature could have been better described and the consequence for scientific validity in deliberately confining eligibility to participate in the CRT only to those with pre-existing relationships with researchers better communicated. In five CRTs, non-relational eligibility criteria were developed and applied to maximize the number of clusters and sampling frame. In this approach, bias is more readily assessed. In CRTs conducted in remote locations, cluster randomization meant that the community's only accessible health service, store or school was in a CRT. Pre-existing relationships may have safeguarded against potential harms from research activity. These relational conditions for CRTs were intriguing and require further enquiry beyond text abstraction to better understand and codify for ethical review. In addition, it was not always clear why randomization of entire 'social units' enhanced intervention impact. As stated by Campbell (2019), the CRT design should be avoided if the RCT design better answers a research question about individual therapeutic benefit unless there is concern about contamination. While logistics and contamination were common reasons for deploying the CRT design in these 18 CRTs, for others there was either an implicit or explicit intent to engage with clusters as social units as part of the intervention. Six CRTs targeted all three levels (the cluster as a functional unit plus the staff working within schools or health services plus individual service recipients, students or community members). For future CRTs randomizing entire communities, there would be merit in further investigating how cluster-level interventions could be better informed by theories of community agency, empowerment or co-design to maximize insights about the importance of Aboriginal and Torres Strait Islander community engagement in CRTs and future knowledge transfer.

Permission, consent and data

Cluster gatekeepers are never in a position to provide proxy consent on behalf of individual cluster members (Weijer et al 2012). Details as abstracted from these 18 CRTs varied as to how the researchers explained their proposed management of ethical complexities inherent in the CRT design including multi-layered interventions, exposures and measurements. Despite feasibility, patterns of consent by level to participate in these CRTs were highly variable.

Any research poorly conceptualized or disrespectfully conducted with Aboriginal and Torres Strait Islander peoples compromises cultural safety, community trust and self-determination. Harms inadvertently introduced by a CRT may extend beyond the life of the CRT itself. In health service provision, cultural safety is conceptualised as both an ethical standard of health care practice and an outcome of the quality of care provided (Elvidge et al 2020). When conducting research about Aboriginal and Torres Strait Islander health, cultural safety could span significant epistemic risks such as misrepresenting or misappropriating what happened or was achieved in any specific research study. For this reason, culturally unsafe health and medical research can abet continuing colonization through research activity of Aboriginal and Torres Strait Islander peoples (Cameron et al 2010; Jennings et al 2018; Mackean et al 2019; Bond et al 2021; Sherwood et al 2020).

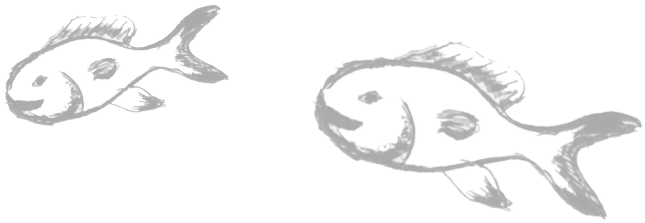
As described in the Ottawa Statement (Weijer et al 2012), gatekeepers are individuals or bodies who may be called upon to protect the group-based interests of the cluster that are affected by enrollment in a CRT. They play an important role in the protection of cluster interests but this responsibility can be met only when they have legitimate authority. Criteria for identifying gatekeepers are emerging (Weijer et al 2012). In these 18 CRTs we identified in this systematic review, procedures to identify, inform and heed 'gatekeepers' appeared non-standardised however. Expectations of researchers about these 'gatekeepers' and the authority they hold on behalf of individuals in their respective cluster were unclear. There was little transparency regarding the role of Native Title organisations including Prescribed Body Corporates (PBCs), community-controlled service organisations created under ORIC legislation or acknowledged Elders as 'gatekeepers' in these 18 CRTs. Gatekeepers ensure that risks of participation in the CRT including randomization are commensurate with the benefits for the cluster of the proposed research (CIOMS 2016; Martin 2008).

Having obtained cluster permission, individual consent for participating in interventions was lacking in almost all of those CRTs with interventions targeting individual participants. Researchers' omitting to obtain individual informed consent for interventions (or obtaining a waiver) has been found elsewhere (Taljaard et al 2011; Taljaard et al 2017). Furthermore, consent for data access was similarly variable in these CRTs. Ten CRTs required access at individual level to routinely collected data for primary outcome measurement. Individual consent for data collection was not obtained for nine (90%). Waivers for data access were reported for three (33%). Adequacy of ethical processes to invite and obtain informed consent for interventions and data collection are context-specific. Whether transfer of de-identified data from routine clinical information systems to researchers without prior individual consent is ethical is highly dependent on stakeholder viewpoints (Weijer et al 2011; Hey et al 2018; Lin et al 2021; de Hoop et al 2015; London et al 2020). A systematic review by a cross-cultural Australian team assessed the process of seeking informed consent for research with Aboriginal and Torres Strait Islander participants (Fitzpatrick et al 2016). As such, these processes were confined to individual RCTs. As concluded elsewhere by the same research team (Fitzpatrick et al 2017; Fitzpatrick et al 2019), contemporary health and research designs can be 'so complicated' that informed consent can be difficult for any researcher to facilitate and for any participant to provide. Consent form construction in any context requires a clear conceptualization of research purpose, harms, benefits and procedures (Goldstein et al 2017). Progress has certainly been made. In 2002, 44% of Australian human research ethics committees reported no procedures to include Aboriginal and Torres Strait Islander people in reviewing Aboriginal and Torres Strait Islander health research applications (Stewart et al 2006a; Stewart et al 2006b). In 2021, there are five independently constituted Aboriginal and Torres Strait Islander ethics committees recognized by the NHMRC (2021). It is imperative that local, regional and jurisdictional perspectives for consent and waivers all must be incorporated (Martin 2008; Studdert et al 2010; NAILSMA 2007; Lincoln et al 2017).

We also found that formal data and safety committees or structures to oversight data access and data interpretation were uncommon in these 18 CRTs.

Cultural authority

Third, our finding about impact on primary outcome was intriguing but remains speculative. Across time and place, CRTs are a resource-intensive design not always delivering statistically significant results (Taljaard et al 2017; Siebenhofer et al 2018; Taljaard et al 2020; Al-Jaishi et al 2020; Prost et al 2015). If previous critique of research generally undertaken in Australia affecting Aboriginal and Torres Strait Islander peoples similarly applies to CRTs (Jennings et al 2018; Bond et al 2021), structural power imbalances and inadequate control asserted by Aboriginal and Torres Strait Islander peoples over design and implementation could similarly have contributed to negative trial results. Unfortunately, different approaches to decision-making and co-design were incomplete in the majority of publications as would be necessary to examine this with validity. Across these 18 CRTs, governance to secure the necessary cultural authority in research affecting Aboriginal and Torres Strait Islander peoples varied. Where in place, mechanisms ranged from advisory groups without clear decision-making power over researchers to steering committees with authority to co-design and, importantly,



maximize positive intervention impact. In research publications, communities of any kind could be better described in terms of their characteristics (particularly their cohesiveness), the spectrum of ethical risks posed to communities and individuals within them from research and details about appropriate protections and their effectiveness (Weijer et al 2000). In these 18 CRTs, local ethical protocols also appeared to be in place but not always, and not always unambiguously described to assist understanding.

Self-reported ethical practices in subset of SW-CRTs

It is noteworthy that seven (39%) of these 18 CRTs had been designed and conducted as SW-CRTs. As a design choice, SW-CRTs expose all clusters to untested interventions by the end of the trial. SW-CRTs present challenges for articulating equipoise, communicating the rationale for the study choice and discussing risks with potential participants when all clusters will be exposed (Hey et al 2018). Unique ethical assessment is required for the SW-CRT because its basic premise is

> … that all clusters start in the control condition, and they switch to the intervention condition in an order determined by randomisation. SW-CRTs differ from cluster crossover trials in that the switch is only in one direction, from control to intervention condition (Campbell et al 2019: 253).

As these and other authors also explain, SW-CRTs might appeal to policy makers who wish to implement an intervention under a strong but untested belief that it will be beneficial yet the universal exposure of clusters to an intervention not yet considered so beneficial that its implementation should be universal might be a contestable stance for public policy (Campbell et al 2019; London et al 2020). Through randomization, SW-CRTs expose every cluster (and individuals within it as a social unit) to an intervention which may be ineffective, harmful or beneficial however (Prost et al 2015). Seven CRTs among these 18 CRTs were SW-CRTs. Debate continues. Some justify the use of the SW-CRT design to ensure all of a population receives the intervention at some point while others are less comfortable with the unscientific premise of this justification that requires an assumption of inherent effectiveness rather than an assumption of equipoise as the starting point for embarking on the trial because research requires genuine uncertainty about the benefits and harms of the intervention requiring a randomized trial to resolve (see Mdege et al 2012; Hemming et al 2019; Kotz et al 2012a; Kotz et al 2012b; Prost et al 2015; Hargreaves et al 2015; Taljaard et al 2017; Al-Jaishi et al 2020). Abandoning equipoise as a prerequisite for ethical experimental health and medical research is problematic (Conrad & Edwards 2011). Use of the SW-CRT is increasing, and the most commonly cited reasons for choosing a SW-CRT are its perceived logistical, social and ethical advantages (Hemming et al 2020). Alternative designs may be preferable such as a parallel CRT in which the control group is wait-listed until results are known (Hemming et al 2020). These alternative designs might also better address concerns about statistical efficiencies, risks of bias and the impact of secular changes.

Elsewhere, it has been recognized that large, expensive and pragmatic trials such as SW-CRTs could be better anchored to and reported against their intended purpose (Nicholls et al 2020). This approach would encourage full disclosure in study protocols of the purpose of the trial in relationship to the policy or practice decisions that its findings are intended to inform – and in which settings. Providing this detail need not be 'an aspirational ideal' but a 'necessary component' in research conceptualization and protocol development (Nicholls et al 2020). Such has been specifically recommended for SW-CRTs in mainstream settings based on a comprehensive analysis of ethical issues in two examples (Hemming et al 2019). Detailed analysis of the decisional intent for policy or practice in each of the seven SW-CRTs identified here would be beneficial.

Methodological strengths and limitations of this systematic review

The majority of these 18 CRTs were retrieved through a replicable electronic search strategy which is a major strength of this systematic review. Searching the ANZCTR was a worthwhile addition to our search method. We adapted robust data extraction methods to compile a detailed overview of self-reported ethical practices. As

at February 2015, eleven SW-CRTs had been identified as having been conducted in Australia as at February 2015 (Grayling et al 2017). Of these, two had been conducted in Australian Aboriginal settings and both of these we found through our own search strategy [EC2 and EC3].

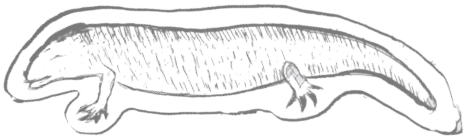
Despite our confidence that we were unlikely to have missed any CRT undertaken in Australia in Aboriginal and Torres Strait Islander settings, we accept that this systematic review was limited by the lack of resources to contact authors directly for additional details and to explore their views about ethical practices in CRTs. For example, we could not explore whether different ethical practices were implemented because the majority or all of the respective lead researchers at the level of Chief Investigator was Aboriginal or Torres Strait Islander. Direct contact with researchers to establish this was not undertaken and, as found, no articles in our cohort indicated whether authors were Aboriginal or Torres Strait Islander people. Others have recommended consideration of the structural and institutional characteristics aiding Aboriginal and Torres Strait Islander community control in every step of the research enterprise (Duke et al 2021). In a Western epistemic paradigm, research is technically completed once findings are produced and articles written. For Indigenous researchers including Aboriginal and Torres Strait Islander researchers for whom their relationships to their communities brings significant additional accountabilities, dissemination requires a deeper reciprocity: 'No matter how much knowledge (or qualification) a person accumulates, if the knowledge, research or stories do not reach the collective consciousness of the wider group, then the person is failing to act in an Indigenous manner' (Xiiem et al 2019:7). Systematically establishing the extent of academic leadership of Aboriginal and Torres Strait Islander researchers at the level of Chief Investigator would permit a broader analysis of research impact beyond the primary quantitative outcome measure for each CRT considered here. In addition, our exclusive focus here on changes in primary outcome measures meant that we had no line of sight to changes in secondary outcome measures. Secondary outcome measures can provide useful insights about intervention implementation, processes and surrogate endpoints (Campbell et al 2012). As secondary outcome measures are methodologically subservient to primary outcome measures, our approach retains merit.

We also acknowledge that engaging researchers in an initiative to share their research documents such as research partnership contracts or the terms of reference for advisory groups and steering committees would cast complementary light on current practice and potentially create a warehouse of practical examples. Further enquiry would also lead to a better understanding of researchers' approaches to sampling frames and recruitment strategies for clusters. Those CRTs in our sample restricting participation to those clusters with existing relationships with research teams have strengths for research implementation but weaknesses for generaliseability. Researchers' reflections on these trade-offs in CRTs and their ethical resolution would be informative.

Most importantly, and to address the limitations of our own positionality (Smith 2014), we welcome and would support an open and iterative process to explore views of Aboriginal and Torres Strait Islander peoples themselves about these ethical complexities in CRTs. With Aboriginal and Torres Strait Islander leadership of such an initiative, a wide range of stakeholders could be consulted about the ethical ground rules and requirements for in complex designs such as the CRT. Others have initiated this scope of enquiry in the context of consent (Lin et al 2021).

CONCLUSION

This is the first systematic review of ethical practices in CRTs conducted in Australian Aboriginal and Torres Strait Islander settings. As for all experimental research, CRTs must have both sound methodological design and ethical processes, such that the risk for harm is '… reasonable in relation to the knowledge that may be gained' (Weijer & Miller 2004:571). When clusters such as schools, health services, shops or entire communities are randomized, unique ethical issues are introduced. Ethical review is not straightforward. Nontherapeutic harms for the 'social unit' may not be immediate, visible or measurable. By contrast, individual RCTs where ethical checks and balances including carefully delineated consent procedures are generally much clearer. As a baseline snapshot, variations in self-reported ethical practices described in these 18 CRTs invite specific effort to strengthen conceptualisation and conduct of



experimental trials in which large social units comprising Aboriginal and Torres Strait Islander peoples or services they receive are randomised. As at the time of writing, there is no specific guidance from NHMRC or AIATSIS about the unique ethical complexities of CRT designs in these circumstances or recommendations for acceptable ethical practices.

While international guidelines such as the Ottawa Statement are useful, we are mindful of limitations inherent in guidance put forward to support action in Australia with consequences for Aboriginal and Torres Strait Islander peoples yet developed without Aboriginal and Torres Strait Islander perspectives and control. This criticism has been raised in reference to the development of the Ottawa Charter (McPhail-Bell et al 2013). Continued use of the term 'vulnerable populations' in any future re-issue of the Ottawa Statement for CRT research may be somewhat discordant in the Australian political context (Munari et al 2021). Nonetheless, the Ottawa Statement remains to date the only international guidance dedicated to ethical aspects of CRTs. The findings of this systematic review are now under active consideration by an independent Aboriginal and Torres Strait Islander research ethics committee in Australia whose direction we welcome for next steps regarding guidelines specifically for future CRTs in such settings. Aboriginal and Torres Strait Islander research occurs in the context of a continuing 'settler state' in which First Nations peoples have been and continue to be systematically marginalized and disempowered. There are unique ethical issues inherent in experimental Aboriginal and Torres Strait Islander research particularly when studies are led by or disproportionately advantage non-Indigenous researchers: this continues disempowerment and colonization (Pantazatos 2017; Bond et al 2021; Manathunga et al 2021). Hence, there may be interest in the citations, impact and implications for policy and practice of the findings of each of these CRTs as a means of gaining insight into epistemic justice and research translation.

REFERENCES

AHMRC. (2020) AH&MRC Ethical Guidelines: Key Principles. Sydney: AHMRC. Accessed 2 January 2021 at https://www.ahmrc.org.au/publication/ahmrc-guidelines-for-research-into-aboriginal-health-2020/

AIATSIS. (2020). AIATSIS Code of Ethics for Aboriginal and Torres Strait Islander Research. Canberra: AIATSIS.

AIATSIS. (2012). Guidelines for Ethical Research in Australian Indigenous Studies (GERAIS) (revised second edition). Canberra: AIATSIS. Available at http://aiatsis.gov.au/sites/default/files/docs/research-and-guides/ethics/GERAIS.pdf

Al-Jaishi A, Carroll K, Goldstein C et al. (2020). Reporting of key methodological and ethical aspects of cluster trials in hemodialysis require improvement: a systematic review. Trials 21: 752.

Anderson I, Crengle S, Kamaka M, Chen T, Palafax N and Jackson-Pulver L. (2006). Indigenous health in Australia, New Zealand and the Pacific. Lancet 367: 1775- 85.

Arabena K. (2006). The universal citizen: an Indigenous citizenship framework for the twenty-first century. Australian Aboriginal Studies 2: 36-46.

Arrow P, McPhee R, Atkinson D et al. (2018). Minimally Invasive Dentistry Based on Atraumatic Restorative Treatment to Manage Early Childhood Caries in Rural and Remote Aboriginal Communities: Protocol for a Randomized Controlled Trial. JMIR Res Protoc 7(7): e10322.

Arrow P, Piggott S, Carter S, McPhee R, Atkinson D, Mackean T, Kularatna S, Tonmukayakul U, Brennan D, Nanda S, Palmer D and Jamieson L. (2020). Atraumatic Restorative Treatments in Australian Aboriginal Communities: A Cluster-randomized Trial. JDR Clinical & Translational Research. First published online 3 October 2020; then hard copy 2021; 6(4): 430-439.

Bainbridge R, Tsey K, Calman J et al. (2015). No-one's discussing the elephant in the room: contemplating questions of research impact and benefit in Aboriginal and Torres Strait Islander Australian health research. BMC Public Health 15: 696.

Bar-Zeev Y, Bonevski B, Bovill M, ICAN QUIT in Pregnancy Pilot Group, et al. (2017). The Indigenous Counselling and Nicotine (ICAN) QUIT in Pregnancy Pilot Study protocol: a feasibility step-wedge cluster randomised trial to improve health providers' management of smoking during pregnancy. BMJ Open 7: e016095.

Benveniste T and King L. (2018). Researching together: Reflections on ethical research in remote Aboriginal communities. Learning Communities special issue 23: 52-63.

Bond C, Singh D, and Tyson S. (2021). Black bodies and Bioethics: Debunking mythologies of benevolence and beneficence in contemporary Indigenous health research in colonial Australia. Bioethical Inquiry 18: 83–92

Borg K, Sutton K, Beasley M et al. (2018). Communication-based interventions for increasing influenza vaccination rates among Aboriginal children: A randomised controlled trial. Vaccine 36: 6790-6795.

Bradley K, Smith R, Hughson J et al. (2020). Let's CHAT (community health approaches to) dementia in Aboriginal and Torres Strait Islander communities: protocol for a stepped wedge cluster randomised controlled trial. BMC Health Serv Res 20: 208. doi. org/10.1186/s12913-020-4985-1.

Brimblecombe J, Ferguson M, Chatfield M et al. (2017). Effect of a price discount and consumer education strategy on food and beverage purchases in remote Indigenous Australia: a stepped-wedge randomised controlled trial. The Lancet Public Health 2(2): e82-e95. https://doi.org/10.1016/S2468-2667(16)30043-3.

Brimblecombe J, Ferguson M, Liberato S et al. (2013). Stores Healthy Options Project in Remote Indigenous Communities (SHOP@RIC): a protocol of a randomised trial promoting healthy food and beverage purchases through price discounts and in-store nutrition education. BMC Public Health 13: 744. https://doi.org/10.1186/1471-2458-13-744.

Brimblecombe J, Ferguson M, McMahon E et al. (2019). Reducing Retail Merchandising of Discretionary Food and Beverages in Remote Indigenous Community Stores: Protocol for a Randomized Controlled Trial. JMIR Res Protoc 8(3): e12646.

Brimblecombe J, McMahon E, Ferguson M et al. (2020). Effect of restricted retail merchandising of discretionary food and beverages on population diet: a pragmatic randomised controlled trial. The Lancet Planetary Health 4(10): e463-e473.

Brown CA and Lilford RJ. (2006).The stepped wedge trial design: a systematic review. BMC Med Res Methodol 6:54.

Cameron M, Andersson N, McDowell I and Ledogar RJ. (2010).Culturally Safe Epidemiology: Oxymoron or Scientific Imperative. Pimatisiwin 8(2): 89-116.

Campbell M. (2019). Cluster randomised trials. MJA 210(4): 154-156.

Campbell MJ, Hemming K and Taljaard M. (2019). The Stepped Wedge Cluster Randomised Trial: what it is and when it should be used. Med J Aust 210(6): 253-254.

Campbell M, Piaggio G, Elbourne D and Altman D for the CONSORT Group. (2012). Consort 2010 statement: extension to cluster randomised trials. BMJ 345: e5661.

Conrad E and Edwards SJ. (2011). Inequalities and fairness in cluster trials. Research Ethics 7(2):58-65.

Council for International Organizations of Medical Sciences (CIOMS). (2016). International Ethical Guidelines for Health-related Research Involving Humans (fourth edition). Geneva. CIOMS. https://cioms.ch/wp-content/uploads/2017/01/WEB-CIOMS-EthicalGuidelines.pdf

Crooks K, Clark K, Allan N, Taylor P, Miller A and Campbell S. (2019). Letter to the Editor in response to the article by Borg et al. Vaccine. 37(26): 3381.

de Hoop E, van der Tweel I, van der Graaf R, Moons KGM et al. (2015). The need to balance merits and limitations from different disciplines when considering the stepped wedge cluster randomized trial design. BMC Medical Research Methodology 15(1):93.

Duke DLM, Prictor M, Ekinci E, Hachem M and Burchill LJ. (2021). Culturally Adaptive Governance: Building a new framework for equity in Aboriginal and Torres Strait Islander health research: Theoretical basis, ethics, attributes and evaluation. International Journal of Environmental Research and Public Health 18(15):7943.

Dwyer A. (2012). Pukarrikarta-jangka muwarr – stories about caring for Karajarri country. Australian Community Psychologist 24(1): 11-23.

Elvidge E, Paradies Y, Aldrich R and Holder C. (2020). Cultural safety in hospitals: validating an empirical measurement tool to capture the Aboriginal patient experience. Australian Health Review 44: 205-211.

Fitzpatrick E, Macdonald G, Martiniuk A et al. (2019). The picture talk project: Aboriginal community input on consent for research. BMC Med Ethics 20: 12.

Fitzpatrick E, Martiniuk Ah, D'Antoine H et al. (2016). Seeking consent for research with indigenous communities: a systematic review. BMC Med Ethics 17: 65 https://doi.org/10.1186/s12910-016-0139-8.

Fitzpatrick E, Macdonald G, Martiniuk A et al. (2017). The Picture Talk Project: Starting a Conversation with Community Leaders on Research with Remote Aboriginal Communities of Australia. BMC Med Ethics 18: 34. https://doi.org/10.1186/s12910-017-0191-z.

Goldstein CE, Brehaut J and Weijer C. (2017). Does consent form follow function? American Journal of Bioethics 17(12): 29-31.

Gould G, Bovill M, Pollock L et al. (2019). Feasibility and acceptability of Indigenous Counselling and Nicotine (ICAN) QUIT in Pregnancy multicomponent implementation intervention and study design for Australian Indigenous pregnant women: A pilot cluster randomised step-wedge trial. Addictive Behaviors 90: 176-190.

Grayling MJ, Wason JM and Mander AP. (2017). Stepped wedge cluster randomized controlled trial designs: a review of reporting quality and design features. Trials 18: 33.

Guy R, Natoli L, Ward J et al. (2013). A randomised trial of point-of-care tests for chlamydia and gonorrhoea infections in remote Aboriginal communities: Test, Treat ANd GO- the "TTANGO" trial protocol. BMC Infect Dis 13: 485. https://doi.org/10.1186/1471-2334-13-48.

Guy R, Ward J, Causer L et al. (2018). Molecular point-of-care testing for chlamydia and gonorrhoea in Indigenous Australians attending remote primary health services (TTANGO): a cluster-randomised, controlled, crossover trial. The Lancet Infectious Diseases 18(10): 1117-1126.

Hargreaves J, Copas A, Beard E et al. (2015). Five questions to consider before conducting a stepped wedge trial. Trials 16: 350.

Harrison K, Lee K, Dobbins T et al. (2019). Supporting Aboriginal Community Controlled Health Services to deliver alcohol care: protocol for a cluster randomised controlled trial. BMJ Open 9: e030909. doi: 10.1136/bmjopen-2019-030909.

Hemming K and Taljaard M. (2020). Reflection on modern methods: when is a stepped wedge cluster randomized trial a good design choice? International Journal of Epidemiology 49(3): 1043-1052. doi:10.1093/ije/dyaa077.

Hemming K, Taljaard M, Forbes G, et al. (2018). Ethical implications of excessive cluster sizes in cluster randomised trials BMJ Quality & Safety 27: 664-670.

Hemming K, Taljaard M, Marshall T, Goldstein CE and Weijer C. (2019). Stepped-wedge trials should be classified as research for the purpose of ethical review. Clinical Trials 16(6): 580-588.

Hey SP, Weijer C, Taljaard M and Kesselheim A. (2018). Research ethics for emerging trial designs: does equipoise need to adapt? BMJ 360: k226.

Hunt J, Smith D, Garling S and Sanders W (eds). (2008). Contested governance: culture, power and institutions in Indigenous Australia. Canberra: Australian National University.

Jamieson L, Paradies Y, Eades S et al. (2012). Ten principles relevant to health research among Indigenous Australian populations. Med J Aust 197: 16-18.

Jennings W, Bond C and Hill PS. (2018). The power of talk and power in talk: a systematic review of Indigenous narratives of culturally safe healthcare communication. Aust J Prim Health 24: 109–15.

Kiran A and Knights J. (2010). Traditional Indigenous Games promoting physical activity and cultural connectedness in primary schools? Cluster Randomised Control Trial. Health Promotion Journal of Australia 21: 149-151.

Kotz D, Spigt M, Arts I et al. (2012a). Use of the stepped wedge design cannot be recommended: a critical appraisal and comparison with the classic cluster randomized controlled trial design. J Clin Epidemiol 65: 1249-1252.

Kotz D, Spigt M, Arts I et al. (2012b). Researchers should convince policy makers to perform a classic cluster randomized controlled trial instead of a stepped wedge design when an intervention is rolled out. J Clin Epidemiol 65: 1255-6.

Laycock A, Walker D, Harrison N, Brands J. (2011). Researching Aboriginal Health: A Practical Guide for Researchers. Melbourne: The Lowitja Institute: Australia's National Institute for Aboriginal and Torres Strait Islander Research.

Liaw S, Wade, V, Furler J et al. (2019). Cultural respect in general practice: a cluster randomised controlled trial. Med J Aust 210: 263-268.

Lin Y, Jochym N and Merz J. (2021). Refusal rates and waivers of informed consent in pragmatic and comparative effectiveness RCTs: A systematic review. Contemporary Clinical Trials 104. https://doi.org/10.1016/j.cct.2021.106361.

Lincoln G, Austin B, Dobbs R et al with the Balanggarra, Bardi Jawi, Dambimangari, Karajarri, Nyul Nyul, Wunambal Gaambera and Yawuru Traditional Owners prepared by the Kimberley Land Council for the Kimberley Indigenous Saltwater Science Project (KISSP). (2017). Collaborative Science on Kimberley Saltwater Country - A Guide for Researchers V17.03 Broome: Kimberley Land Council.

London A, Taljaard M and Weijer C. (2020). Loopholes in the research ethics system? informed consent waivers in cluster randomised trials with individual-level intervention. Ethics and Human Research 42: 21-28.

Lovett R, Lee V, Kukutai T et al. (2019). Good data practices for indigenous data sovereignty and governance. In Daly A, Devitt S, Mann M (Eds.) Good Data. Amsterdam: Institute of Network Cultures, pp. 26–36.

Mackean T, Fisher M, Friel S and Baum F. (2019). A framework to assess cultural safety in Australian public policy. Health Promotion International 35(2): 340-351. doi:10.1093/ heapro/daz011.

Manathunga C, Qi J, Bunda T and Singh M. (2021). Chapter 6: Working towards future epistemic justice: incorporating transcultural and Indigenous knowledge systems in doctoral education. In Lee A and Bongaardt R. (Eds) The Future of Doctoral Research. London: Routledge.

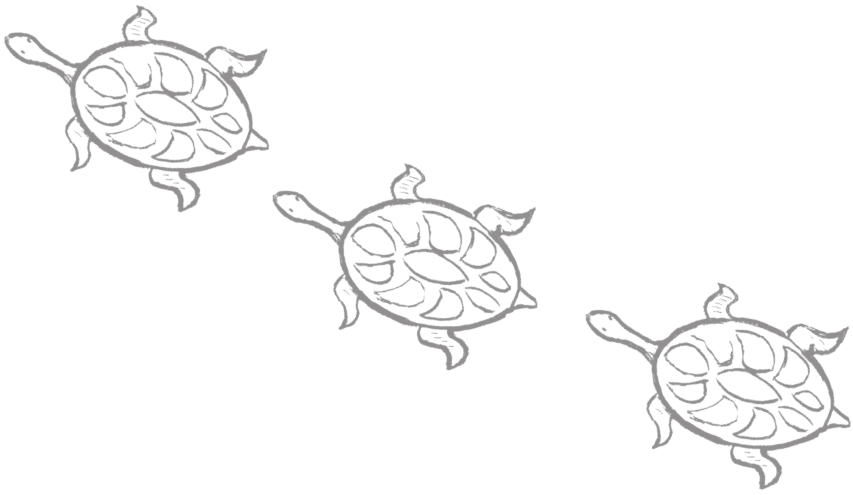
Martin K. (2008). Please knock before you enter: Aboriginal regulation of outsiders and the implications for researchers. Teneriffe: Post Pressed. ISBN 9781921214370

McAullay D, McAuley K, Marriott R et al. (2016). Improving access to primary care for Aboriginal babies in Western Australia: study protocol for a randomized controlled trial. Trials 17: 82. https://doi.org/10.1186/s13063-016-1206-7.

McDermott R, Schmidt B, Preece C et al. (2015). Community health workers improve diabetes care in remote Australian Indigenous communities: results of a pragmatic cluster randomized controlled trial. BMC Health Serv Res 15: 68.

McPhail-Bell K, Fredericks B and Brough M. (2013). Beyond the accolades: a postcolonial critique of the foundations of the Ottawa Charter. Global Health Promotion 20(2): 22-29.

McPhail-Bell K, Nelson A, Lacey I, Fredericks B and Bond C. (2018). Using an Indigenist framework for decolonizing health promotion research. In Liamputtong P (ed). Handbook of research methods in health social sciences. Singapore: Springer.



Mdege ND, Man MS, Taylor Nee Brown CA and Torgerson DJ. (2011). Systematic review of stepped wedge cluster randomized trials shows that design is particularly used to evaluate interventions during routine implementation. J Clin Epidemiol 64:936-48.

Mullane MJ, Barnett TC, Cannon JW et al. (2019). SToP (See, Treat, Prevent) skin sores and scabies trial: study protocol for a cluster randomised, stepped-wedge trial for skin disease control in remote Western Australia. BMJ Open 9: e030635. doi:10.1136/bmjopen-2019-030635.

Munari SC, Wilson AN, Blow NJ, Homer CSE and Ward JE. (2021). Rethinking the use of 'vulnerable'. Aust N Z J Public Health 45(3): 197-199.

NAILSMA. (2007). Guidelines and protocols for the conduct of research. Darwin: NAILSMA. http://www.nailsma.org.au/nailsma/downloads/NAILSMA_Guidelines_Jun07.pdf

NHMRC. (2018). Ethical conduct in research with Aboriginal and Torres Strait Islander Peoples and communities: Guidelines for researchers and stakeholders. Canberra: Commonwealth of Australia.

NHMRC. (2021). List of all registered HRECs. Available at https://www.nhmrc.gov.au/research-policy/ethics/human-research-ethics-committees

Nicholls S, Zwarenstein M, Hey S, Giraudeau B, Campbell M and Taljaard M. (2020). The importance of decision intent within descriptions of pragmatic trials. Journal of Clinical Epidemiology 125: 30-37 https://doi.org/10.1016/j.jclinepi.2020.04.030.

Ninomiya M and Pollock N. (2017). Reconciling community-based Indigenous research and academic practices: knowing principles is not always enough. Soc Sci Med 172: 28-36.

Pantazatos A. (2017). Chapter 35: Epistemic injustice and cultural heritage. In Kidd I, Medina J and Pohlhaus G. (Eds). The Routledge Handbook of Epistemic Injustice. London: Routledge.

Paradies Y.(2016). Colonisation, racism and indigenous health. Journal of Population Research 33 : 83-96. doi:10.1007/s12546-016-9159-y

Pearson N. (2012). The Aboriginal 'community' amounts to a dangerous myth for some and an alibi for others. The Australian: 8 December 2012, p. 20.

Peiris D, Usherwood T, Panaretto K et al. (2012). The treatment of cardiovascular risk in primary care using electronic decision support (TORPEDO) study: intervention development and protocol for a cluster randomised, controlled trial of an electronic decision support and quality improvement intervention in Australian primary healthcare. BMJ Open 2: e002177.

Peiris D, Usherwood Y, Panaretto K et al. (2015). Effect of a Computer-Guided, Quality Improvement Program for Cardiovascular Disease Risk Management in Primary Health Care: The Treatment of Cardiovascular Risk Using Electronic Decision Support Cluster-Randomized Trial. Circulation: Cardiovascular Quality and Outcomes 8: 87–95.

Prost A, Binik A, Abubakar I et al. (2015). Logistic, ethical, and political dimensions of stepped wedge trials: critical review and case studies. Trials 16: 351.

Ralph A, de Dassel J, Kirby A et al. (2018). Improving delivery of secondary prophylaxis for rheumatic heart disease in a high-burden setting: Outcome of a stepped-wedge, Community, randomized trial. Journal of the American Heart Association 7(14). https://www.ahajournals.org/toc/jaha/7/14

Ralph A, Read C, Johnston V et al. (2016). Improving delivery of secondary prophylaxis for rheumatic heart disease in remote Indigenous communities: study protocol for a stepped-wedge randomised trial. Trials 17: 51.

Rigney L. (1999). Internationalisation of an Indigenous Anticolonial cultural critique of research methodologies. Wicazo SA review Fall: 109-121

Rix E, Wilson S, Sheehan N and Tujague N. (2018). Indigenist and decolonizing research methodology. In Liamputtong P (ed). Handbook of research methods in health social sciences. Singapore: Springer.

Schmidt B, Wenitong M, Esterman A et al. (2012). Getting better at chronic care in remote communities: study protocol for a pragmatic cluster randomised controlled of community based management. BMC Public Health 12, 1017. https://doi.org/10.1186/1471-2458-12-1017.

Schnarch B. (2004). Ownership, control, access, and possession or self-determination applied to research: A critical analysis of contemporary first nation's research and some options for first nations communities. Journal of Aboriginal Health 1(1): 80-95.

Segal L, Nguyen H, Schmidt B, Wenitong M and McDermott R. (2016). Economic evaluation of Indigenous health worker management of poorly controlled type 2 diabetes in north Queensland. Med J Aust 204: 196-196.

Sherwood J and Anthony T. (2020). Chapter 2: Ethical conduct in Indigenous research: It's just good manners. In George L, Tauri J, Macdonald L (eds). Indigenous research ethics: claiming research sovereignty beyond deficit and the colonial legacy. Advances in Research Ethics 6: 19-40.

Siebenhofer A, Erckenbrecht S, Pregartner G et al. (2016). How often are interventions in cluster randomised controlled trials of complex interventions in general practices effective and reasons for potential shortcomings? Protocol and results of a feasibility project for a systematic review. BMJ Open 6: e009414.

Siebenhofer A, Paulitsch M, Pregartner G et al. (2018). Cluster-randomized controlled trials evaluating complex interventions in general practices are mostly ineffective: a systematic review. JCE 94: 85-96.

Slade G, Bailie RS, Roberts-Thomson K et al. (2011). Effect of health promotion and fluoride varnish on dental caries among Australian Aboriginal children: results from a community-randomized controlled trial. Community Dent Oral Epidemiol 39(1):29-43.

Smith LT. (2014). Chapter 2: Social justice, transformation and Indigenous methodologies. In Rinehart RE, Barbour K and Pope C (eds). Ethnographic worldviews: Transformations and social justice. Netherlands: Springer, pp. 15-20.

Stewart P, Anderson I, Dunbar T, Shibasaki S, Pyett P and Devitt J. (2006). Aboriginal and Torres Strait Islander participation in the ethical review of health research. Aborig Isl Health Worker J 30(6): 22–5.

Stewart P, Shibasaki S, Anderson I et al. (2006). Aboriginal and Torres Strait Islander participation in ethical review of health research. 3 Australian and New Zealand Journal of Public Health 30 (3): 291-2.

Studdert D, Vu T et al. (2010). Ethics review of multisite studies: the difficult case of community-based Indigenous health research. MJA 192(5): 275-280.

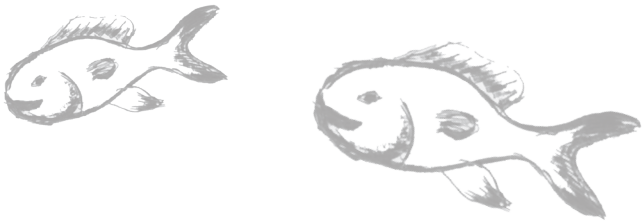
Sullivan C. (2020). Who holds the key? Negotiating gatekeepers, community politics, and the "right" to research in Indigenous spaces. Geographical Research 58: 344–354.

Taafe L. (2008). Research in Aboriginal Contexts: Kimberley Voices. Unpublished Honours dissertation. School of Arts and Sciences; University of Notre Dame Australia.

Taljaard M, Goldstein CE, Giraudeau B et al. (2020). Cluster over individual randomization: are study design choices appropriately justified? Review of a random sample of trials. Clinical Trials. 17(3): 253-263.
Taljaard M and Grimshaw JM. (2014). Concept, characteristics and implications of cluster randomization. Clin Invest 4(1): 1–4.

Taljaard M, Hemming K, Shah L et al. (2017). Inadequacy of ethical conduct and reporting of stepped wedge cluster randomized trials: results of a systematic review. Clin Trials 14(4): 333-341.

Taljaard M, McGowan J, Grimshaw JM et al. (2010). Electronic search strategies to identify reports of cluster randomized trials in MEDLINE: Low precision will improve with adherence to reporting standards. BMC Med Res Methodol 10: 15.



Taljaard M, McRae A, Weijer C et al. (2011). Inadequate reporting of research ethics review and informed consent in cluster randomised trials: review of random sample of published trials. BMJ 342: d2496.

Thomas D and Anderson I. (2006). Getting the most from Indigenous health research. Med J Aust 184: 500-501.

Wagner B, Fitzpatrick JP, Mazzucchelli TG et al. (2017). Study protocol for a self-controlled cluster randomised trial of the Alert Program to improve self-regulation and executive function in Australian Aboriginal children with fetal alcohol spectrum disorder. BMJ Open 8: e021462. doi: 10.1136/bmjopen-2017-021462.

Wagner B, Latimer J, Adams E et al. (2020). School-based intervention to address self-regulation and executive functioning in children attending primary schools in remote Australian Aboriginal communities. PLoS ONE 15(6): e0234895.

Ward J, Guy R, Rumbold A et al. (2019). Strategies to improve control of sexually transmissible infections in remote Australian Aboriginal communities: a stepped-wedge, cluster-randomised trial. The Lancet Global Health 7(11): e1553-e1563.

Ward J, McGregor S, Guy R et al. (2013). STI in remote communities: improved and enhanced primary health care (STRIVE) study protocol: a cluster randomised controlled trial comparing 'usual practice' STI care to enhanced care in remote primary health care services in Australia. BMC Infect Dis 13: 425. https://doi.org/10.1186/1471-2334-13-425.

Ward JE, Thorburn K, Girgis S, Oliver S, Weijer C and Taljaard M. (2018). Ethical practices of researchers conducting cluster randomised trials (CRTs) in Australian aboriginal settings. PROSPERO 2018 CRD42018106463 Accessed 1 January 2021.

Weijer C. (1999)Protecting communities in research: Philosophical and pragmatic challenges. Cambridge Quarterly of Healthcare Ethics 8(4): 501-513.

Weijer C and Emanuel E. (2000). Protecting Communities in Biomedical Research. Science 289(5482): 1142-1144. doi: 10.1126/science.289.5482.1142.

Weijer C, Grimshaw JM, Eccles MP et al. (2012). The Ottawa Statement on the ethical design and conduct of CRTs. PloS Med 9(11): 1-9.

Weijer C, Grimshaw JM, Eccles MP et al. (2012). The Ottawa Statement on the ethical design and conduct of CRTs (S1: Glossary of terms). PloS Med Available at https://doi.org/10.1371/journal.pmed.1001346.s001.

Weijer C, Grimshaw JM, Eccles MP et al. (2012). The Ottawa Statement on the ethical design and conduct of CRTs (S3 General ethical principles). PloS Med Available at https://doi.org/10.1371/journal.pmed.1001346.s003.

Weijer C, Grimshaw JM, Taljaard M et al. (2011). Ethical issues posed by cluster randomized trials in health research. Trials 12: 100.

Weijer C and Miller PB. (2004). When are research risks reasonable in relation to anticipated benefits? Nat Med 10(6): 570-3.

Wyatt K. (1991). The rights of Aboriginal communities: The obligations of health researchers. Aboriginal and Torres Strait Islander Worker Journal 15(2): 7-8.

Xiiem J, Lee-Morgan J and de Santolo J. (2019). Introduction. In Xiiem J, Lee-Morgan J and de Santolo J. (2019). Decolonizing research: Indigenous Storywork as methodology. London: Zed Books.

Yu P. (1994). Part 4: Kimberley: the need for self-government and a call for radical change. In Fletcher C (Ed). Aboriginal self-determination in Australia. Canberra: Aboriginal Studies Press, pp 115-124.

Authors' Notes

Our review team included two internationally recognized experts in ethical and methodological aspects of CRTs (CW and MT) and four Australian-based non-Indigenous authors with technical disciplinary backgrounds including Aboriginal political science, epidemiology, behavioural science and public health (JEW, SG, KT, SO). Three of us (JEW, CW, MT) have been chief investigators in CRTs although none in Aboriginal and Torres Strait Islander settings.

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