Australian Clinical Trials Alliance

Activities critical to success and growth of Clinical Trials Networks: Sector consultation

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GLOSSARY OF TERMS AND ACRONYMS

ACTA	Australian Clinical Trials Alliance
Clinical Trial Coordinating Centre (CTCC)	Dedicated centres for conducting multi-site clinical trials.
Coordinating CTN	A CTN model based on self-reporting that the CTN is directly involved in clinical trial coordination and project management of CTN-endorsed trials as well as undertaking many of the activities that define a facilitating network.
Clinical Trials Network (CTN)	A group of researchers who are active in a defined area of clinical trials research, with agreed and documented processes for the governance of collaborative development, conduct and publication of multi-site investigator-initiated clinical trials, have published at least one multi-site investigator-initiated clinical trial in a peer-reviewed journal, and demonstrate an ongoing commitment to work collaboratively and conduct further trials to improve the evidence base for high-quality health care.[1]
Clinical Quality Registry (CQR)	An organisation that systematically monitors the quality (appropriateness and effectiveness) of health care within specific clinical domains by routinely collecting, analysing and reporting health-related information. The information is used to identify outcome benchmarks, significant outcome variance, and inform improvements in healthcare quality.
Executive Officer	CTN staff member in charge of operational processes. May also be known as Manager, Operations Manager, Chief Executive Officer, Network Manager.
Facilitating CTN	A CTN model based on self-reporting where the CTN does not maintain direct project management or coordination of CTN-endorsed clinical trials and acts to support trial activity by facilitation only.
Governance committee	The committee that governs the CTN. It may also be known as the Executive Committee or Steering Committee. In some CTNs, a Board may be appointed that fulfils this role, with advisory committees comprising people with various expertise to advise the Board.
Investigator-initiated clinical trial	Trials that are conceived and conducted by independent clinicians and academic researchers. These trials serve the broad purpose of generating clinical evidence to improve health care rather than commercial imperative. Investigator-initiated clinical trials may be funded from public sources or industry sources but if funded by industry the investigators retain primary control of trial design, conduct, and reporting and own the data from the trial.
Learning healthcare system	A healthcare system characterised by the continuous generation and implementation of knowledge from clinical research 'embedded' within healthcare delivery.
Memorandum of understanding (MOU)	A non-binding agreement between two or more parties outlining the terms and details of an understanding, including each party's requirements and responsibilities.
Newly established/establishing CTN	A CTN that has been in existence for five years or less.
Network site	A healthcare facility where the clinical trial activity involving participants recruited to network-led clinical trials takes place.
Standard Operating Procedures (SOPs)	Written procedure described for repetitive use as a practice, in accordance with agreed specifications aimed at reaching a desired outcome.
Terms of Reference (ToR)	A document that outlines the purpose, structure and operating rules of a committee.
Trial coordinator	An individual researcher with primary responsibility for daily coordination of the trial. They may be responsible centrally for the entire trial or based at the network site and responsible for local coordination.

EXECUTIVE SUMMARY

The delivery of high-quality health care relies on the availability of high-quality evidence to inform practice. An emerging concept is the Learning Healthcare System, which provides a cost-effective system embedded within healthcare delivery to identify priority research questions, undertake high-quality research, understand the knowledge gained from clinical research, to implement findings where appropriate, and to measure the resulting change in health practice. A sustainable, cost-effective and efficient model for clinical research is an integral component of the Learning Healthcare System.

In Australia and New Zealand, clinical trial networks (CTN) design, conduct and publish investigator-initiated clinical trials, generating evidence that contributes to a high-quality healthcare system. Utilising qualitative descriptive activities in a sector-wide survey and focus groups, ACTA consulted the CTN sector to identify the structures, operational processes and activities that are critical to effective and efficient network operations, and to identify any unmet needs of CTNs.

A matrix of operational activities and structural components that build on earlier ACTA work[1] was created, and then extended by sector review. Three focus groups were conducted, including sixteen participants representing twelve CTNs. Each focus group represented one of three CTN types: facilitating CTNs, coordinating CTNs and newly established/establishing CTNs. The CTNs involved in these focus groups were from a wide range of disciplines and at varying levels of maturity, clinical trial program breadth and success. Focus group participants were asked questions to encourage discussion about critical factors for successful and sustainable operations; to describe any unmet needs for effective and efficient CTN operations, and to identify any tools and resources critical to successful CTN operations.

Focus groups discussions were recorded, transcribed and analyses undertaken. Three key themes that underpin network operational efficiency and effectiveness were identified:

- an engaged membership
- an established infrastructure, and
- sustainability.

Critical success factors that supported each of these key themes were described, although many discussion points encompassed more than one theme. Tools and resources that support these key themes were identified.

'An engaged membership' was the predominant theme, and is commonly supported in CTNs by network champions and key leaders promoting a culture of research, passion and goodwill; uniting the membership with a clear mission and vision; representative governance committees with accountable and transparent processes; an annual meeting of the membership and regular small group meetings; and communications across the membership.

An Executive Officer was critical to 'an established infrastructure', although this role is integral to all three themes and was identified as an unmet need by some CTNs. Other critical success factors identified as part of 'a defined CTN structure' included prioritisation of research, peer-review, trial endorsement and authorship guidelines, clinical trial development support and, for coordinating CTNs, trial coordination services. A challenging area of CTN structural operations was network site activity, including expansion beyond a core group of high-performing sites, and establishing reasons why there is variation in clinical trial activity between sites.

'Sustainability' encompassed the need for multidisciplinary representation and consumer involvement, succession planning for CTN champions and key leaders, and responsiveness to a changing environment. Building the CTN reputation and brand, and maintaining that brand, was facilitated by peer-review and trial endorsement processes, and may be enhanced by advocacy and raising community awareness, and sometimes by external collaborations. Ensuring timely publication of trials is critical to CTN brand, with networks taking a variety of approaches to overcome this acknowledged challenge.

Funding for infrastructure and operations was critical to CTN sustainability, however few CTNs have secure ongoing funding. Maintaining an effective clinical trial workforce at network sites arose as a deficiency, hampering effective clinical trial participation. Possible solutions discussed included sharing site trial coordinators between disciplines, defining a career pathway for trial coordinators that attracted and retained quality staff, and conducting more pragmatic or embedded trials that used the existing healthcare service and staff in a more efficient manner. A role for healthcare facilities to assimilate and support research into routine healthcare arose as a discussion point in the focus groups, highlighting the importance of the Learning Healthcare System.

The research conducted identified the activities and attributes of a CTN that allows the network to operate successfully. These are:

- a shared vision and motivation
- strong leaders, governance and succession planning
- transparent processes
- effective communication
- an Executive Officer
- sustainable funding
- diverse representation and consumer input
- prioritisation of research
- a strong trial pipeline of trials
- a reputable and recognised CTN brand
- an effective group of network sites with skilled site workforce
- embedded trials
- innovation and adaptation.

Future work could systematically evaluate the strength of networks across the sector, both at an operational and membership level, assessing these critical success factors, and making recommendations for individual CTNs that will improve the effectiveness and efficiency of their own operations.

INTRODUCTION

The delivery of high-quality health care relies on the availability of high-quality evidence to inform best practice. An emerging concept is the Learning Healthcare System, which provides a cost-effective system embedded within healthcare delivery to identify priority research questions, undertake high-quality research, understand the knowledge gained from clinical research, to implement findings where appropriate, and to measure the resulting change in health practice (Figure 1).

Clinical trials that generate the evidence to inform best practice are largely divided into two groups: (i) commercial clinical trials, conducted by organisations who own or have a financial interest in the intellectual property related to the intervention being tested; and (ii) investigator-initiated clinical trials, that are conceived, conducted and published by clinicians, healthcare providers and academic researchers in order to generate evidence to advance health care where insufficient evidence exists. A sustainable, cost-effective and efficient model to conduct clinical trials is an integral component of the Learning Healthcare System (Figure 1).

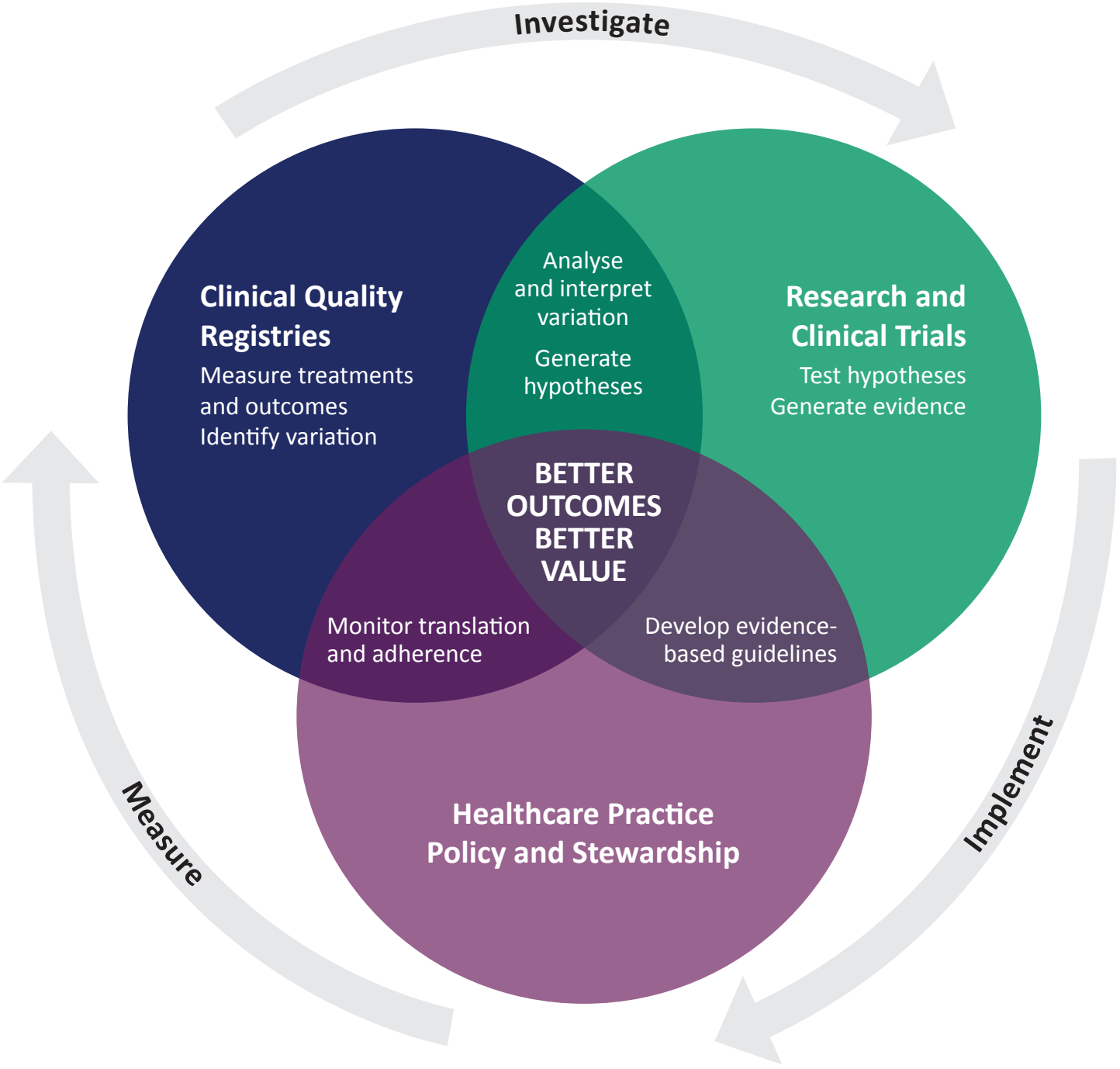


Figure 1: A Learning Healthcare System

CLINICAL TRIALS NETWORKS

In Australia, and throughout the world, clinical trials networks (CTNs) have been formed as a means of bringing together communities of geographically dispersed and multidisciplinary clinical researchers that are active in defined areas of clinical trials research. Some CTNs may use the network structure to assist the conduct of commercial clinical trials, but CTNs primarily exist to design, conduct and publish investigator-initiated clinical trials proposed and supported by the CTN membership.

CTNs are typically clinician-led and maintained by a collective objective among the membership to conduct high-quality, multi-site clinical trials. Common to all CTNs is the involvement of multiple healthcare facilities and practising clinicians to enable the conduct of clinical trials with sufficient sample sizes to answer clinically relevant questions, while ensuring close integration with the healthcare system. CTNs provide the capacity for peer and consumer review in the development and design of clinical trial hypotheses, ensuring that the CTN generates high-quality, relevant and feasible clinical trial protocols. With its size and geographical reach, both nationally and internationally, a CTN is capable of providing a diverse and sizeable recruitment pool of clinical trial participants, which enhances the timely completion and generalisability of results (Box diagram 1).

Clinical trial networks have:

- Broad and diverse membership encompassing trialists and healthcare providers who facilitate trial recruitment
- Peer and consumer review and endorsement process to develop high quality patient and clinician-relevant clinical trial proposals
- Successful track record of practice-changing trials
- Established central and site infrastructure and skilled workforce
- Capacity for enhanced translation and implementation of clinical trial findings
- Infrastructure to support multiple clinical trials
- Wide variety of stakeholders including international partnerships

Box diagram 1

The majority of CTNs undertake a process of trial selection, where protocols are reviewed, and if they meet criteria are supported and endorsed by the membership, earning the right to use the CTN name when applying for funding and publishing. While the option to propose a trial for endorsement is open to the entire membership, there is often a core group of trialists who design and lead clinical trials, with the remainder of the membership contributing by recruiting participants to the trials in the CTN portfolio. The effectiveness of the CTN relies on the quid pro quo premise that members will recruit participants to trials conducted by other members.

The continuous initiation of pilot studies and clinical trials from the CTN membership creates a pipeline of research, which aims to ensure the optimisation and sustainability of an established infrastructure and workforce that conducts the clinical trials, both at sites and in central administration. The stringent peer-review processes and commitment to publication of trial outcomes contributes high-quality evidence to the advancement of healthcare practices. Involvement of an extensive network of healthcare providers in the clinical trial should also facilitate the seamless and widespread integration of consequent practice change, where such implementation is appropriate.

Together with the endorsement, conduct, completion and publication of high-quality clinical trials, is the building of the CTN brand, which includes a reputation for completing high-quality, clinician- and patient-relevant clinical trials on time and within budget. This hallmark of quality adds to the competitiveness of clinical trial funding submissions, enhances merit in publication and presentation of clinical trial results, and can attract further collaboration in clinical trials from international CTNs. Early career researchers benefit from the track record and brand of the CTN in competitive funding applications, and access opportunities for learning and mentoring from experienced member trialists.

While many clinical trials, including some high-impact trials are conducted in Australasia with no CTN involvement, networks enable a more structured sharing of tools, infrastructure, knowledge, experience, and processes that avoid the need to “reinvent the wheel”. Together with the factors identified above, this creates a synergy so that a CTN is substantially more than the sum of its constituent parts, generating efficiencies and effectiveness that would not be possible without the network.

AUSTRALIAN CLINICAL TRIALS ALLIANCE

The Australian Clinical Trials Alliance (ACTA) – www.clinicaltrialsalliance.org.au – is a national body that supports and represents CTNs, Clinical Quality Registries (CQRs) and Clinical Trial Coordinating Centres (CTCC), and is driven by the vision of better health through best evidence. ACTA is uniquely positioned to strengthen the capacity, efficiency and effectiveness of CTNs in Australia through encouraging collaboration and sharing of practice, contributing knowledge, and possessing a common vision to that of many CTNs to advance healthcare and patient outcomes through the generation of high-quality evidence.

In 2015 ACTA profiled the activities and achievements of 34 CTNs in Australia, many of which are bi-national Australian and New Zealand networks.[1] The report highlighted the immense contribution these CTNs have made to the global evidence base and healthcare policy across numerous clinical disciplines both within Australasia and internationally. This report defined a CTN as a group led by clinician researchers that are active in a defined area of clinical trials research, that have agreed and documented governance processes for the collaborative development of clinical trial proposals, that conduct and publish multi-site investigator-initiated clinical trials, and that demonstrate an ongoing commitment to work collaboratively to conduct further trials and improve the evidence base for high-quality health care.

The same report identified two main models for CTNs in Australasia that can be approximated into (i) coordinating and (ii) facilitating CTNs, based on their activities and management of clinical trials. Table 1 summarises the responsibilities and activities associated with each of these models, noting that some CTNs will undertake some, but not all, trial coordinating activities. Both facilitating and coordinating CTNs undertake collaborative development, funding and execution of trials, but coordinating CTNs also undertake direct project management of trials. Regardless of the CTN model, the *Report on Activities and Achievements of Clinical Trials Networks in Australia 2004–2014*[1] concluded that CTNs are a vital component of a high-quality healthcare system that conducts clinical trials capable of changing global practice, and contribute markedly to a strong and competitive clinical trials enterprise in Australasia.

Table 1: Core activities and responsibilities of Clinical Trials Networks

Activities and responsibilities of 'facilitating networks'	Additional activities and responsibilities of 'coordinating networks'
Identification of important/priority clinical questions	Direct trial coordination and management
Collaborative study protocol development	Site management
Peer review and endorsement of trials	Data management
Convene scientific meetings	Enrolment of trial participants
Grant writing	Trial monitoring
Education/training/mentoring of researchers	Statistical analysis
Advocacy and industry/consumer liaison	Regulatory affairs
Clinical guideline development	Study sponsor Assistance with site selection and trial oversight

Note: Many CTNs are closely aligned with CCTC that undertake some of the activities described.

In 2017 ACTA and the Australian Commission on Safety and Quality in Health Care published a landmark report detailing a series of case studies used to evaluate the health and economic benefits of trials conducted by CTNs.[2] In this report, 'Economic Evaluation of Investigator-initiated Clinical Trials Conducted by Networks', investigator-initiated clinical trials that were conducted by established CTNs demonstrated high value for money for funding bodies and the broader health system, with a conservative estimate of the overall consolidated benefit-to-cost ratio for trials conducted by CTNs showing a return of AUD$5.80 for every $1 invested.

The current ACTA work program, 'Lifting Clinical Trials and Registries Capacity – Clinical Trials Networks Program', divided into eight Reference Groups, engages the sector for relevant expertise and best practice to strengthen the capacity, efficiency and effectiveness of CTNs. The work described in the present report has been produced by ACTA Reference Group A that is responsible for identifying best practices for the effective and efficient operations of CTNs. Through both the continued clinical trial experience within CTNs and the sharing of experiences between CTNs, operational processes, structures and activities that underpin the CTN success can be optimised to deliver maximum efficiency and effectiveness across the sector.

AIMS AND OBJECTIVES

The aim of this project was to engage with senior CTN members who have current or prior experience on CTN governance committees (hereafter referred to as Chairs) and Executive Officers, to identify key activities undertaken by CTNs that are critical to the success and sustainability of networks, and to identify any unmet needs. A secondary aim was to identify tools that support successful structural and operational processes within CTNs.

METHODS

RESEARCH TEAM AND GOVERNANCE

The project was undertaken with the oversight of ACTA Reference Group A, an expert advisory committee established to undertake projects that promote efficient and effective CTN operations, comprising representatives from CTNs, the ACTA Board of Directors, and the broader clinical trials sector. The primary researcher for this project is an ACTA Senior Project Officer who has previously been employed as a Program Manager in an ACTA member CTN. The researcher received training in qualitative research methods prior to developing focus group questions and facilitating focus group discussions. The Chair of ACTA Reference Group A, who attended all focus groups, is also the Chair of an ACTA member CTN. A Report Working Party was convened after the conduct of the focus groups and included representatives from two additional CTNs; both of whom were present at one focus group, and are members of ACTA Reference Group A. As outlined in the National Statement on Ethical Conduct in Human Research, organisations are permitted to identify and undertake ethical review of projects that are low or negligible risk. The project was reviewed by ACTA's internal ethical review committee and determined to be low risk.

SECTOR-WIDE CONSULTATION

Combining information from the *Report on Activities and Achievements of Clinical Trials Networks in Australia 2004–2014*[1] and expertise provided by ACTA Reference Group A, a matrix of the structural components and operational activities of CTNs was created. This was sent by email to the administrative contact and current Chairperson of 38 CTNs (including, but not restricted to, CTNs that were members of ACTA) requesting that they review the matrix and identify any additional structural components or operational activities of CTNs. CTN contacts were not required to respond if they did not have any additions. This matrix was used to establish the focus group question guide. A request to share CTN operational procedures, policies and other tools was included and a request to consider participation in the planned focus group activities.

FOCUS GROUPS

Due to the diversity in CTNs previously identified in the *Report on Activities and Achievements of Clinical Trials Networks in Australia 2004–2014*[1], three focus groups were planned to be specific to the needs of the participating CTNs:

- Coordinating CTNs
- Facilitating CTNs, and
- Newly established and establishing CTNs.

The short-listing of CTNs for invitation to participate in the focus groups was a sample of convenience that considered the disease or clinical area and geographical location to encourage in person attendance in Melbourne, Australia, although attendance by videoconference was permitted. A balance between cancer and non-cancer CTNs was specifically considered, as cancer CTNs have a dedicated funding source for some CTN infrastructure that is not available to CTNs in other clinical areas. Apart from newly established and establishing CTNs, all invited CTNs were full members of ACTA. Invitations were sent by email to Chairs and Executive Officers from four of the short-listed coordinating CTNs and four of the short-listed facilitating CTNs. When responses indicated that not all CTNs would be available to contribute, further invitations were issued to four coordinating CTNs and three facilitating CTNs. Chairs and Executive Officers of three establishing CTNs were invited by email to attend the newly established/establishing CTNs focus group.

Three focus groups were held during September and November 2018 in Melbourne, Australia, with videoconferencing facilities available. Focus groups were recorded using Zoom videoconferencing software (Zoom Video Communications, Inc.) and transcribed by intelligent verbatim using a professional transcription service. Consent for recording and use of deidentified verbatim quotes in the final report was sought and provided in writing by all participants prior to commencement. The focus groups were facilitated by the primary researcher, with the assistance of an additional Project Officer.

The focus group question guides consisted of semi-structured, open-ended questions, informed by the results of the sector-wide consultation, and developed by two researchers with the assistance of an external qualitative research expert. The proposed question guide for the coordinating and facilitating CTNs focus groups is presented in Table 2. A separate question guide was developed for the focus group involving representatives from newly established and establishing CTNs, as some of the questions were not relevant for recently established CTNs, and is presented in Table 3. Some further questions were added for this group as the discussion presented an opportunity for ACTA to assess the facilitatory role ACTA provides during CTN establishment. In practice, in all the focus groups, pre-defined questions were not asked if appropriate discussion had already been elicited from earlier questions. At the discretion of the facilitator, if an area was not adequately covered, further questions were asked *ad libitum*.

Table 2: Focus group questions for coordinating and facilitating Clinical Trials Networks

Questions
Identify one enabler and one barrier to running your CTN as efficiently and as effectively as you would like.
Identify and describe essential tools that will allow a network to operate effectively.
What makes your network successful?
Describe the factors that help shape the goals of your network.
If you had to apply blue-sky thinking, how would your network look if there were no limitations to growth?
Tell us about the governance structure of your network and what works well.
Talk about the 'culture' that your network strives to promote.
How does your network ensure different stakeholders feel engaged?
Can you describe which of these activities are essential to the effective running of your network?
How does the network decide which of these activities to undertake?
Describe some other operational activities that you undertake that could be made more efficient or effective.
Describe any opportunities for your network and others to share resources or services to facilitate effective operations.
Describe any key roles or processes that strive towards ensuring your network is sustainable now and for the future

Table 3: Focus group questions for establishing and newly established Clinical Trials Networks

Questions
Describe the activities/elements/plans that you feel will make your network successful and the work you have undertaken or are planning to undertake to achieve these.
What other activities and processes did you undertake to establish your network?
Can you comment on ACTA's facilitation of the CTN establishment? What could have been done better?
Describe your plans for sustainability.
Describe any challenges and how you overcame them.
Talk about the culture that your network strives to promote.
How does your network work to ensure different stakeholders feel engaged?
Describe any opportunities for your network and others to share resources or services to facilitate effective operations.

IDENTIFICATION OF CRITICAL TOOLS

During the focus groups with coordinating and facilitating CTNs any operational tools that were identified as being critical to success and growth were listed. After completion of all focus groups, participants and members of ACTA Refence Group A were supplied with this list of operational tools by email and asked to identify and rank their five most critical tools in order of importance to their current network operations.

ANALYSES

At completion of data collection, the focus group transcripts were analysed and relevant points collated under themes emerging from the discussion defined by the primary researcher. Themes were further refined, and appropriate discussion points reclassified where necessary. The results of the thematic analysis were reviewed by the Report Working Party to exclude bias that may arise from a sole individual undertaking the analysis. Discussion pertaining to activities specifically related to clinical trial coordination were deemed out of scope and not included in the thematic analysis.

RESULTS

SECTOR-WIDE CONSULTATION

Five of the 38 CTNs responded with additional items to both structural components and operational activities of CTNs. The original list and the additional items are presented in Table 4 (overleaf). Several CTNs shared internal operational tools such as strategic plans, risk management plans and trial endorsement procedures.

Table 4: The structural components and operational activities of CTNs identified during sector-wide consultation

	Structural components	Supporting operational activities and resources
Organisational structure	Independently registered company or association Sub-entity of a parent organisation Informal entity Registered charity Deductible gift recipient status	Appropriate supporting documentation
	Governance committee	Committee Terms of Reference Meetings
Membership structure	Membership categories	Scientific meeting Education and training workshops Mentoring Communications platforms and policies Membership database
Subcommittee structure	Finance, Audit and Risk Committee	Committee Terms of Reference Meetings Risk management
	Scientific Advisory Committee	Committee Terms of Reference Meetings
	Consumer Advisory Board	Committee Terms of Reference Meetings
Business Operations	Finance	Financial software Business Case Report Business continuity plans Funding strategy Budgets
	Human resources	Human resources Operational staff position descriptions
	Legal	Policies Business insurance
	Strategic	Strategic plan Strengths, weaknesses, opportunities and threats analysis
Trial Program	Endorsement and prioritisation	Peer review guidelines Authorship policy Endorsement guidelines Research Prioritisation guidelines Presentation guidelines
	Collaborative development of clinical trials	Grant writing guidelines Budget and quoting systems Trial pilot scheme Protocol development
	Consumers	Consumer involvement policy
	Safety oversight	Meetings Committee Terms of Reference Clinical Trials Insurance policy
	Trial management	SOPs
	Site management	Selection and acquisition procedures Capability assessment
	Research staff: health economics, biostatistics, research translation coordinator, events coordinator, data manager	Business case Position descriptions

FOCUS GROUP COMPOSITION

Twelve CTNs were involved in the three focus groups as a representative sample of more than 38 CTNs known to operate in the sector (Table 5).

1) The coordinating CTN focus group included representatives from five CTNs with a median of 13 years (range 12-47 years) since establishment. One Chair and five Executive Officers were present, with one CTN represented by both a Chair and Executive Officer. Four participants attended remotely via video or teleconference, and two participants attended in person. The focus group facilitator, a project assistant and the Chair of Reference Group A attended in person. This focus group ran for 180 minutes.
2) The facilitating CTN focus group included representatives from four CTNs with a median of 18 years (range 14-23 years) since establishment. In the facilitating CTN focus group, three Chairs and two Executive Officers all attended in person. One CTN was represented by both a Chair and Executive Officer. The same facilitator, project assistant and Chair of Reference Group A attended. This focus group ran for 165 minutes.
3) The newly established or establishing CTNs focus group was conducted with three CTNs. Chairs and Executive Officers of each CTN were invited to attend, however only Executive Officers were available. This focus group was only offered via remote video or teleconference and the Chair of Reference Group A was also a remote participant. No project assistant was present. Two of the CTNs had commenced operation during the current year, and the other had commenced operations five years previously. This focus group ran for 100 minutes.

Table 5: Clinical Trials Networks represented at focus groups

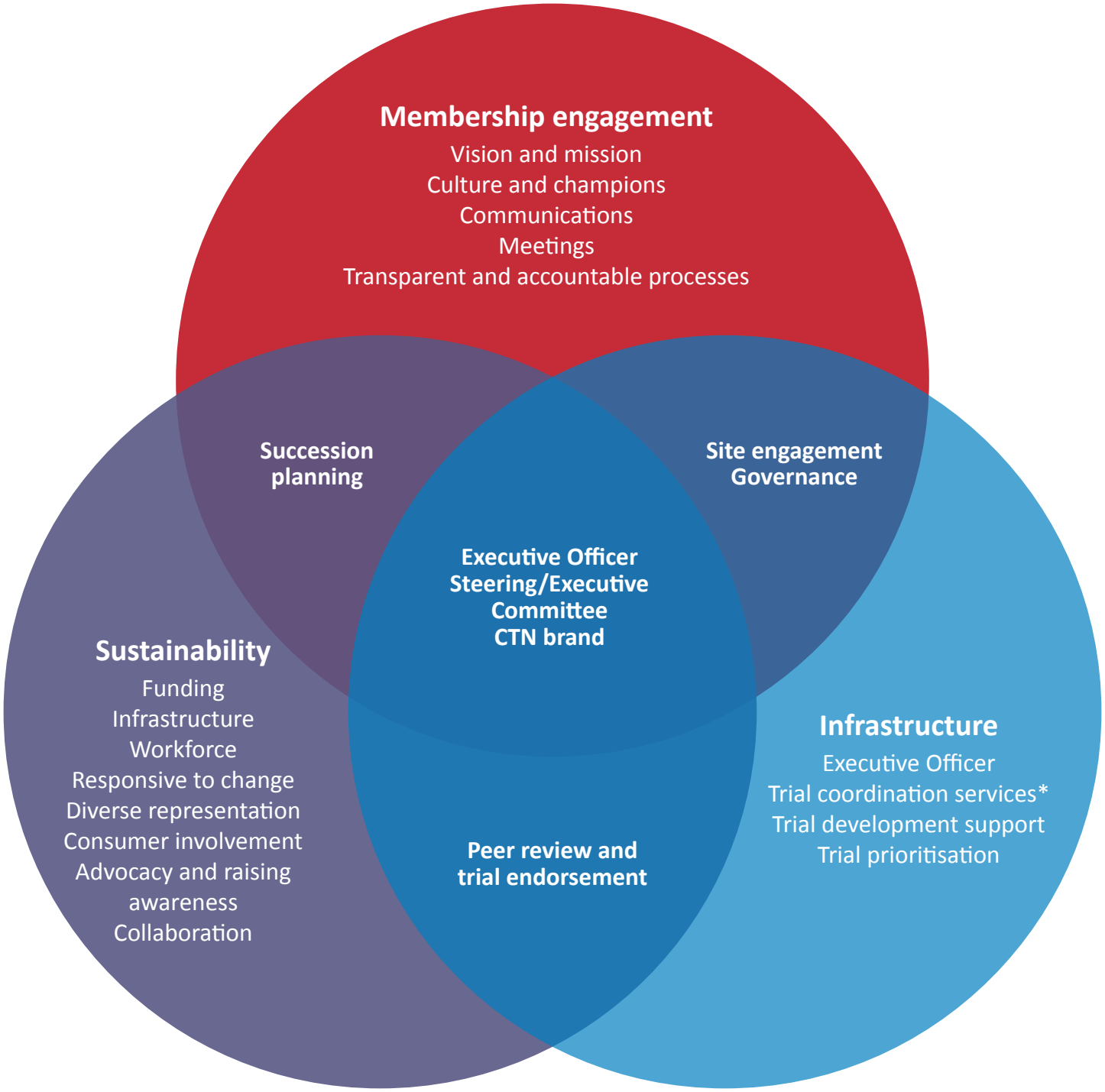
Clinical Trials Network	Year of establishment	Core function
Palliative Care Clinical Studies Collaborative (PaCCSC)	2006	Coordinating
Australasian Leukaemia and Lymphoma Group (ALLG)	1973	Coordinating
Australasian Gastro-Intestinal Trials Group (AGITG)	1991	Coordinating
The Australasian Kidney Trials Network (AKTN)	2005	Coordinating
Australian and New Zealand College of Anaesthetists Clinical Trials Network (ANZCA)	2002	Coordinating
Australasian Stroke Trials Network (ASTN)	1996	Facilitating
Australasian Lung Cancer Trials Group (ALTG)	2004	Facilitating
Paediatric Research in Emergency Departments International Collaborative (PREDICT)	2004	Facilitating
Interdisciplinary Maternal Perinatal Australasian Collaborative Trials Network (IMPACT)	1995	Facilitating
Australia and New Zealand Musculoskeletal Clinical Trials Network (ANZMUSC)	2015	Newly established
Australian and New Zealand Alliance for Cardiovascular Trials (ANZACT)	2018	Establishing
Child and Youth Mental Health (CYMH)	2018	Establishing

OVERVIEW OF THEMES CRITICAL TO SUCCESS AND GROWTH

Qualitative data analysis of the focus group transcripts revealed three key themes identified that were critical to CTN success and growth. These were:

- an engaged membership
- an established infrastructure, and
- sustainability.

These themes and their associated factors identified in the focus groups are presented in Figure 2 (overleaf). Some factors discussed were unique to a particular theme. Many factors were relevant to more than one theme, with their overlap presented in Figure 2.



* Directly for coordinating CTNs and indirectly for facilitating CTNs (often via CTCC)

Figure 2: Clinical Trials Network themes and activities

IDENTIFICATION OF TOOLS AND RESOURCES CRITICAL TO CLINICAL TRIALS NETWORK OPERATIONS

Table 6 (overleaf) lists the tools and resources identified as critical to CTN success and growth during the focus group discussions; these are presented in the ranked order of importance to CTN operations identified by consultation following the focus group. Identifying the tools to support the critical operations for success and sustainability of a CTN provides a basis for sharing knowledge and resources which can be shared between CTNs. This is potentially a key foundation to maximising efficiency and effectiveness in the sector. Table 7 (overleaf) connects the identified themes and activities linked to success with these tools. This has the potential to support almost all areas of successful CTN operations.

Table 6: Key tools and resources to facilitate Clinical Trials Network operations

Clinical Trials Network	Description
1. CTN Membership structure	Describes the options CTNs may consider for fees, membership categories, membership approval and meetings of the membership.
2. CTN Governance structure and documents	Describes the options for CTN organisational structures and models, governance frameworks, responsibilities of various committees and considerations for committee Terms of Reference.
3. CTN strategic plan development	Describes the process for developing a CTN mission, vision and strategic plan, and the process for implementing strategic plan objectives and their evaluation.
4. Website	A website shell that can be easily modified by each CTN to include CTN-specific information.
5. Executive Officer duties	Describes the duties of the CTN Executive Officer and provides an editable position description.
6. Trial review, endorsement and prioritisation process	Describes options that a CTN may consider when establishing a clinical trial review and endorsement procedure; to accompany a guidance document on options to determine areas of research prioritisation.
7. Communication strategies	Describes options a CTN may consider in communicating with members and the public.
8. Management of trial metrics – pipeline, active trials, impact of completed trials	A database that keeps a record of clinical trial milestones from development through to publication and impact.
9. Authorship and publication policy	Describes options that a CTN may consider when establishing policy for publication of trials, and the process or criteria for determining authorship.
10. MOU for collaboration with other CTN trials (international and local)	A document covering key considerations and suggested responsibilities when collaborating with another CTN on a clinical trial.
11. Agreement for collaboration with parent organisation	A document covering key considerations and suggested responsibilities if a CTN is a sub-entity of a parent organisation.
12. SOPs for trial management	SOPs for the conduct of multi-site clinical trials (e.g., site activation checklist).
13. Options for funding structures	Description of the opportunities for funding CTN operations and central infrastructure
14. Roles and responsibilities for network trial Chief Investigator	Allocation of responsibilities and requirements in clinical trials endorsed by the CTN
15. Safety Committee policy and procedures	Suggested procedures, considerations and template documents for oversight of CTN clinical trial safety
16. Network meetings and workshops	Description of types of meetings that can be conducted by a CTN
17. Evaluation of site network capabilities	A process of conducting a needs-analysis for clinical trial sites
18. Customer relation management database for CTN member management	Database to record CTN member details, and to track communications
19. Risk management plans for identification and mitigation of risks	Identification of serious risks, development of risk mitigation strategies and procedures for effectively management of risks
20. Formal mentoring structures and processes	Describes the different options a CTN can utilise to undertake mentoring of new Investigators and trialists
21. Fundraising and marketing plan	Describes fundraising and marketing goals and targets
22. CTN consumer engagement guidelines	Describes the options CTNs may consider for involvement and engagement of consumers in research-related activities, outlining objectives and commitments for both parties.

Tools and resources identified by focus group discussion. Ranking in order of importance to successful CTN operations by ACTA Reference Group A members and focus group participants.

Table 7: Relationships between tools and activities that support critical success in Clinical Trials Networks and accompanying themes

Tool	Success factor	Theme
CTN membership structure	Activity of network sites	An established infrastructure
	Multidisciplinary representation and consumer involvement	Sustainability
Governance structure and documents (ToR)	Governance committee membership (Steering and Executive Committee)	An engaged membership An established infrastructure Sustainability
	Accountable and transparent processes	An engaged membership An established infrastructure
	Succession planning for network champions and key leaders	Sustainability An engaged membership
Strategic plan	Uniting the membership with a clear vision and mission	An engaged membership
Website	Communications	An engaged membership
	Building reputation, brand development and brand maintenance	Sustainability An engaged membership
	Advocacy and raising community awareness	Sustainability
Executive Officer duties	Executive Officer	An established infrastructure An engaged membership Sustainability
Trial review, endorsement and prioritisation process	Peer review, trial endorsement and authorship guidelines	An established infrastructure
	Building reputation, brand development and brand maintenance	Sustainability An engaged membership
	Trial development support	An established infrastructure
Communication strategies	Communications	An engaged membership
	Advocacy and raising community awareness	Sustainability
Management of trial metrics- pipeline, active trials, impact of completed trials	Building reputation, brand development and brand maintenance	Sustainability An engaged membership
	Trial development support	An established infrastructure
Authorship and publication policy	Accountable and transparent processes	An engaged membership An established infrastructure
	Building reputation, brand development and brand maintenance	Sustainability An engaged membership
	Trial development support	An established infrastructure
MOU for collaboration with other CTN trials (international and local)	Collaboration	Sustainability
Agreement for collaboration with parent organisation	Building reputation, brand development and brand maintenance	Sustainability An engaged membership
	Sustainable source for funding, resource and infrastructure	Sustainability
	Collaboration	Sustainability
SOPs for trial management	Trial coordination services	An established infrastructure
Options for funding structures	Sustainable source for funding, resource and infrastructure	Sustainability
	Collaboration	Sustainability

Tool	Success factor	Theme
Roles and responsibilities for network trial Chief Investigator	Accountable and transparent governance	An engaged membership An established infrastructure
Safety Committee Policy and Procedures	Trial coordination services	An established infrastructure
Network meetings and workshops	Meetings: scientific, smaller group workshops and social events	An engaged membership
Evaluation of site network capabilities	Activity of network sites	An established infrastructure
Customer relation management database for CTN member management	Communications	An engaged membership
Risk management plans for identification and mitigation of risks	Building reputation, brand development and brand maintenance	Sustainability An engaged membership
Formal mentoring structures and processes	Succession planning for network champions and key leaders	Sustainability An engaged membership
Fundraising and marketing plan	Sustainable source for funding, resource and infrastructure	Sustainability
	Advocacy and raising community awareness	Sustainability
Consumer engagement guidelines	Multidisciplinary representation and formal consumer involvement	Sustainability
	Trial development support	An established infrastructure
	Advocacy and raising community awareness	Sustainability

KEY THEMES CRITICAL TO CLINICAL TRIALS NETWORK SUCCESS

1. An engaged membership

The most consistent theme associated with success identified by all CTNs was membership engagement, and specifically, the culture that the membership strives to promote. When reflecting on barriers and enablers to CTN success, one Chair highlighted the challenge posed in achieving membership engagement as, *"One of our enablers is engagement and in broader terms one of our barriers is lack of engagement of investigators"*. When membership engagement is high, key CTN operations will flourish through commitment of members to these activities. In a circular relationship, when the CTN is operating successfully, membership engagement remains high. A number of key factors contribute to membership engagement (Figure 2) and several activities and tools support these factors (Table 7).

Network culture, network champions and key leaders

A key factor in membership engagement is the intangible network culture that promotes passion, goodwill and research. One Chair noted, *"I think it's the culture of the people, the enthusiasm, the goodwill. The network runs 90 percent, like all the other networks, on goodwill of clinicians. Without that it would be non-existent."* This culture is often driven by champions and Executive Committee members who are seen as senior influential leaders in their field. One Executive Officer expressed this as, *"Champions are leaders. I think our trial network was started by two very strong leaders and there has been a lot of buy-in from all the subsequent leaders and champions at individual hospitals to keep this collaborative network going"*. Another Chair noted that an Executive Committee that engaged and communicated with the rest of the membership was critical to maintaining membership engagement. *"The operational component of the group is actually managing a large organisation in a way, and you have to deal with your people. Engagement at the leadership level very much requires people skills."* An Executive Officer felt that leaders introducing their own personal connections and network into the CTN was critical to their CTN success. *"Connectivity is actually probably one of our key items. A number of the positions within our governance structure, and I think the Chairs are critical, are really quite well-connected individuals in their own right. Whilst that might mean we lean on people on occasions it does mean that we get engagement, that they have a lot of famous friends if you like, and that actually aids the way our trial group is perceived both upstream and downstream."*

Uniting the membership with a clear vision and mission

Uniting members through a clear vision to improve health care is critical to member engagement, and this was highlighted in the focus groups (Box diagram 2). Vision and mission statements of CTNs often draw upon the motivating factor of generating evidence through clinical trials and consequent improvement in healthcare practice and outcomes for patients to facilitate member engagement.

Uniting the membership with a clear vision and mission facilitates engagement

There is a *"… strong motivation among the members to improve outcomes for their patients. … this is partly because outcomes are so poor for many diseases, that gives that group of physicians a very strong imperative to try and improve outcomes."* – Chair

"For us, I think our biggest enabler is a huge desire for disease speciality clinicians and disease specialty departments to be involved in clinical trials or clinical improvement work led by the network. We cannot engage everyone that wants to be engaged. We just don't have the resources. I think that's our biggest enabler. We won't stop functioning because of lack of interest." – Chair

"I think it is a passion to try and deliver best care and the recognition of the centrality to clinical research to that." – Chair

"Our success is definitely the number and the quality of the trials that we've done." – Chair

"I think we have what I would call a proud tradition of essentially completing studies that have changed global practice…I think there were some very influential people who essentially … what the trials have discovered have changed practice not only in Australia but beyond. I do think that's what motivates us because we can see the reach of this." – Chair

Box diagram 2

The vision and mission of a CTN should be clearly developed within a strategic plan that can then be operationalised by governance committees, Executive Officers and network operational staff. As described by one Executive Officer, *"The organisation needs a strategic plan, there needs to be a structure and there needs to be clear delegations of accountability and responsibility. Those things are just essential for a good organisation."*

Governance committee membership

A critical role for CTN members is representation on CTN governance committees. For practical reasons, CTN governance is usually the responsibility of a small number of members that comprise a Steering or Executive Committee, and it is critical that this group is structured, engaged and adheres to transparent terms of reference. The governance committee should be responsible to, and representative of, its membership. One Executive Officer considered *"… having a very engaged executive group and governance structure to facilitate operations and/or to stimulate the network and support operations"* as a fundamental reason for success of their CTN. Member engagement is greatly facilitated by the perception that each member may have the opportunity to become a leader by ensuring governance committee members serve a finite number of terms, and encouraging a committee composition reflective of the diversity and specialties within the membership, so there are designated spokespersons for all areas of a CTN clinical trial portfolio.

Accountable and transparent processes

Some CTN activities that contribute to the success of a network may impose on the autonomy of individual trialists. Governance processes that are transparent and accountable should enable confidence in decisions made by the network and support membership engagement. Tools to facilitate transparency and accountability range from committee terms of reference, pre-defined priority areas for clinical trial development and allocation of CTN resources, authorship guidelines and endorsement criteria.

Scientific meetings, workshops and social events

Activities that support membership engagement include creation of opportunities for members to meet. These include annual scientific meetings, smaller group workshops, social events and educational opportunities. One Executive Officer stated that *"… getting members together at workshops, running networking events"* were critical CTN activities to keep members engaged, while another CTN conducted *"smaller working groups to reach out to more members"*.

Communications

Communications across the membership occurs mostly via electronic means, such as the website, newsletters by email and, for some CTNs, social media platforms such as LinkedIn, Twitter and Facebook. However, not all CTNs are convinced that the investment in maintaining social media platforms is worthwhile. Different platforms should be targeted for different stakeholder groups, for example CTN members are most likely to access Twitter, but Facebook is more likely to be effective in raising community awareness. Critical to the efficiency of CTNs communications is a clearly defined membership and an effective system that records membership information.

Management of differing expectations between investigators and capacity of the CTN operations through effective communication, is a critical component to maintaining engagement. *"I think that some sort of agreement before the whole process runs, this is what you have to do and what we will provide and that communication is quite important"*, noted one Chair. Operational tools that limit member dissatisfaction and reduce disengagement include agreements and policies that support transparent processes for CTN governance, prioritisation of research, trial endorsement, authorship, and clinical trial responsibilities.

Communication with individual members who are contributing at a high level to the CTN must also be considered. *"It's crucial to keep that communication going and it's often at the operational level easy to think things are flowing fairly nicely, but then if investigators are not up to date and they suddenly get a question about X or Y or they get an update that there's a problem, that can cause issues. Communication is important."* One solution employed by a CTN to ensure regular and consistent communication has been to establish a project manager role in the CTN that communicates updates from all trials to relevant investigators.

2. An established infrastructure

A CTN needs a structure with effective central network activity that can support and facilitate a pipeline of clinical trials across multiple network sites. A coordinating CTN Chair suggested, *"Having a good organisational structure whereby the pathway from presentation of trial concept to final trial completion is clear and structured is very helpful."* A number of key factors contribute to a well-defined CTN structure (Figure 2) and several activities and tools support these factors (Table 7).

Executive Officer

An Executive Officer is central to the efficient operation of CTNs. Activities critical to the success of a CTN that require administrative and project management duties are usually delegated to a CTN Executive Officer, including duties critical to the network structure such as support of the governance committees; coordination of events, smaller interest groups and meetings; successful implementation and measurement of the impact of strategic objectives; and management of the operational budget. However, the Executive Officer is also expected to maintain membership and key stakeholder engagement through communications, including the CTN website, and to coordinate activities to maintain the CTN's reputation and promote community awareness. In focus group discussions the Executive Officer was described as a 'key staff' member and lack of an Executive Officer was identified as a critical barrier to reaching operational effectiveness and efficiency. Outside the cancer field, options for CTNs to obtain dedicated funding for an Executive Officer are extremely limited, and include short-term, competitive grants or funding from a parent organisation.

Prioritisation of research

Prioritisation within a CTN refers to the areas of healthcare where the CTN preferentially or actively seeks to conduct their research and clinical trials. This may be done subjectively or more formally. One Chair described their objective prioritisation process as, *"We have formally gone and looked at what the priorities for our researchers are. We went through a Delphi process, three or four years ago, where we came up with a list of priorities in ranks."* In contrast, an informal prioritisation process was described by another Chair as, *"We have a concept development workshop just to talk about new ideas and I guess if people bring those ideas and there is passion and people come up afterwards and say, 'Yes, I want to do that trial, thanks' then that's how we get that groundswell of interest in something."* However, that same Chair also reflected, *"We do want to think more strategically about prioritisation though; where are the issues and where are we going to get our greatest value from."*

Peer review, trial endorsement and authorship guidelines

A valuable process undertaken in most CTNs is peer-review of clinical trial and funding proposals, often accompanied by endorsement and support of the trial by the CTN. Intensive peer-review is usually undertaken in smaller workshops or by specific committees, but most CTNs also require that trials endorsed by the CTN meet specified requirements, such as peer-review publication and presentation at the annual scientific meeting. A common feature of trial endorsement is a commitment by the lead investigator group to publish the trial results.

A common feature of a network's endorsement conditions is detailing the requirements for authorship of collaborative projects, and the use of the CTN name and logo on publications and presentations. During focus group discussions, authorship and publications arose as a frequent source of tension in CTNs, either through delays in finalisation of manuscripts, or determining which members that participated in a study warranted authorship. This was captured by one Chair as *"Sometimes it's the simple things that cause trouble early on, and on our first few projects authorship caused an issue. So, we created an authorship guideline that people have to agree to before they come on board with the project"*. Many CTNs have pre-defined authorship policies detailing the requirements for authorship and CTN acknowledgement, but there is an awareness that this is an evolving area[3], and many CTNs may need to keep refining their guidelines.

Trial development support

Development of clinical trial protocols was provided as an internal process by many CTNs, most often with a view to enhancing success in competitive funding applications. Structural supports ranged from a dedicated staff member to help with preparation of the protocol, assembly of multidisciplinary and consumer groups to critique and review the clinical trial proposal, and either supporting funding applications or providing CTN funding for the conduct of pilot or feasibility trials. Specific examples provided by CTN Executive Officers include, *"We award those pilot grants to fellows who can then lead that feasibility or pilot study which can lead to a large multicentre clinical trial"*, *"We have a new concept symposium at our annual scientific meeting held each year. Concepts may be presented there and then we also have our Innovation Fund which awards $200,000 annually for pilot studies,"* and *"a workshop is for all our site PIs and our trial coordinators to come together to develop brand new research proposals and give peer review."*

Being able to support pilot studies to demonstrate feasibility of clinical trial proposals is seen as an effective way to enhance success in major project funding bids. It also provides an opportunity to optimise successful trial conduct, increasing the likelihood of timely trial completion once funded.

Activity of the network sites

Successful engagement and efficiency of recruiting sites (network sites) within the network infrastructure is essential to network success and growth. In some CTNs membership is via organisation or site and already encompasses site accreditation, but in others the CTN engages with investigators directly, who then take responsibility for their site's participation and evaluation of the network site capabilities.

While engagement is required in both models, it is critical for the success of clinical trials supported by individual members. As described by one Chair, *"Because we are a facilitating network, site accreditation is not a role that we take on. We facilitate groups of investigators to run trials. The interaction with the sites has been with the groups of investigators, rather than the network."*

Facilitating CTNs also described an inability to move beyond recruitment at a small but experienced core group of sites, primarily due to lack of resources and time to train new sites in CTN and clinical trial procedures. One Chair described a potential barrier as, *"given that there is variable expertise all trials go to the same sites over and over again and there is an overburden of some sites and then other sites don't have the infrastructure or have a very hard time to build their infrastructure to do the clinical trials. If we were to expand and do trials quicker and be attractive to industry or trialists building bigger capacity at sites, even rural sites, would be very important."*

This was echoed by another Chair who described training new sites to CTN procedures as, *"you've been talking about the importance of new sites coming on board but the pain of that is immense, isn't it?"* The burden of introducing new sites to a CTN may be somewhat overcome in the setting of a coordinating CTN or by a well-resourced central network administration, and one Chair proposed that *"… having the CTN office being able to provide good infrastructure is very helpful because by far the majority of sites don't have the infrastructure to actually run a multisite trial."*

Tools that may provide more structure to support network site activities include a network site performance tracking system and network site capability assessments. As one Chair stated, *"we know if we're running a trial, which sites we want to go to. We know who is going to perform and who can get it up and running but it's how do we engage those others and make them work as well"*. This was echoed by another Chair, *"I think that's a real challenge for all the networks, working out which of your sites do well and also why they do well because then it helps you with the ones that are underperforming."* Another CTN suggested a less formal approach to a site accreditation scheme where sites may see CTN involvement as an opportunity to demonstrate their research capabilities, noted by their Chair, *"If you walk into the hospital and you've got your badge there that says we do research and we do it well because we've met these criteria. We're thinking we're going to take that approach because we are not a coordinating Network. So, we don't have to be so didactic in terms of accreditation."*

Trial coordination services

Trial coordination services are offered by some CTNs, although others (i.e., facilitating CTNs) rely on the services of CTCCs. Generally, these trial coordination activities adhere to a set of standard operating procedures (SOPs), that may be common within a CTCC for trials conducted by various networks, but differ between CTCCs and CTNs offering trial coordination services. One Executive Officer commented, *"As far as the SOPs, I think that's a massive amount of work for any network and I think we all tend to just do them separately for our own network. It's crazy, isn't it? It's so much work."*

3. Sustainability

The third key theme identified for CTN success, sustainability, is a measure of success in itself. Several key factors contributing to CTN sustainability are the past successes of the network (Figure 2) and activities and tools to support these factors also focus on maintaining that success (Table 7).

Multidisciplinary representation and consumer involvement

Most CTNs cater for a membership that includes a variety of disciplines and diseases or diagnoses, and which establishes membership and other structures for inclusive representation, such as sub-diseases. One described strategy was, *"We have seven sub-disease committees and they allow members, clinicians and researchers to engage with any disease areas where they have a particular interest. They meet about three or four times a year and help to drive the program of research in that particular area"*. This representation of different sub-diseases enhances sustainability, as clinical trials in different areas can run concurrently and ensure that the pipeline and trial program is maintained, without exhausting the patient population.

Sustainability also requires engagement of consumers to ensure the continued development of patient-relevant clinical trials. One particular disease area presented challenges in engaging consumers locally due to the short-term nature of patient presentation and type of treatment. Some examples of consumer participation described in the focus groups include: representation on governance or other network committees, participation in a consumer advisory panel, involvement in prioritisation of research, input into clinical trial consent procedures, and writing social media posts to raise community awareness. However, many CTNs identified a requirement for guidelines on how to best engage consumers and align both interests of the consumers and CTN (Box diagram 3).

Guidelines for consumer engagement are an unmet need for CTNs

"Often the consumers that engage are semi-professional consumers who are representing groups who have very much got their own agenda. Unfortunately, when they then get together and their agendas conflict it can cause some disharmony within your consumer group. I think guidelines or leadership of the consumer group is really important to make them effective. They are essential, and in some ways how you manage them, it can be tricky… ACTA particularly have identified this need to show some leadership in how to engage and interact and make them a fundamental part of the process. I think that is a challenge." – Chair

"They are given a certain amount of training in the research process and they go through most of the documentation from a consumer perspective. Their feedback is valuable, very valuable, when it's within the right context. They have those roles and responsibilities. It does get a bit sticky because a lot of the smaller groups or the networks, a lot of them transfer between or have worked in another group and can see that work." – Executive Officer

"Consumers are critical to our network growth and sustainability. They need to have clear roles of responsibility and a lot of the networks don't necessarily have that outlined. …They have their expectations and we have ours, but they are not aligned, and they are not reviewed. We've come into a couple of situations where we weren't aligned. It didn't work out and that's unfortunate because we are here for that purpose. Ultimately that's why we do the research. That's one thing for us. That is a tool that we need." – Executive Officer

Box diagram 3

Succession planning for network champions and key leaders

Network champions and Executive Committee leaders are key to an engaged network membership, and thus succession planning is crucial for sustainability. The difficulties of fostering commitment to the CTN leadership in a new generation was acknowledged by one CTN as, *"we do have our champions that have been with us for a number of years. That's also a double-edged sword, because we are trying to bring in a new generation to attract them into our group to see the benefit of doing the research, as well as the clinical work, which is always difficult."*

Formal mentorship programs and other activities can be developed to facilitate succession planning. The CTN structure and trial portfolio naturally lends itself to mentoring, by enabling engagement of new investigators as associate investigators on trial protocols championed by more experienced investigators, thereby providing unique opportunities to become involved in the design, data collection and ownership of clinical trials. Ideas included an *"Emerging research leaders' workshop during scientific meetings … to develop our next generation of research leaders,"* and, *"At our CTN researchers' strategy workshop we have an emerging research leaders' workshop where we identify active players in our CTN who are undertaking higher degrees and are ready to step up."*

Building reputation, brand development and brand maintenance

A number of activities support these factors including timely completion and publication of high-quality trials; advocacy and awareness; collaboration with other networks and organisations; and continuing commitment to the CTN vision. The quality of trials and likelihood of their success is greatly enhanced by the processes of peer review and endorsement, which facilitates maintenance of the CTN brand. Early- and mid-career investigators, can benefit from the brand and combined track record of the CTN in competitive grant funding applications, manuscript submissions and clinical guideline development.

Delays in publication of manuscripts is a challenging but critical area for brand maintenance. and described by one Chair as, *"it's a very difficult area and I think we all struggle with it. As much as you can plan, you've just got to manage it."* One CTN placed members of the governance committee on each authorship committee, and made them accountable for manuscript finalisation, but another CTN had discontinued this strategy as it had caused tension in the membership. A further CTN recounted a unique strategy that they had included retired clinician members on writing committees to provide mentorship; "There are retired clinician members around that are still wanting to have an intellectual input and help out their colleagues but aren't necessarily worried about whether or not their name appears on the paper. We've found them a good resource for helping on writing committees just to help keep the motivation going".

A CTN's ability to track the timely completion and publication of trials supports brand development and maintenance, and focus group participants proposed options such as technology tools (i.e., apps) that collated all CTN publications, or specialised software to manage clinical trial activities. Other metrics that may be tracked for its contribution to brand maintenance are timelines for clinical trial start up and recruitment, trial completion within budget, and impact of trial publication. Other risks to the CTN could be identified with proposed mitigation strategies through the development of formal risk management plans.

Advocacy and raising community awareness

Most CTNs have engaged in some advocacy work but found that as a single CTN, their available resources and ability to successfully raise awareness of CTNs or clinical trials, is limited. One Executive Officer described *"trying to get your message out there amongst everybody else's message"* as a barrier. Another Chair described his CTN's efforts, which included invitations to annual scientific meetings, as *"We fail miserably in every way to interact with policy makers".*

Some CTNs use their website to raise community awareness: *"The website includes information on all of our trials, whether they be in development or recruiting. Each trial has two sections you can either click on as a consumer or as a health professional."* Others used social media, but acknowledged that it needs a prospectively designed communications strategy: *"… we specifically use Facebook to engage the community, not really to engage the members"*. Other CTNs have consumer representatives who contribute to raising awareness through their own social media networks: *"… she's a consumer and she puts these questions out on Twitter and she gets thousands of responses".*

Collaboration

Collaboration with other CTNs, both internationally and cross-disciplinary can contribute to the pipeline of clinical trials, development of the track record and sustainability of Australasian CTNs. One Executive Officer from a CTN with collaborations in Canada and Asia described this as, *"We've been proactive in collaborating with the Canadian trials group and we actually have a Memorandum of Understanding with the Canadian trials group around sharing trials, that's then allowed us to access studies that they've negotiated for and they will then negotiate almost on our behalf, and we'll join that collaboration … Obviously the focus is Australasia, but you can build on that by having potentially formal collaborations internationally. That's been a success for the group."* Another Executive Officer agreed that *"an enabler is for us that we are part of a worldwide network of clinical trials".*

Maintaining infrastructure and a research workforce

A strong and effective pipeline of trials ensures an ongoing portfolio of trials can be offered to the membership allowing network sites to maintain infrastructure and experienced core research staff (Box diagram 4). These staff are seen as essential to sustainability, as noted by one Executive Officer: *"the trial coordinators at the sites are the success of our CTN and if we lose them, we lose our backbone really".*

Lack of resources at sites is a barrier to CTN operational efficiency and effectiveness

"Our number one barrier is lack of resource at participating member sites to perform the setup and the conduct of the clinical trials." – Executive Officer

"I think we are so inefficient how we – there's funding there, people are recreating the wheel all the time. Sometimes it's trial coordinators who are experienced, sometimes they are quite inexperienced. Sometimes the person who gets there has never really run a life study and they're really floundering from day one." – Chair

"A large number of our sites are exactly as you said. They get a research assistant, they get point four of an RA and when that's gone that sticks and then it's two years before they get another research project that they're involved in. Yes. We have a lot of sites like that and it is incredibly inefficient." – Chair

"Our sites who are the most efficient are those that have staff who are employed who present a portfolio of studies." – Chair

Box diagram 4

The challenge of providing appropriate remuneration to the sites for the costs and work effort of participant recruitment to investigator-initiated clinical trials, has potential to: lead to excessive workload for site trial coordinators, hamper engagement with the CTN, and may contribute to turnover of staff at sites, necessitating retraining of new staff in CTN-specific clinical trial processes. Some CTNs offer educational opportunities to engage and train trial coordinators, but inappropriate levels of funding still limit the ability for these opportunities to be realised. Lack of site resource and expertise can also manifest in decreased recruitment to clinical trials and was summarised by one Executive Officer as, *"A barrier to efficient CTN operations that I see quite often is that there's a bit of a mismatch between feasibility survey results and actual recruitment which delays clinical trials and causes cost blowouts".*

A potential solution is to share trial coordinators between clinical areas at sites, but the limitations discussed included accessing funding and prioritising what is clearly a large unmet need. *"If you do that, who controls them and who decides what their priorities are? Clearly every group will want to say I've got enough work for you, so no one else can use you,"* stated one Chair, and supported by an Executive Officer, who corroborated, *"Because, there is still that extra oversight that we can't control. If that person doesn't work for us, we give some funding into positions we can't control".*

Another possible solution to the demands that a clinical trial places on trial coordinators is to embed trials more successfully into the healthcare system (Box diagram 5, overleaf), to limit development and training of staff in specific procedures pertaining to an individual clinical trial. As described by one Executive Officer, *"Trials shouldn't be an add-on to good clinical environments and yet they still are; from the staffing that are at the trial sites, the way the hospitals engage in terms of governance processes, etcetera. It's still very much an add-on. I'd like to see it become more of core business … with some cost recovery on the hospital side from their participation in trials as part of their core business."* In an effort to design trials that facilitate embedding, some CTNs are now exclusively running trials that use standard of care visit schedules for data collection points.

Integrating research into routine healthcare supported by clinicians

"I think that if we are talking about a clinical trial network, we should be [talking] about highly efficient clinical trials generating the evidence and thinking about how the implementation, the whole continuous improvement cycle occurs. It is that knowledge generation – I do think it should be the core purpose of that network." – Chair

"Research is not the bottom line for most [healthcare institutions] and that is the big problem, right? If it was part of their mission, then all these things would happen. But it is seen as separate from healthcare. That's a big barrier, I think." – Chair

"I think we are lacking [hospitals providing resource for clinical trials] in Australia because research is not in the mission of the hospitals, to create clinical trial centres and create an infrastructure. There is ethics. There is some research governance, but there is not the infrastructure to help people build that." – Chair

"We need healthcare institutions to realise that it is not just activity and finance that should drive their priorities. It is knowledge improvement." – Chair

Box diagram 5

Many focus group participants also supported better integration of research into standard healthcare, as a sustainable means of conducting research to drive knowledge generation, improved practice, and better patient outcomes. The provision of CTN infrastructure to conduct multisite clinical trials was considered a critical step to achieve this.

Several CTNs highlighted the lack of a recognised career pathway for research staff, such as trial coordinators and research nurses, as a barrier to network sustainability. It was proposed that defining a career pathway for trial coordinators may lead to greater recognition of this role at sites, potentially better funding for the position from the sites, and less turnover, with consequent retention of talent, skills and knowledge. One Chair proposed that facilitating the development of a defined professional group could highlight the trial coordinators' crucial contribution to high-quality clinical trials research (Box diagram 6).

Site trial coordinators are a critical, but inadequately recognised, component of clinical trial research

"I think something that would be very useful to do as a group would be to help develop the trial coordinator/clinical trial manager role as a career in its own right. It can be difficult to explain to groups, such as hospital administration and nursing, or even at a site level, what clinical trial staff do, their expertise and the appropriate remuneration because they don't come from a defined professional group. Trial coordination at the site level is crucial to clinical trial research so if we can in any way facilitate this, it would be good." – Chair

"Career pathways for these staff are very limited. Pay rates are just not at the level where we often get staff that are high performers, and so we have to put in a lot of energy training them. Whenever there is a change of staff at a site, we have to go back in and re-educate, not only about the trials that they're running but just about the collaborative more generally and how we interact, and so that's quite a time investment from a national office perspective."
– Executive Officer

Box diagram 6

Sustainable source for funding, resource and infrastructure

It was unsurprising that ongoing funding and resources were identified as critical to CTN sustainability. Many CTNs have only limited or short- to mid-term funding, and very few have certain long-term funding. Some CTNs have become involved in fundraising activities to generate income, but it was acknowledged that the investment required for fundraising was significant, and the cost-benefit ratio was not assured, particularly for those CTNs with limited resources. Alignment with parent societies and medical colleges provides some CTNs with ongoing support, but this is not applicable to some CTNs, including those that are more multidisciplinary in nature. Support from universities and hospitals might be more suitable for multidisciplinary CTNs, but this model usually only provides infrastructure support rather than direct funding. There may also be some disadvantages to either of these funding structures, including a lack of autonomy and possible instability if the network is no longer prioritised by the institution.

Responsiveness to change

For successful operations, CTNs need to remain agile and adaptable, not only because they are operating in the dynamic area of research and with limited funding, but also because the clinical trial environment is constantly evolving. One Executive Officer suggested, *"Responding to the services and the regulatory environment is absolutely critical to maintain yourself as a successful clinical trial organisation. The regulatory environment influences significantly where your business efforts need to be shifted to at various points in time, and what types of roles the business needs and being able to be responsive to that, I think, is very important".*

FACTORS FOR SUCCESS SPECIFIC TO A NEWLY ESTABLISHING CLINICAL TRIALS NETWORK

The newly establishing CTNs identified some factors specific to success in the early processes of network establishment (Table 8). All newly establishing CTNs were cognisant of the need to establish governance procedures early to provide transparency and consistency and reduce the likelihood of disagreements, as well as providing a prospective framework if it did arise. They were keen to gain knowledge of the types of organisational structures that could be adopted. Sharing simple resources, such as strategic plan templates and communication plans, were also sought.

Table 8: Key factors of success for establishing Clinical Trials Networks

Mission and vision Established early Diverse representation involved, but must include champions Developed by agreement as an initial bonding exercise and then by evolution
Leadership Identify early and ensure involvement in establishment meeting and succession planning Lack of leaders' time may be a barrier
Establishing network culture Flagship project to initially unite the network Mentoring and welcoming younger or new members
Operational staff position descriptions
Knowledge when making choice about organisational structures

Establishing a vision and mission early is key, and provides opportunity to enhance an evolving network culture, as noted positively by one Executive Officer, *"I think actually getting people together in a room to work through those things is like a bonding exercise".* This opportunity was potentially missed by another CTN, *"We've pulled together a very basic strategic plan. What I feel is missing in our development is the coming together of the committee members to really clarify for themselves their vision and their objectives".*

In support of developing the network culture, a flagship clinical trial was identified as a way to unite the network. Similar to the more established networks, diverse and multidisciplinary representation with champions to lead the network, were also identified as key factors to drive success in establishment.

Access to funding to establish a CTN was acknowledged as a challenge and, in comparison to established CTNs, further complicated by the lack of a track record. One idea suggested was collaboration as part of an internationally-led clinical trial: *"If you get something that's already up and running and you get some local funding for it, that might be a really good opportunity to start building the network".*

DISCUSSION

CTNs have made an immense contribution to cost-effective generation of clinically- and consumer-relevant evidence, and implementation of best practice healthcare across many disciplines. In alignment with our vision of better health, best evidence, and as a representative of CTNs and the investigator-initiated clinical trial sector, ACTA has utilised a qualitative descriptive approach consisting of sector-wide consultation and focus group study to identify the activities undertaken by CTNs that contribute to successful operations of the CTN, to identify any unmet needs that limit the effectiveness and efficiency of CTN operations, and potential shared tools and resources to support future activity. This type of qualitative descriptive research is commonly used and well-accepted in the healthcare sector, and was particularly suitable for this project, as limited frameworks for evaluation of network operations are available (reviewed in [4–6]).

Three main themes were identified as critical to success and growth of CTNs: an engaged membership; an established infrastructure; and sustainability. The sector-wide consultation and focus group discussions also identified tools and resources that could be developed as common resources for all CTNs to support activities within these themes.

Strengths of this research include sector-wide consultation that provided an opportunity for a comprehensive overview of all operational processes undertaken by CTNs. The focus groups allowed more detailed discussion with leaders and operational staff that were representative of a broad range of CTN types and disciplines. This allowed identification of those operational processes that were most critical to success.

A limitation of the focus groups is that it was conducted with participants strongly invested in the CTN, which did not allow perceptions of members with weaker ties to the CTN to be incorporated. Operational success of a CTN could also be perceived differently by the community, the hospitals, policy makers, funders and trial participants, and the focus groups did not include representation from those areas to determine this.

The twelve CTNs participating in the focus groups may not have been sufficient to reach saturation, thus factors identified may not be entirely representative of the wider group of CTNs that exist in the sector. To mitigate against this, the CTNs selected for the focus groups represented various disease specialties, differing levels of maturity and funding availability, and different organisational structures. Despite representing diverse CTNs, participants within the focus groups demonstrated consensus, built on other CTN experiences and initiated sharing of tools, and similar factors were identified across the focus groups, suggesting that activities and key themes underpinning successful CTN operations were applicable to all CTNs.

While critical tools were identified, the focus group discussion did not overtly obtain information on whether these were integral to operational efficiency of all CTNs. This was partially overcome by the subsequent request to rank and prioritise the tools identified. Further potential for bias may exist, as the focus group transcripts were only coded by one researcher, however, the results and themes were agreed upon with other individuals who were present for focus group discussions.

The information gathered contributes to a growing picture of what defines an operationally successful network (Figure 3, overleaf), noting that there is extensive diversity among the CTNs known to ACTA, and there is unlikely to be a network operations model that will suit all CTNs. Literature on successful networks for the conduct of investigator-initiated clinical trials is sparse, despite the presence of similar networks for the conduct of clinical trials in Northern Europe, the USA and Canada. However, many of the features identified in this study are common to other healthcare-based networks, such as practice-based research networks[7,8], and examination of critical success factors in evaluation of these practice-based research networks, and networks that conduct investigator-initiated clinical trials[9], supports the findings of this current study.

Similar elements of a successful clinical research network as depicted in Figure 3 were identified following an external business review and internal survey of a Canadian Cancer Pain Network. These elements encompassed shared vision; formal governance policies and terms of reference; infrastructure support; regular and effective communication; an accountability framework; a succession planning strategy to address membership change over time; multiple strategies to engage network members; regular review of goals and timelines; and a balance between structure and creativity[10]. At a more basic level, and using the example of the Population-based Palliative Care Research Network (PoPCRN), Kutner[8] describes necessary elements for successful operations as a definition of who is in the network; how network recruitment operates; how people maintain membership; a system for deciding how studies are selected and how members decide to participate in a given study; a mechanism for the network to interface effectively with other agencies; the development of a

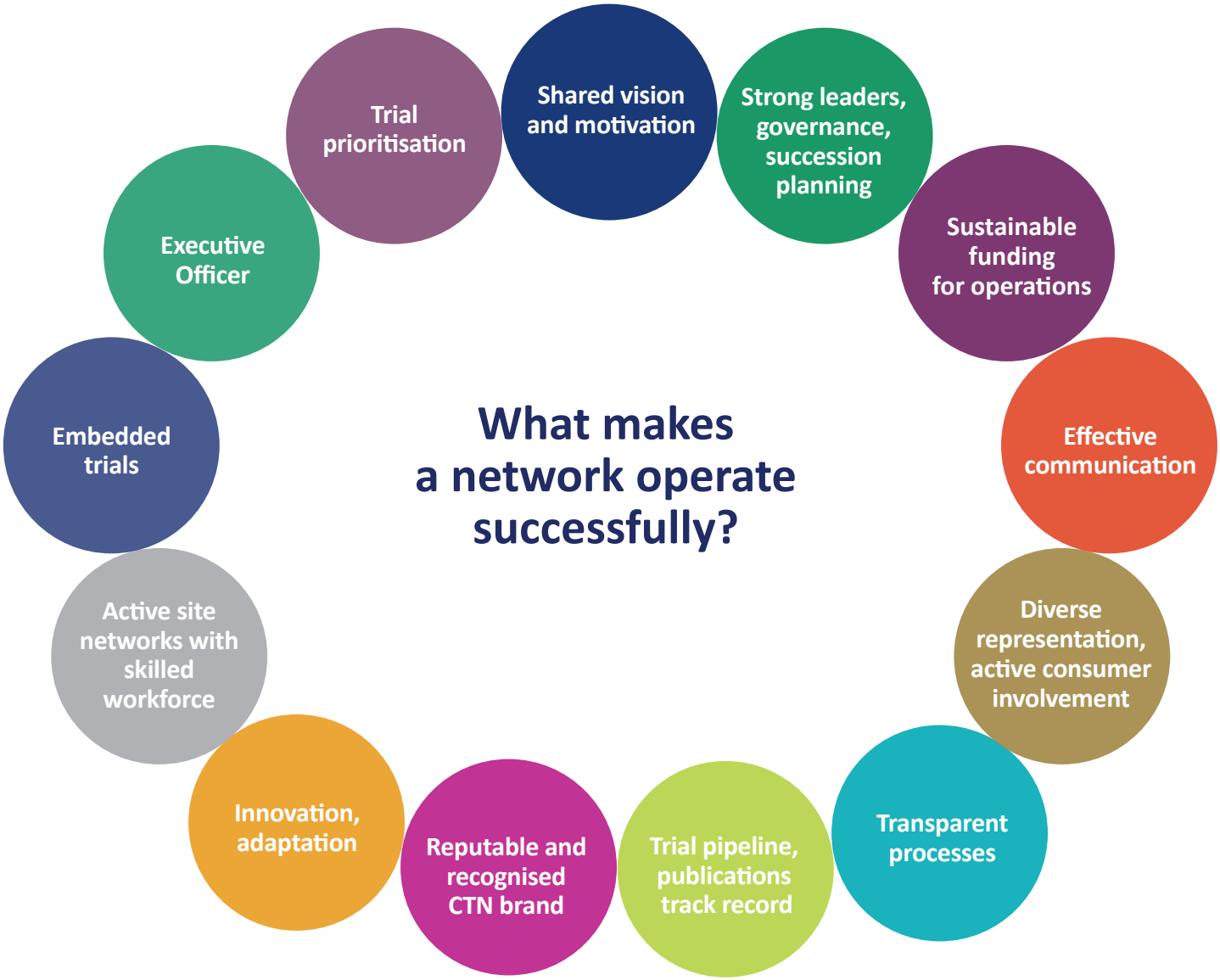


Figure 3: Key success factors for a Clinical Trials Network

network identity; the development and maintenance of a basic database about network members; a governing body and; a process by which network members can interact with each other. Areas that emerged as an ongoing challenge during focus groups, such as managing member expectations, particularly around authorship, were also noted as potential sources of tension within other networks[7–9].

Good organisation of the CTN is a critical component identified in the literature on network evaluation[7,9,10], and recognised as critical to successful network operations by the CTNs participating in the focus group discussion. One of the findings emerging from the external business review of the Canadian Cancer Pain Network was to implement defined procedures for moving research ideas to concrete proposals and then active research studies[10]. Already identified as an unmet need in some CTNs participating in the focus groups, the Executive Officer plays an essential role in defining this pathway and the organisational efficiency of a CTN, through provision of support to the governance and other committee meetings, execution of the operational processes, management of the operational budget and allocation of resources, implementation of the strategic plan and management of timelines[10].

Despite the pivotal role of the Executive Officer, there are currently limited options for sustainable and dedicated funding for this role. Beyond the cancer CTNs, many networks need to rely on funding from a parent organisation or short-term, competitive funding applications to fund their Executive Officer. By exception, the cancer networks receive a dedicated, albeit still competitive, funding stream for infrastructure that can be utilised to support Executive Officers. However, even for CTNs with Executive Officers, the lack of sustainable funding for network operations can still give rise to operational inefficiencies that were commonly identified in this research, such as not expanding clinical trial recruitment beyond a core group of experienced sites, and not evaluating sites to identify high performers or provide support to lesser performing sites to ensure that they contributed maximally to clinical trial recruitment.

Sustained site infrastructure is a key benefit of CTNs, however, even the very established networks felt that their engagement with sites was a significant ongoing challenge, despite undertaking activities to facilitate this engagement. Engagement with trial coordinators can be hampered by the perception that CTNs do not meet the true costs to the site of recruiting a participant to a clinical trial, in comparison to trials sponsored by the commercial sector. The disparity between the per-participant payment and the true costs of managing that participant in an investigator-initiated clinical trial[11], and clinicians' concerns about demands on staff have been reported as reasons for decreased trial recruitment in National Institute of Health Cancer Cooperative Group trials[12], and may be one reason why despite appropriate feasibility studies, timely trial recruitment remains a barrier for efficient CTN operations. Delayed recruitment to trials can have negative effects on a CTNs brand, and detract from other network operational activities, as resources are targeted to activities that enhance trial recruitment.

Throughout the focus group discussions, participants commented on the inability of current healthcare facilities to assimilate research into the healthcare system (Box diagram 7). Epitomised by the Learning Healthcare System model, integration of research enables decisions about health and healthcare to be supported by continuously updated, high-quality evidence that is obtained and implemented through research activities embedded into routine patient care. Among elements that support embedding of research activities into routine healthcare described in an earlier ACTA report[13], a secure, skilled research workforce and pragmatic clinical trial designs that can be 'embedded' or conducted within the usual parameters of routine healthcare, would provide potential solutions to the unmet need of inexperienced or inadequate site trial coordinator resourcing, that was identified during this research. Many of the existing strengths and characteristics of CTNs ideally place them at the forefront of the implementation of a Learning Healthcare System model.

Key features of CTNs that contribute to a Learning Healthcare System include:

- the size, breadth and diversity of membership that enables efficient and diverse patient recruitment onto statistically powered clinical trials
- the generation of clinical trial questions relevant to advancing healthcare through the contribution of clinicians who work 'at the coalface' and consumer input
- the process of peer-review and endorsing trial by the CTNs that refines clinical trial protocols to high quality, efficient and feasible designs
- the establishment of reuseable clinical trial infrastructure and a clinician and site network that is successfully engaged in research
- cost-effective clinical trials utilising relevant endpoints to facilitate translation of clinical trial results into healthcare
- the creation of a consistent, knowledgeable, skilled and widespread workforce that is already familiar with procedures from clinical trial participation greatly facilitates implementation of research findings beyond the trial population.

Box diagram 7

One feature of successful network operations previously identified that did not emerge during focus group discussion was intrinsic evaluation of network success.[7] In other healthcare networks this has been conducted by surveying the membership[7,9,10], and allows evaluation of the network operations by those with looser ties to the CTN than the Chairs and Executive Officers that participated in the focus group discussions. Key questions included in network evaluation surveys include strengths and weaknesses of the network[9], and commentary on the achievement of the network in certain areas such as communication, leadership and organisation[7,10]. A further tool that can be developed by ACTA is a CTN evaluation framework that networks can adapt to gain feedback from their membership on their success.

A further activity that could be undertaken to support this work would be to use the critical success factors defined in this report to complete a full evaluation of all CTNs within the sector. This would provide an opportunity to identify areas where shared resources could improve effectiveness and efficiency across networks, and to make recommendations for individual CTNs that could improve the effectiveness and efficiency of their own operations.

In conclusion, the qualitative research conducted for this report has identified themes, activities and factors critical to CTN operation efficiency, effectiveness and success. Tools and resources supporting these activities have been identified and prioritised. Unmet needs specifically identified by CTNs are Executive Officer support, a sustainable funding source for central CTN operations and optimal resources at participating clinical trial sites. In the future, dedicated funding that supports central and site activity of all CTNs could maximise the cost-effective contribution that investigator-initiated clinical trials and CTNs can make to the advancement of healthcare and patient outcomes as part of a fully integrated Learning Healthcare System.

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Lead Researcher Dr Megan Sanders

Project Assistant Mrs Anitha Balagurunathan

Chair of ACTA Reference Group A A/Professor Katie Groom

Report Working Party Dr Megan Sanders, A/Professor Katie Groom, Ms Karen Goulding, Ms Donna Reidlinger

ACTA Reference Group A members Dr Allison Bourne, Ms Linda Brown, Dr Julie Chapman, Ms Melanie Gentgall, Ms Donna Goldsmith, Ms Susan Goode, Ms Rebecca James, Professor Paul Komesaroff, Dr Kurt Lackovic, Professor Henry Ma, Professor Maria Makrides, Ms Margaret McJannett, A/Professor Ed Oakley, Ms Elizabeth Paton, Professor Tim Price, Professor Ralph Stewart, Dr Angela Watt, Ms Cate Wilson

Focus Group Participants

Australian
Clinical
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