



What works best when establishing a translational cancer research centre?

Final research report

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This report was compiled by Siggins Miller on behalf of the Cancer Institute NSW.

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CONTACT DETAILS

Address

Cancer Institute NSW,
Australian Technology Park,
Level 9, 8 Central Avenue,
Eveleigh, NSW 2015

PO Box 41
Alexandria, NSW 1435

Telephone

(02) 8374 5600

Website

www.cancerinstitute.org.au

Email

information@cancerinstitute.org.au

Emails sent to this address are forwarded to the appropriate person for action.

About the Cancer Institute NSW

The Cancer Institute NSW is Australia's first statewide government cancer control agency, established under the Cancer Institute (NSW) Act 2003 to lessen the impact of cancer.

Cancer touches the lives of everyone in our community. The Institute's vision is to end cancers as we know them, by keeping as many people off the cancer journey as possible, and by improving health outcomes for those affected by cancer across the state.

Guided by the objectives outlined in the *NSW Cancer Plan 2011–2015*, the Cancer Institute NSW works across the full spectrum of cancer control to:

- reduce the incidence of cancer
- improve survival from cancer
- improve the quality of life of people affected by cancer
- be a source of expertise on cancer control for the NSW Government, health service providers, medical researchers, and the general community.

The Institute works to achieve this by coordinating priorities, resources and efforts among all individuals, organisations and governments involved in cancer control in NSW.

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Executive summary

This report documents the research commissioned by the Cancer Institute NSW (CINSW) between December 2013 and August 2014, the third year of full operation of a funding program that created four new Translational Cancer Research Centres (TCRCs) and three new Translational Cancer Research Units (TCRUs) in that state. The CINSW investment in TCRCs aims to facilitate more efficient and effective incorporation of research, clinical training, education and service delivery within a formal framework that links leading research centres with leading clinical centres.

The ultimate goal of the investment and effort in translational cancer research is to improve outcomes for cancer patients and the community, through more patient-focused research that more quickly and effectively impacts upon the treatment and support of people affected by cancer.

The purpose of this research project was to establish a portrait of local adaptations of the CINSW's TCRC model; gather local perspectives of the characteristics, mechanisms, processes and contexts which have facilitated a TCRC's success; and to identify the key

characteristics and enablers of success for TCRCs, in the form of a model which maps the salient elements and features of successful translational research centre implementation.

A mixed methods approach was employed to gather qualitative data, consisting of a preliminary literature and document review, an extensive review of internal documents relating to the establishment and operations of each Centre, interviews with key CINSW informants, reflective workshops and interviews with key stakeholders in each TCRC.

A draft model was developed that grouped the possible factors influencing the success of TCRCs in five domains: Leadership, Governance, Research strategy, Collaboration and Capacity building for sustainability. This model was enhanced, modified and validated through both internal and external stakeholder consultations and feedback from the CINSW.



The model and the factors that appear to influence the success of a TCRC are presented in this report. The NSW TCRCs vary in many ways, including the types and number of partner organisations within a collaboration, the history and traditional practice of cancer research and service delivery within the collaboration or geographic location, the extent of existing collaborations within the membership, and the age and size of the health services, universities and research groups involved. Informants were of the view that no single model necessarily fits all TCRCs, but that the development of a model will be useful as a 'menu' or as 'guideposts' for those attempting to establish these 'institutes without walls' which aim to bring together a range of new collaborators who are located in various institutions, professions and sectors.

The TCRCs were described by informants as something of a 'social experiment' that attempts to break down traditional research, professional and institutional silos. Stakeholders also thought it was too early to establish whether success factors in implementation will predict longer term outcomes such as patient and community benefit. It is hoped, however, that documenting the lessons learned for the existing centres will assist them and others in the future to know more about the significant implementation issues involved in developing structures and processes to support effective translational research efforts.

The key success factors identified included altruistic leadership that enables the success of others, governance arrangements that generate trust and provide clear policy direction, research strategies that are specific to the TCRC's context, focusing on engaging the members and enabling new collaborations, and strategically building capacity that will contribute to the sustainability of translational research within the workforce and the health system.

A 2-3 page summary of the key success factors is included in this report, in the form of a "What works best?" guide, modelled on similar publications by the NHS Service Delivery and Organisation (SDO) Research & Development Programme.¹

1. webarchive.nationalarchives.gov.uk/20090322012542/sdo.nihr.ac.uk/

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Introduction and background

Introduced by the Cancer Institute NSW (CINSW) in 2010–2011, the Translational Cancer Research Centre (TCRC) Program aims to facilitate more efficient and effective incorporation of research, clinical training, education and service delivery within a formal framework that links leading research centres with leading clinical centres.

The model of translational research adopted by CINSW is adapted from Westfall et al (2007) and the Wills Review (2012),² in essence categorising the stages of translational research as:

T1 Developing treatments and interventions

T2 Testing the efficacy and effectiveness of these treatments and interventions

T3 Dissemination and implementation research for system wide change

The key objective is to facilitate closer collaboration between researcher and clinician to drive the generation of practice-improving research and its more rapid adoption for improved patient outcomes.

Initially, there were two levels of grants offered in the program – Centre (TCRC) and Unit (TCRU).³ Seven NSW consortia were awarded funding that commenced in 2011. There was some flexibility as to funding use, with the exception of mandated activity in biobanking and governance arrangements that required the quarantine of specific funds for biobanking and the creation of the positions of a Director (fractional) and a Manager⁴ for each TCRC/U. From 1 July 2014, the former Units were awarded competitive grant funding to become centres with a further five years' funding.

Areas of flexibility in the use of funding included organisational structure and membership, which could be organised as a single free-standing organisation or a formal consortium under central leadership. Collaborating facilities were expected to collectively demonstrate excellence across at least

basic and clinical research but could also include complementary programs in other areas, such as health services, psychosocial and population research. The collaborating organisations were required to include clearly-defined networks for biobanking, cancer treatment programs, clinical care activities, professional education and training.

The funding was intended to support, for example, governance activities and personnel, professional development and training for research and clinical staff such as research scholars, clinical fellowships, travel and education scholarships, networking and outreach activities and research activities, especially in improving the science of uptake of evidence into practice.⁵

A critical element of the TCRC program is intended to be the establishment of effective collaboration and networking that will enable:

- continued development and translation of current best evidence into care (including an active research program addressing how to improve the uptake of evidence into practice)
- continued development and translation of current and new diagnostic and prognostic tests, new therapies and interventions into patient care
- translation of clinical problems into research questions
- collaborations between clinical and research disciplines, leading centres of research and clinical services.

The purpose of this project has been to:

- establish a portrait of local adaptations of the CINSW's TCRC model
- gather local perspectives of the characteristics, mechanisms, processes and contexts which have facilitated a TCRC's success
- identify the key characteristics and enablers of success for TCRCs, in the form of a model which maps the salient elements and features of a successful translational centre.

The research took place between December 2013 and August 2014.

2. NSW Health (2012). NSW Health and Medical Research Strategic Review www.health.nsw.gov.au/ohmr/Documents/medical_strategic_review_.pdf; and Westfall JM, Mold J, Fagnan L (2007). Practice-based research—"Blue Highways" on the NIH roadmap. JAMA 297 (4): 403–406.

3. A maximum \$1.3m per annum is available to fund each TCRC for five years (or a maximum of \$500,000 per annum for each TCRU for three years), which includes a minimum \$100,000 per annum towards a collaborative biobanking fund (\$40,000 per annum for collective biobanking in each TCRU).

4. In TCRUs, the Manager position could also be fractional. In TCRCs the Manager position was full-time.

5. Cancer Institute NSW Guidelines for Applicants.

Methodology

Select literature review

Siggins Miller was asked to use a 'mixed methods' approach that commenced with a select literature review of peer-reviewed international literature and grey literature on evaluation of translational research and research centres, transforming translational research, and the effectiveness of translational research.

This preliminary literature review informed the development of a research framework and methodology. During the course of the project, informants provided additional sources that have been included in the final version of the literature review which forms *Appendix B* of this report.

Siggins Miller developed a research framework that mapped likely data sources against the research questions. This framework was used when reviewing the documentation for each TCRC.

Document review

Approximately 200 documents were reviewed, consisting of CINSW Guidelines, TCRC/U applications, progress reports, reporting spreadsheets, case studies, supporting documentation and the reports of CINSW External Expert Reviewers. In addition, the websites of the seven consortia were examined, particularly for updated information and for details of their membership approach.

Some data quality issues that needed to be considered include:

- consistency of data collection, recording and reporting
- relevance of data items to the program logic, the research questions and the activities of new types of research organisations
- clarity of data collection methodology and data terms employed
- potential for data 'doctoring'
- extent and frequency of existing analyses and reporting of data
- the relatively short timeframe for delivering outcomes that could be evidenced as 'success' in a TCRC.

From the document review, a draft portrait of the local approach of each TCRC was developed, together with a draft sub-program logic that conformed to the style and approach of the CINSW's overarching program logic for its entire translational cancer research investment. These documents form *Appendix C* of this report.

From the document review and the literature review, a draft model of good practice in implementing TCRCs was developed for discussion with stakeholders.

Stakeholder consultations

Consultations were both individual and group-based, using consultation plans and protocols developed to address the research questions. CINSW stakeholders were consulted, both as a group and in individual telephone interviews.

Site visits occurred later in the project, after the completion of the document review. Protocols consisted of a generic format, with aspects tailored towards different sites where relevant. The protocols and research tools developed for the project, together with the thematically arranged, qualitative data from interviews and workshops were submitted to the CINSW in a Progress Report on 15 August 2014.

The key stakeholders for inclusion in the review project were identified by the Cancer Institute NSW and included:

- Cancer Institute NSW Executive
- Cancer Institute NSW Strategic Research Investment Division
- TCRC/U Directors
- TCRC/U Managers
- Members of TCRCs, as nominated by their Directors and Managers.

Site visits: face-to-face reflection workshops

Siggins Miller facilitated eight⁶ reflection workshops to discuss the draft model. The workshops involved small groups of people (5 –10 members; most of whom were involved in some aspect of TCRC governance and leadership) who participated together, responding to each other's comments. Some advantages of the group approach for qualitative inquiry, as identified by Patton,⁷ include cost-effectiveness, interaction among participants enhanced data quality (through checks and balances) and easy identification of shared views.

Where a critical informant was not available on the date of the site visit, a phone interview (using the draft model as the basis of the interview) was used as an alternative.

Data analysis

A large amount of qualitative data was generated from consultations. We applied a 'framework analysis' approach to the analysis of data from interviews and reflective workshop groups.⁸

The linear steps were: familiarisation; identifying a thematic indexing; charting; mapping and interpretation. Themes were developed both from the responses to the draft model and the research questions and from the narratives of stakeholders consulted. All consultants (including the external expert) involved in the site visits and interviews were involved in the analysis to ensure continuity and to check reliability of interpretations and analysis of the qualitative data.

Confirmatory input from stakeholders

For confirmation purposes, each TCRC was provided with the summary of the qualitative data collected from their site's reflective workshop, the draft sub-program logic for their TCRC and the draft 'portrait' of their local adaptation of the CINSW's model of translational research. TCRCs were asked to check each document for currency and accuracy prior to inclusion in this report. At the time of writing, four of the seven TCRCs had submitted updates to their 'portraits' and four TCRCs had modified the sub-program logic for their centre.

6. One TCRC, split over two metropolitan hospitals, required two separate site visits to accommodate clinical rosters. An additional preliminary presentation was made to Centre Directors prior to the site visits.

7. Patton MQ (2002). *Qualitative Research and Evaluation Methods* (3rd edition). Thousand Oaks, CA: Sage Publications.

8. Krueger RA, Casey MA (2000) *Focus Groups: A Practical Guide for Applied Research*, 3rd ed. Thousand Oaks, CA: Sage Publications; and Ritchie J, Spencer L (1994). *Qualitative Data Analysis For Applied Policy Research*. In Bryman A, Burgess RG (eds). *Analyzing Qualitative Research*. London: Routledge.

Issues from the literature review applied to this study*

Key success factors

The literature points to success factors that are specific to delivering on the promises of translational research, which Chubb (2012) describes as having “a key part to play in improving our lives and also in justifying taxpayer dollars [spent on research]”.

Research to develop frameworks and guidelines for translational research centres points to the pivotal role of organisational policies and strategies (Rajan et al 2013; Dilts 2013), with emphasis on achieving a shared understanding of the purpose of the total investment, clear and transparent prioritisation processes (Grazier et al 2013; NCI 2010), greater attention to context and external validity (Schillinger 2010; Glasgow and Emmons 2007), and coordinated management of research collaborations that involve partnership with relevant decision-makers and target audiences from the outset (Glasgow and Emmons 2007; Wallerstein and Duran 2010).

Tailored funding programs can underpin and demonstrate a centre's priorities, through providing incentives, selecting promising early translational research (NCI 2010), encouraging collaborations that use the complementary strengths of diverse research partners (Bahr and Cohen 2008; NCI 2010), and supporting targeted training programs and career incentives for researchers (NCI 2010).

It is important that centres have the capacity to:

- identify gaps and opportunities, in terms of resources and access to those resources (NCI 2010)
- identify, attract, develop and retain the right people – both staff and network partners (Grazier et al 2013)
- develop clear recruitment strategies (Rajan et al 2013)
- develop sound management systems (NCI 2010) that include the capacity to document the reach, adoption, implementation and maintenance of interventions (Glasgow et al 2003).

All of these factors identified in the literature emerged in this study of NSWTCRCs, albeit with different emphases or approaches.

Terminology

There are varying uses and understandings of terms like ‘translational’ and ‘translation’ research in the international literature. The definition of translational research that is agreed by the TCRCs and was used in this study is based on the adaptation of the Westfall et al (2007) model and the Wills Review (2012) as outlined above. Therefore, for the purposes of this study, the term ‘*translational research*’ covers the continuum from upstream bench science (T1), through trials of intervention effectiveness or efficacy (T2), to studies of dissemination, implementation or diffusion of the research (T3). Participants in this study commonly referred to T1/T2 research (basic science and clinical trials) and the newer area of ‘implementation research’ (T3).

The term ‘knowledge translation’ appears in the literature to describe a dynamic and iterative process that includes synthesis, dissemination, exchange and application of knowledge to improve health, health services and the healthcare system. This term also appears in the strategic decision-making of several of the NSWTCRCs, particularly in prioritising the development of platforms for engagement and information exchange between the members of TCRCs.

In attempting to explain why “one of the most consistent findings from clinical and health services research is the failure to translate research into practice and policy” (Grimshaw et al (2012), some authors point to the key differences between efficacy intervention studies (“*Did the treatment cause the effect?*”) and effectiveness intervention studies (“*Can you generalise the results?*”) (e.g. Schillinger 2010; Glasgow et al 2003). These authors argue that most interventions that are assessed as efficacious tend to be intensive and demanding of both staff and participants, but these measures may also limit the generalisability of the findings. Differences in emphasis between the NSWTCRCs regarding efficacy versus effectiveness intervention studies were evident during the consultation process, and were often reflected in research strategies and priorities.

* See the bibliography in the Literature Review for the details of references in this section.

Interpretations of the end point of translational research can differ (Woolf 2008; Venter 2010). This was evident in differences in priorities and emphases between some of the NSW TCRCs. One interpretation is that translational research means the “bench-to-bedside” where the end point is a promising new treatment that can be used clinically. Another interpretation is that translational research means translating research into practice, ensuring that new treatments and research knowledge actually reach the patients or populations for whom they are intended. The end point for “bench-to-bedside” translational research is only the starting point for this second area of translational research which seeks to close the gap and improve quality by improving access. This often requires behaviour change and culture change within traditional systems and professions. Consequently, different emphases have emerged within different TCRCs, depending on their context and leadership.

Measures of success

There is considerable discussion in the literature about appropriate measures of success for translational research efforts, reflecting the particular challenges in assessing the impact of investments in TCRCs as new ways of working. The *Stockholm Declaration* (2008) committed European Union (EU) cancer clinicians and scientists to a consensus based framework for translational cancer research. An 18-month consensus-building exercise clearly found that assessing excellence in translational research should be based on qualitative rather than quantitative criteria. EU participants felt that the assessment of excellence itself should focus more on how efficiently the results are being used and the quality of their outputs.

The “roadmap” program launched in 2002 by the US National Institutes of Health (NIH) explicitly states that funded institutions are given wide latitude to choose the structure and methods for evaluating their local program (Kane et al 2013). The common view of TCRC participants in this NSW study (i.e. that traditional measures of research activity have limited relevance to TCRC success) reflect the EU experience and endorse the USA NIH approach. TCRC participants in this study commonly suggested that, particularly in the early stages of a TCRC’s development, the most relevant measure is ‘new collaboration’. The literature suggests that an increase in cross-disciplinary, collaborative team science initiatives has spurred interest by multiple stakeholder groups in empirical research on scientific teams, giving rise to an emergent field referred to as the science of team science (Falk Krzesinski et al 2011). It is not yet empirically clear exactly how and when collaborative efforts actually enhance the scientific enterprise, although Dozier et al (2013) have developed a method to document emerging research networks and collaborations to describe their productivity and viability over time; and some early work has been conducted at one of the NSW TCRCs to study collaboration within networks (Long et al 2014). Similarly, Tillman et al (2013) suggest there is a need to develop new tools for detecting causal linkages among and between education, training, and other research support services and effective translational research.

Collaboration

NSW TCRC study participants consistently expressed the view that their most tangible achievement in their first three years has been building new collaborations. The literature suggests that the key factors contributing to collaboration are social and professional interaction (Cunningham et al 2011), physical co-location that facilitates even brief and focused face-to-face interaction (Boudreau et al 2012) or, where network sites are geographically dispersed, reliable virtual communication technology to support personal and professional interactions (Long et al 2014). The importance of these factors was consistently raised by TCRC informants in this NSW study.

In 2001, Pober et al observed that translational research was hindered by, among other things, a shortage of qualified investigators, an academic culture that hindered collaboration between clinical and laboratory-based investigators, a traditional structure that favoured departmental efforts over interdisciplinary programs, and an increasing regulatory burden. Similar barriers were reported to this 2014 NSW study, where participants spoke of: the scarcity of some key disciplines (e.g. biostatisticians, bioinformaticians, implementation scientists and psycho-oncologists); structural barriers posed by professional silos and by institutions; and the need to acknowledge the concerted effort and the time required to achieve behaviour change and culture change within the networked organisations of a TCRC.

Westfall et al (2007) observed that the vast majority of patients receive medical care in the ambulatory primary care setting, yet the majority of clinical research happens in an academic clinical setting.

While this may not be relevant to some NSW TCRCs (e.g. children's cancer, where the majority of treatment occurs in tertiary settings), the need to expand collaborations and research activities beyond professional groups and beyond sectors (particularly into the primary care sector and allied health professions) was commonly identified by TCRC informants. An emerging issue in NSW is the increasing trend for cancer treatment to take place in private sector institutions in some TCRC geographical areas. Informants suggest this increases the complexity of the nature of partnerships and the breadth of collaborations required for effective TCRCs.

Collaboration with the community is a key factor for success in many TCRC contexts. Schillinger (2010) suggests that the mismatch between a research design on the one hand and the realities in the target practice setting leads to low adoption and implementation, and proposes community-based participatory research, methods and practical clinical trials as a means of enhancing the relevance and effectiveness of public health interventions.

Some TCRCs have involved people affected by cancer in key roles in the design, planning and prioritising of research. Other TCRCs are exploring ways to involve the community in research prioritisation. Westfall et al (2009) remind us that participatory research is not simply about using a group of neighbourhoods or community members to pursue a particular research agenda—it is really about an attitude to research that embraces sharing power. It could be argued that Westfall's notion of 'sharing power' is an underlying principle of TCRCs and that this principle influences leadership, governance, research strategy and collaboration activities of a successful TCRC.

Findings



The factors influencing the success of TCRCs can be grouped in five domains: Leadership, Governance, Research strategy, Collaboration and capacity building for sustainability. Not all the factors identified within a domain are relevant to all the types of TCRCs operating in NSW. However, informants felt that the five domains captured the essential areas for effectiveness in a TCRC.

TCRC informants identified some issues where the extent of culture and system change required to enable translational cancer research may be beyond the control of a single TCRC to effectively address. These issues have been included as *Appendix A* “System level enablers” and the following discussion of the findings refers to the operations of TCRCs, as opposed to broader system level factors.

Variables, such as the types and number of partner organisations within a collaboration, the history and traditional practice of cancer research, and service delivery within the collaboration, geographic location, the extent of existing collaborations within the membership, the age and size of the health services, universities and research groups involved can all influence the relative importance of certain factors within each domain. These variables are referred to as the ‘context’ of each TCRC in the following presentation of the findings, which describes the factors influencing success within each domain.

Leadership

Leaders accept a generative role that is facilitating others and has no personal career benefits. A skilled TCRC leader is aware that their main role is to work with leadership of other disciplines and sites to create the space and resources for others to do the translational work (in the laboratory, the clinic, the health service). TCRCs are an unusual organisation type and the leadership role can bring significant risks to the capacity of that individual to meet the metrics that determine career progression and promotion in traditional research structures and processes. These risks have significant implications for succession planning and sustainability.

Consequently, TCRC leaders need to be motivated by a deep concern for others—for consumers, for the population as a whole, for global health, for colleagues and for the institution(s) in which they work. Leadership, therefore, is ascribed based on a hierarchy of competence for a functional task, rather than a hierarchy of seniority or rank. In most contexts, leaders who understand the complexities of (and have connections in) both the health services and the research/academic institutions within the network can be a critical factor for success. The cross-sectoral and multidisciplinary nature of most translational research effort requires leaders who have credibility in their own profession and sector, as well as the ability to persuade, influence and collaborate with researchers, clinicians, educators and decision-makers in longer established and more traditional institutions.

TCRCs are, in effect, ‘institutes without walls’, spread across multiple sites, sectors and disciplines. A leadership team that supports the Director; spans the whole collaboration network; and spans institutions, disciplines and sectors is crucial in underpinning a TCRC. This team of leaders needs mutual trust, a shared understanding and language about translational cancer research.

Therefore, the role of the TCRC Director is focused on coordination and guidance of effort across all sites, sectors and disciplines; and minimising the negative aspects of individual and organisational competition.

“ TCRCs are communities of interest—it’s a matter of leaders channelling that common interest. A TCRC can be a focal point for people who are wandering around with good ideas, so the ability for a leader to engage with people, communicate with them about translational research and bring them along on the journey is important. ”

The leadership approach needs to be inclusive. Including early-to-mid-career scientists and clinicians in leadership roles within the network potentially brings freshness of ideas, currency of knowledge, intergenerational sustainability and peer networking that encourages an interest in translational research, from undergraduate to post doctoral levels.

Building support within the leadership of health services is also crucial: explaining ‘what’s in it for them’ to build and support translational research within their institutions. Some successful strategies for inclusion have been to include leaders of local health services in the TCRC governance structure, or to collaborate with health services leadership in promotional, educational or community engagement activities.

Governance

Some informants described TCRCs as ‘social experiments’, requiring adaptability and the capacity to respond to new opportunities as they arise, while at the same time steering activities of the membership toward clearly defined and shared goals. In translational research efforts, these goals are patient- and community-focused, rather than institution- or career-focused.

Governance structures need to match the key collaborations, and be flexible enough to allow for the diversity of effort or shifts in focus over time. In some contexts (e.g. a greenfield site) or populations (e.g. children’s cancer), the focus of effort or the disciplines involved may be evolving or different.

Informants suggested that governance structures need to support relationships and trust, but there were differing views of how trust can best be achieved within a TCRC. The networking of long-established institutions may pose potential barriers to collaboration and innovation unless formal agreements determine governance structures and decision-making. Informal arrangements may be appropriate for other networks (e.g. where fewer ‘players’ are involved, such as in a regional collaboration).

The process of developing governance arrangements needs to address inter-institutional sensitivities. Freedom to develop and evolve appropriate governance arrangements for the context is important.

The governance structure needs to reduce the process burden and to develop new paradigms/metrics that fit the translation space, while at the same time ensuring that the reporting system doesn’t overload the researchers and clinicians. The development of sound management systems and investment in capable managers in TCRCs is uniformly reported as a crucial factor for success. Using existing reporting systems and administrative facilities can be an enabling factor in reducing process burden.

A balance needs to be achieved between accountability for the use of funds and resources, freedom to innovate (and to necessarily take some risks) and avoiding unnecessary duplication of effort or inappropriate use of ‘traditional’ governance approaches in a context of innovation and ‘newness.’ TCRCs need to work with their networked institutions, funding bodies, health system leaders and the community to develop mutually-acceptable reporting arrangements that may not be traditional.

Where groups of institutions and disciplines are joined in a network, decision-makers in the TCRC are governing for the whole, not representing parts of the whole. Consistently articulating this essential requirement to those involved in governance, and gaining the commitment of decision-makers, was reported as a major challenge, but crucial for success.

“ We were very up-front about the leadership group not deriving any personal benefit from the centre. If you don’t like it, don’t sign up. We see ourselves as ‘custodians of the process’, not the beneficiaries. Our governance structure was carefully planned to reflect our ethos of cross-sector, cross-disciplinary collaboration. ”

Good TCRC governance relies on open, transparent, continuous two-way communication with those involved in the ‘social experiment’ of establishing TCRCs. A commitment to openness, listening, sharing information and the provision of feedback is important to maintain the morale and commitment of translational researchers within a TCRC, and for the development of collegial relationships between TCRCs.

At the same time, external communications need to focus on the benefits of translational cancer research to the member organisations, the system and the community. Continually explaining the benefits of translational cancer research to the system and the community includes creating realistic expectations of what is achievable for success within timeframes.

TCRCs need to facilitate streamlining of cross-institutional governance (e.g. inter-institutional, cross-boundary research approval approaches or staffing arrangements) within their local sphere. Through collaboration with other TCRCs and the funding body, barriers to innovative ways of working can be reduced by streamlining system-level governance, so that local success in system change that facilitates translational research can be replicated or extended to the broader system.

In order to support creativity and innovation in research, governance processes need to accommodate learning from failure. TCRCs need to create a culture where failure is not automatically punished by withdrawal of support, but rather used diagnostically to develop the next round of research questions or to improve research protocols, processes or capacity. In addition, governance groups and the leadership need to actively learn from colleagues in the broader translational research community. Some TCRCs have commissioned, or are considering, external expert reviews by interstate and international colleagues for continuing quality review purposes. Advice from critical friends can lead to shifts in direction and focus that may keep a TCRC on the path towards T3, rather than staying predominantly in the T1/T2 space, or can evaluate the success or sustainability of TCRC interventions in the medium and longer term. Openness to advice and willingness to listen were identified as key characteristics for success in TCRC governance.

Good governance can be enhanced by including early or mid-career professionals in decision-making. The type and extent of involvement of the next generation will depend on the context of the TCRC, with some informants suggesting that their inclusion may be more effective after the initial start-up phase of a TCRC, as the network evolves and overcomes the inevitable early institutional barriers. Other TCRCs have actively involved the next generation from an early stage, particularly in decisions about research priorities and ways to facilitate collaboration. Mid-career researchers who are involved in TCRC governance strongly endorsed this approach and its importance for demonstrating and promoting the inclusive ethos of translational cancer research and for sustainability of the TCRC.

Similarly, some TCRCs have actively involved people affected by cancer in influencing research priorities, advising researchers in the planning and design phase, and in overall governance decisions for the network. This is a key strategy of some TCRCs to maintain the patient-centred focus of their effort. Other TCRCs are considering the involvement of people affected by cancer in the next stage of their development.

Research strategy

In formulating overarching research strategy, best practice involves working backwards from desired outcomes for patients and the community to identify ways of changing research practice (rather than forward from the needs of existing institutions or professions). Successful TCRCs will have reflected this approach in the articulation of their vision, their governance policies and procedures, and their research priorities. The TCRC provides the infrastructure and mechanisms to bring the respective strengths of different fields and backgrounds to bear on a question or problem that has been prioritised.

TCRCs need to develop strategies that will facilitate the patient-centred research of others, conducted in a range of settings across the collaboration, rather than strategies to build the reputation and research strengths of a single institution.

Strategies for generating research can be bottom-up or top-down, or a combination of both, depending on the context. Flexibility and adaptability is the key.

“With this little bit of money you’re making relationships, making time, seeding. Strategies can’t be set in concrete—you might find something that makes you see something new. Strategies need to be a living document.”

Auspecting the development and oversight of flagship programs that raise the profile of translational cancer research and disseminate their results can be a successful top-down strategy; or can be the result of having the capacity to seize opportunities to collaborate with other partners (e.g. local contribution to global translational research initiatives). For flagship programs to be successful, TCRCs need to develop a clear, shared understanding of what flagship programs are, and of their purpose. Flagships can serve the dual purpose of engaging a range of potential research collaborators and educating the TCRC membership and the health system about translational research across the T1,T2,T3 continuum.

TCRCs can have success with projects where minimal intensity is sufficient for maximum change. Such projects are often developed from a bottom-up, inclusive approach to identifying research questions. This bottom-up approach is part of a broader strategy to seed and support early stage research, through inclusive grants processes and targeted funding.

Building on existing strengths (e.g. in research methods) and applying them to different content is an important factor in success and in ‘early wins’. However, informants identified a risk that ‘working to existing strengths’ could encourage researchers to stay in their ‘comfort zone’ (principally T1, T2 research). Consequently, TCRCs need to provide support and incentives for researchers to move outside the T1, T2 arena and form new collaborations to apply their skills and knowledge to T3 research problems.

“We need to look beyond our existing strengths—that is, towards things that aren’t existing strengths in oncology. Otherwise there’s a danger that nothing new will be done. It’s a challenge to give funding to something outside your own area, but it needs to be done.”

Key to TCRC support moving into new research areas, is the strategy of providing advice and expertise to researchers, ranging from general guidance on research design to expert advice on specific projects. This includes access to expertise in implementation science, psycho-oncology, bioinformatics and biostatistics.

Projects that address local need and local context are considered a good practice for TCRCs. This good practice applies more at the T2, T3 end of the continuum than at T1, T2 (where, for example, drug or biomarker discoveries potentially have global relevance). Addressing local need and local context has been a successful strategy for TCRCs to maintain their focus on patient outcomes, maximise the impact of relatively limited resources and influence practice and collaboration within their member organisations. A local focus serves the dual purpose of achieving successful local T2, T3 and culture change to support and value T3 as part of day to day operations.

The 'virtual' nature of TCRCs (i.e. as a research facilitator—an 'institution without walls' rather than an 'edifice') has fostered strategies to adapt and influence existing facilities and practices for translational research purposes. These can include existing biobanks, lab facilities, equipment or existing clinical team structures. Innovative approaches have included: embedding TCRC pathologists in existing biobanking facilities; assigning biostatisticians as mentors of early-stage researchers; and embedding scientists and researchers in multidisciplinary clinical teams.

TCRCs work with health service providers and university partners to facilitate access to data that will inform research by the membership. It is a complex undertaking to address issues of data access, data linkage and the capacity to track the patient journey (including comorbidities, side effects and survivorship). As the composition of TCRC membership evolves (e.g. to include more geographically dispersed partners, or to include private health services which increasingly deliver cancer treatment), this will become an even more complex undertaking. Best practice in this research-enabling strategy will involve facilitating and streamlining system-level data collection and accessibility. This will be most feasibly achieved through collaboration with other TCRCs, the funding body, policy makers and data custodians within the health system.

Another key strategy is to enhance access of the TCRC's current and potential research workforce to education and training in translational research skills. Activities can range from raising awareness and exposure of undergraduate science students to potential translational research careers, through providing opportunities for experienced clinical staff to learn about and become involved in translational research, to enhancing the skills and understanding of experienced researchers with existing track records in traditional research groups. Including education expertise in the TCRC leadership team has proved critical in the capacity-building activities of some TCRCs.

As TCRCs evolve from the set-up phase, developing the capacity to facilitate and coordinate access to training programs offered across the whole network of TCRCs, enhance cooperation and reduce duplication of effort will enable best practice in research capacity-building.

Collaboration

A fundamental aspect of translational research effort is the need to build new types of collaborations that will generate new research questions, new ideas and new approaches that will accelerate the translation of research into practice.

The foundations of interdisciplinary, cross-institutional and cross-sectoral collaborations in translational cancer research are: a shared understanding of the key research questions; an agreed translational cancer research agenda for the TCRC; and a shared understanding of the contributions of all relevant disciplines to answering the research questions or to the implementation of the research agenda.

Transdisciplinary collaborations need to break down silos, and TCRC policies can provide incentives for new types of collaborations (e.g. as a condition of funding). However, informants identified potential risks to achieving genuinely innovative collaborations, where funding requirements could simply create collaborations of convenience to gain funding. Careful planning of incentives to encourage collaboration is important to achieve the right outcomes, emphasising the need for new rather than existing collaborations.

“ Some research partners were forced together in the interest of getting a grant, rather than in the interest of good science. Done over again, we would have planned it more carefully, and had more or different research partners and key players. ”

Different approaches have been developed by TCRCs to encourage new collaborations that are based on good science and new research questions. These include: specifying the types of collaborators/disciplines expected; providing a step-by-step model for researchers without a track-record in conducting T3 research; requiring cross-disciplinary supervision of PhD students as a condition of scholarship award; and requiring research problems to be generated by MDTs and research projects 'owned' by MDTs.

It is clearer and more credible for TCRCs to measure such things as new collaborations and their outcomes in projects and funds than it is to show a causal link to overall funding of established projects or institutions where partners feel the research would have happened anyway.

To foster new collaborations, TCRCs have developed incentives and policies that facilitate both social and project-related interactions. Informants stressed that interactions need to be at two levels—‘scientific’ socialising and the ‘colloquial’ building of human links between people working together across multiple sites. A key incentive is providing information or opportunities that make potential researchers want to engage with the TCRC. To this end, TCRCs have developed services and platforms for information exchange that attract potential researchers to be engaged with their TCRC network. For example, web-based platforms can provide tools to help researchers find potential collaborators or mentors, and to help groups of investigators do their work together (e.g. sharing documents, sharing ideas, hearing about new opportunities).

“ The membership needs to feel that they belong to an organisation; that it is of value and that it will support them. Strategies we use include a newsletter, website; celebrating excellence; dinners to encourage face-to-face engagement and a more intimate, social atmosphere; and postgraduate and early career colloquia, matching them with mentors. ”

Through policies and incentives, TCRCs should promote a culture that is non-competitive and rewards the sharing of ideas and resources. They need to develop an understanding of how teams work within their member organisations and of each workplace culture, using this knowledge to tailor communication styles and approaches that will develop a shared language and understanding of translational cancer research, and achieve engagement of people working in those organisations.

A priority is for a TCRC to work with its institutional partners to provide access to virtual communications across institutional and geographic boundaries that will support collaboration. Informants stressed that this not a motherhood statement, and that failure to establish reliable communications platforms can seriously diminish collaboration and inclusiveness. Beyond their own members, a TCRC should build and encourage inter-research network collaboration, bringing together the best researchers (local, national and international). Collaborations across the system and outside the health sector are important for innovation, and for the sustainability of TCRCs.

Capacity-building for sustainability

Sustainability is a major challenge for TCRCs in Australia, which are competing with more established, traditional research groups for public research funding or scarce private or philanthropic funding. There are also crucial workforce shortages that have the potential to stymie the development of translational research expertise, particularly in T3 implementation research.

To build the sustainability of the translational cancer research workforce, a TCRC supports new and emerging talent through planned and targeted activities and through financial management that provides sufficient certainty of funding for talent support and development. Successful approaches have involved investing in education programs that span undergraduate to post doctoral levels, across multiple disciplines.

Together, the network of TCRCs and its funding body can work with colleges, professional associations and training bodies to develop a pathway for future translational research careers especially (but not only in disciplines in short supply, such as psycho-oncology, bioinformatics, biostatistics).

In its governance and leadership, a TCRC needs to provide opportunities for early and mid-career professionals in all relevant disciplines to participate in TCRC decision-making. The unusual role of a TCRC leader (as already described under “Leadership”) can mean a disincentive for leaders to stay too long in the role. Consequently, a TCRC needs to plan an agreed approach to leadership succession to ensure that competencies and relationships are maintained.

TCRCs must invest in, and support, sound management practices and managers, and the funding priorities of the TCRC need to acknowledge the importance of management support for the sustainability of the effort.

Diversifying the funding base, including involvement in national and international collaborations, is crucial for sustainability, but was identified by informants as a significant and increasing challenge in the current environment. The capacity of TCRCs to attract funding varies considerably, based on their context (e.g. a greenfield site, or an established group of relatively well resourced institutions; or geographic location) or on their strategic approach and priorities (e.g. system and culture change or supporting new researchers with no track record does not attract funding from the usual sources).

Collaboration is an important aspect of sustainability. Collaboration with other TCRCs and the funding body could explore and promote partnerships with business, research foundations and philanthropic donors that will benefit the whole translational research program.

Some TCRCs have sought, or are exploring, novel collaborations (e.g. with business, IT) both as a collaboration strategy and a sustainability strategy. Some have prioritised investment in programs that have a likelihood of continuation under the auspices of a partner in the collaboration (e.g. education programs in the university; biobanking procedures in the hospital system; changes in the composition and practice of MDTs that could become routine).

“ We thought about sustainability right from the beginning and decided to build things in the member organisations that will endure (beyond the life of the grant or the TCRC) and will be funded by those member organisations. There will always be universities and there will always be hospitals, so we invested in things that can work within their activities.”

Openly and honestly evaluating the success and impact of the TCRC's activities and interventions is a key factor. TCRCs should build an evidence base and document genuine successes that are different from what other research programs generate. As the TCRCs develop, the process of review should become routine: 'Have outcomes been sustained? If not why not?' Highlighting and celebrating what is different about TCRC achievements and approaches is important for sustainability.

TCRCs should consistently and continually promote the benefits of translational cancer research to managers and leaders of their local health services. This can include generating brief stories of success, chunks of information that promote both improved patient outcomes and improved outcomes for health services that arise from research activities facilitated by the TCRC. A strategic effort to keep the TCRC 'front of mind' for decision-makers in the local health system could be important, with the aim of eventually positioning the TCRC as intrinsic to the health service.

“ Engaging the Local Health District is the most critical thing for sustainability. They need to start thinking that a research area is like an x-ray area—part of their business. Research needs to be part of the work and the structure, with time allowed for research.”

Jointly with other TCRCs and the funding body, TCRCs can advocate to, and work with, colleges, professional associations and training bodies to develop the capacity of existing education programs to produce “scientist practitioners” with the capacity to deal with personalised medicine in all relevant disciplines (involving a re-analysis of the vocational training of health professionals in research methods).

Discussion

It is evident from this study that the experience of key stakeholders involved in establishing translational cancer research centres in NSW supports many of the success factors identified in the literature.

Informants endorsed the notion that, particularly because of the difference in approach that is required for successful translational research, organisational policies and strategies are pivotal (Rajan et al 2013; Dिल्ts 2013). Discussions of the model's domain of 'governance' consistently endorsed the notion of achieving a shared understanding of the purpose of the total investment, and clear and transparent prioritisation processes (Grazier et al 2013; NCI 2010). Informants identified governance arrangements as a key contributing factor to establishing trust between research partners. Centres had different approaches to governance, and had experienced varying degrees of difficulty in setting up these processes, often influenced by the context of each centre (the types and number of partner organisations within a collaboration; the history and traditional practice of cancer research and service delivery within the collaboration; geographic location; the extent of existing collaborations within the membership; the age and size of the health services, universities and research groups involved).

This context appears to have an important influence on the approach and trajectory of each centre, leading to caveats from informants about a 'one size fits all' model. At the same time, the importance of a TCRC's context supports suggestions in the literature that a major challenge for TCRCs is to bring together two research traditions (efficacy versus effectiveness) that have evolved different methods and values. This particular challenge for translational research points to the need to apply greater attention to context and external validity (Schillinger 2010; Glasgow and Emmons 2007), avoiding the assumption that effectiveness research naturally and logically follows from successful efficacy research and paying attention to factors that limit robustness across settings, populations and intervention staff (Glasgow et al 2003). This difference in emphasis between TCRCs is relevant to the model's "research strategy" domain, with contextual factors like age and size of the collaboration partners, amount of funding and geographic location appearing to be important.

There was a certain amount of consistency between the approaches of TCRCs to tailored funding programs that underpin and demonstrate the centre's priorities. As the literature suggests, these aim to provide incentives, select promising early translational research (NCI 2010), encourage collaborations that use the complementary strengths of diverse research partners (Bahr and Cohen 2008; NCI 2010), and support targeted training programs and career incentives for researchers (NCI 2010). Informants identified these approaches in the domains of 'governance', 'research strategy', 'collaboration' and 'capacity building for sustainability'. TCRCs uniformly felt that their most tangible successes to date had been in fostering new collaborations between researchers, using tailored funding programs, policy levers, training programs, co-location of diverse professional groups, social and information sharing events and investments in infrastructure to support web-based activity across their collaborative community. All these strategies are identified in the literature and the NSW experience has confirmed their relevance to TCRCs.

Differences between centres were, again, largely in emphasis and the amount of funding allocated, with the exception of eligibility for TCRC membership and therefore eligibility to apply for research support or training. The contextual factors mentioned above again appear to be important in defining, identifying and encouraging potential collaborators (individuals and/or organisations). There were also different TCRC priorities and approaches to encouraging the generation of new research questions and collaborations from applicants spanning a spectrum of research backgrounds, settings and levels of research experience.

This study confirmed the importance of centres having the capacity to: identify gaps and opportunities—in terms of resources and access to those resources (NCI 2010); identify, attract, develop and retain the right people—both staff and network partners (Grazier et al 2013); develop clear recruitment strategies (Rajan et al 2013); and sound management systems (NCI 2010). Several TCRCs identified gaps in professional skill-sets and worked to address them through targeted recruitment of specialised staff who then support and mentor researchers in the collaboration network. Significant effort and funding has been directed towards improving access to biospecimens and data sources that will enhance translational research.

The literature also points to the need for meaningful evaluation of outcomes and the importance of developing the capacity to document the reach, adoption, implementation, and maintenance of interventions (Glasgow et al 2003). Several informants have this 'on the horizon' for future development, regarding evaluation of their efforts using relevant measures of success, as a crucial contributor to the sustainability of TCRCs. Much of the effort in the first three years has been directed towards establishing collaborations, governance, capacity and research strategies. Many of the research participants felt that the second phase of development of TCRCs will increasingly focus on building sustainable systems for innovation, and new collaboration and measures that will identify success in translational research as patient, system and policy outcomes.

A key domain in the model is 'leadership'. All informants spoke of the 'make or break' importance of particular leadership attributes. The 'leadership' domain emerged largely from the consultations in this study, rather than from the literature about translational cancer research centres, although there is some emerging literature about the unique features of leadership in 'extra mural' translational cancer research collaboration. The unique leadership features identified by informants include altruism and the willingness to work to enhance the research of others, while at the same time being willing to put their own research interests on hold or focus their effort on activity that is likely to have no personal career benefit.

Consideration of these TCRC leadership features inevitably led to consideration of sustainability of TCRCs. The domain of 'capacity-building for sustainability' includes consideration of sustainable leadership, as well as workforce and funding sources. Sustainability issues are touched on in the literature but, for participants in this study, sustainability was 'front of mind,' considering the research and health services funding environment in Australia and trend towards increased privatisation of cancer treatment and health services.

This study has been an opportunity to investigate how a semi-structured funding program has been utilised by different collaborative partnerships to build a translational cancer research 'institute without walls' in different contexts. While this type of TCRC is not a unique model (see for example Harvard Catalyst), it was a

first for the state of NSW. By pooling the wisdom of the key players, this study has enabled a reflective learning process that can inform others who are considering greater investment in translational research.

There were also limitations to the study. The TCRCs are at relatively early stages of development, as is the CINSW program as a whole, and over-interpretation of very early outcomes should be avoided. The lead time for many of the activities of TCRCs to produce tangible results is considerable, and the need for more relevant measures of success is identified in the literature. Consequently, attributing causality to any of the activities of a TCRC was not a credible option and identifying the factors contributing to success can only be an early stage in a longer study of the determinants of the successful implementation of translational cancer research centres.

Overall, the five domains of this model are supported by the international literature. However, the outcomes of qualitative research in this study reflect the importance of considering the context of each TCRC investment. There are risks in developing one model for all scenarios, and risks in using standard measures of success that do not allow for local context or the complexity of the health system and the 'behind the scenes' nature of much of the work undertaken by TCRCs. The literature talks about the need to engage external stakeholders (Westfall et al 2009) to demonstrate the extent of translational activity to the public (NCI 2010), and informants advised to create realistic expectations of what can be achieved by a TCRC.

Consequently, as TCRCs move to their next phase of development, further investigation of the leadership, contextual factors and metrics that may impact upon the sustainability of TCRCs may be beneficial.

In the meantime, a series of 'guide posts' for those establishing TCRCs has been developed from the outcomes of the study. This summary of the key success factors is presented below, in the form of a "What works best?" guide, modelled on similar publications by the NHS Service Delivery and Organisation (SDO) Research & Development Programme.

What works best?

Advice from TCRCs and the literature

In 2010, the Cancer Institute NSW (CINSW) commenced a funding program that has resulted in the creation of seven new translational cancer research centres (TCRCs) in NSW. The CINSW investment in TCRCs aims to facilitate more efficient and effective incorporation of research, clinical training, education and service delivery within a formal framework that links leading research centres with leading clinical centres.

The ultimate goal of the investment and effort in translational cancer research is to improve outcomes for cancer patients and the community, through more patient-focused research that more quickly and effectively impacts upon the treatment and support of people affected by cancer.

In August 2014, CINSW completed a qualitative research project that investigated the international literature on best practice in TCRCs, established a portrait of how each NSW TCRC had developed and, through consultation with key stakeholders, pooled the wisdom of those involved in establishing TCRCs to

identify the characteristics, mechanisms, processes and contexts which have facilitated a TCRC's success. The international literature points to key factors for success, including the pivotal role of organisational policies and strategies (Rajan et al 2013; Dilts 2013) and tailored funding programs that can underpin a centre's research and collaboration priorities, through providing incentives, selecting promising early translational research (NCI 2010), encouraging collaborations that use the complementary strengths of diverse research partners (Bahr and Cohen 2008; NCI 2010), and supporting targeted training programs and career incentives for researchers (NCI 2010).

As a result of the literature review and qualitative research, the CINSW has identified five 'domains' that are important in the success of a TCRC.

These domains form a 'model' which is based on learning from the NSW experience. It aims to provide guidance and advice about 'what works best' for those who may be considering investment in translational cancer research.



Leadership

Build a leadership team that:

- consists of people who are respected for their competence, not for their seniority or rank
- has mutual trust, a shared understanding and a shared language
- includes a range of key disciplines and sectors and is dispersed across network sites
- is altruistic and willing to work to facilitate the research of others, not themselves
- minimises the negative aspects of competition between individuals and organisations
- plans for leadership succession and develops future leaders
- works to build support for the TCRC within the leadership of local health districts
- continually explains the benefits of translational research to institutional partners and creates realistic expectations among stakeholders.

Governance

Create a governance structure and approach that:

- matches key collaborations and reflects the ethos of sharing
- is flexible enough to allow for shifts in focus over time and to respond to opportunities as they arise
- minimises process burden
- governs for the whole, doesn't represent parts of the whole
- addresses inter-institutional sensitivities
- develops new metrics for translational research
- ensures that reporting systems don't impede research activity
- supports open, transparent, continuous internal two-way communication
- generates external communications that focus on benefits to system, organisation and the community
- facilitates and streamlines system-level governance (e.g. inter-institutional, cross-boundary research approval approaches)
- builds a culture of innovation that allows for learning from failure
- includes early-stage professionals
- includes people affected by cancer to inform research priorities and approach

- regularly seeks advice from critical friends in translational research (both locally and globally)
- regularly evaluates and documents the effectiveness of interventions facilitated by the TCRC.

Research strategy

Research strategy can be 'top-down' or 'bottom-up', or a combination of both, or the strategy can change over time. Flexibility and adaptability is the key.

Some useful strategies are:

- Work backwards from desired outcomes for patients and the community, rather than forward from needs of existing institutions or professions.
- Enhance access of the TCRCs current and potential research workforce to education and training in translational research skills.
- Develop a clear, shared understanding of what flagship programs are, and their purpose, then auspice the development and oversight of flagship programs that raise the profile of translational cancer research and disseminate their results.
- Support projects where minimal intensity is sufficient for maximum change.
- Provide advice and expertise, ranging from general guidance on research design to expert advice on projects.
- Build on existing strengths (e.g. in research methods) and apply them to different content.
- Support projects that address local needs and local context.
- Adapt and influence existing facilities and workplace structures for translational research purposes.
- Seed and support early-stage research, through inclusive grants processes and targeted funding.
- Provide the infrastructure and mechanisms to bring the respective strengths of different fields and backgrounds to bear on a question or problem.
- Work with health service providers at the system level to address issues of data access and data linkage.
- Work with other TCRCs to coordinate access to training programs offered across the network of TCRCs and reduce duplication of effort.

Collaboration

Develop a shared understanding of:

- the key research questions and an agreed translational cancer research agenda for the TCRC
- the contributions of all relevant disciplines to answering the research questions or implementing the research agenda.

In developing your policy and incentives, make sure that you:

- understand how teams work and the workplace cultures within your member organisations
- acknowledge the diversity of cultures within research networks and develop flexibility in expectations and metrics accordingly.

Use policy and incentives to:

- encourage trans-disciplinary collaborations that break down silos, both in research activity and education
- facilitate new collaborations that are based on good science and new research questions
- promote a culture that is non-competitive and rewards sharing of ideas and resources
- build inter-research network collaboration, bringing together the best researchers (local, national and international)
- develop services and platforms for information exchange that attract potential researchers to be engaged with the TCRC network
- promote both social and project-related interactions
- provide access to virtual communications across institutional and geographic boundaries.

Capacity-building for sustainability

For a TCRC to be sustainable beyond the life of a start-up grant:

- set realistic expectations and time frames for achievement
- allow for the time required for the establishment phase of a new TCRC
- prioritise investment in programs that are embedded in established institutions (e.g. universities and hospitals)
- document and continually promote successes to local health district contacts
- support new and emerging talent
- provide sufficient certainty of funding to enable planning and delivery of talent support and development
- invest in education programs that span undergraduate through to post doctoral, in multiple disciplines
- include early career professionals in decision-making
- invest in and support sound management and managers
- diversify the funding base, including involvement in national and international collaborations
- work with national and international funding bodies to promote translational research and joint effort
- seek diverse partners and donors, including business and IT
- advocate and negotiate with local health district leadership to develop ways of tying translational research activity to funding.

Appendix A: System level enablers

TCRC informants consistently and uniformly identified some issues where the scope of culture and system change required to enable translational cancer research may be beyond the gift of a single TCRC to effectively address.

They suggested that, in concert with the local efforts of a single TCRC, either through collaboration between TCRCs or with the funding body, broader system-wide effort could be a significant enabler. These system-wide enablers included:

- promote a shared understanding of the agreed translational research agenda of the program and the jurisdiction, especially realistic expectations of what can be achieved within the funding envelope and time frames
- build support within the health system and government for new approaches to research
- avoid perverse incentives that may sustain traditional ways of working or reward competition rather than collaboration
- ensure that funding, reporting and accountability mechanisms not only allow for innovative approaches that may not succeed, but lead to 'learning organisation' cultures and processes
- negotiate on behalf of the whole program to resolve issues that are system-wide
- accountability arrangements are flexible enough to allow TCRCs to redirect resources to take advantage of new translational cancer research opportunities
- KPIs of the funding body provide relevant measures
- facilitate and coordinate access to training programs offered across the network of TCRCs and reduce duplication of effort
- through policies and incentives, promote a culture within the whole translational research program that is non-competitive and rewards sharing of ideas and resources
- acknowledge the diversity of cultures within research networks and develop flexibility in expectations and metrics accordingly
- provide sufficient certainty of funding to enable planning
- work with Colleges, professional associations and training bodies to develop a pathway for future translational research careers (e.g. in psycho-oncology, bioinformatics, biostatistics)
- the funding envelope acknowledges the importance of management support
- work with national and international funding bodies to promote translational research and joint effort
- explore and promote partnerships with business, research foundations and philanthropic donors that will benefit the whole translational cancer research program
- work with Colleges, professional associations and training bodies to develop the capacity of existing education programs to produce scientist practitioners with the capacity to deal with personalised medicine in all relevant disciplines (involving a re-analysis of the vocational training of health professionals in research methods)
- advocate and negotiate with health system leadership to develop ways of tying translational research activity to total health service funding. (Informants suggested that the KPIs of Local Health Districts and Cancer Services CEOs do not adequately reflect the role of research in health services (probably for historic reasons) yet T2/T3 in particular are clearly of immediate and local benefit to the service and a campaign to get the benefits of T2/T3 research recognised in KPIs at, say, NSW Ministry of Health would be strongly and happily supported by the TCRCs and could be a major plank in future sustainability. At a broader system level TCRCs could advocate ways of providing incentives to health service managers to support translational research).

Appendix B: Literature review

Rapid literature review: Translational Research Centres

Prepared for the NSW Cancer Institute by:
Ian Siggins & Mary-Ellen Miller

January 2014

Updated August 2014

Translational research – a rapid literature review

This rapid literature review was conducted to help inform development of research questions for the *CINSW's TCRC Review and Modelling Project* (January – August 2014). Relevant and informative articles were identified chiefly through Google Scholar, CINAHL, PubMed, and references and bibliographies in seminal articles. The review focused on recent publications in these categories:

1. Definitions of translational research
2. Frameworks
3. Models
4. The science of science management – evaluation
5. Collaboration
6. Dissemination
7. Barriers
8. Engagement
9. Supporting translational research in Australia

The importance of translational research for Australia

Australia's Chief Scientist, Professor Ian Chubb affirmed the importance of translational research in his keynote address to the 2 Biomelbourne Network in 2012. In part, he said:

"Today, it takes a minimum of 6.3 years for evidence to reach reviews, papers and textbooks. On average it *then* takes an additional 9.3 years to implement evidence from reviews, papers and textbooks into clinical practice.⁵

"Translational research is heralded as the answer. It has a key part to play in improving our lives and also in justifying taxpayer dollars. Because the underlying question is *always* 'is the country gaining the greatest possible practical benefit from its research investment?'

"By comparison to the investment in basic research, relatively little government funding or private capital is available for translational research. Since 2002, the NHMRC has increased its funding for translational research from 0.5% to about 4% – around \$30 million in 2011.⁶ By contrast, the US and Europe have invested heavily in translational research. In the US, the NIH have invested \$480 million in its Clinical and Translation Science Awards, and another \$500 million in a National Centres for Advancing Translational Sciences. And in the UK, they have recently invested 900 million pounds setting up a system similar to the US.

"By funding basic research, we have seen that there is usually little return, certainly very little *immediate* return. Basic research is rarely developed in a practical way for doctors, hospitals or pharmaceutical companies (and it leaves the door open to those who might argue that we should just buy-in what we need).

"But if we invest in translational research, the wealth of knowledge available will be amplified since it all of a sudden has clinical applications. A small investment in translational research, could lead to huge outcomes stemming from the basic research. Translational research, economically speaking, has a multiplier effect. Investing in translation leverages the investments made in biomedical science.

"Translational research is a priority, and the more our international competitors invest in it while we lag behind, the more challenges face us in the future. Funding is not enough. We need to change the way we recognise research, the way we engage between silos and the way we encourage future scientists. For translational research in Australia to be fully effective, we need more than funding, we need cultural change.

"And we need to ask whether, given our commendable research strengths, Australia can afford *not* to fund translational research?"

5. Australian Government 2012, Can Australia Afford to Fund Translational Research, 4 May 2015, accessed 1 August 2013, <http://www.chiefscientist.gov.au/2012/04/can-australia-afford-to-fund-translational-research/>

6. Chubb, I. (2012). Can Australia Afford to Fund Translational Research [pdf]. Retrieved from <http://www.chiefscientist.gov.au/wp-content/uploads/Can-Australia-afford-to-fund-translational-researchV3.pdf>

Definitions of translational research

The Translational Workshop at the 2013 Translational Cancer Research Conference defined translational research as *“a continuum of research in which basic science, such as research conducted in a laboratory, is translated into an intervention or therapy that is then implemented into public health policy and practice. Translational research integrates basic, patient and population science into outcomes that benefit public health”* (Hunter CRA 2014).

Venters (2010) says ‘translation’ refers to applying the results of basic biomedical research to the practice of medicine. It describes the process of converting discoveries made in the laboratory into clinical interventions that provide a direct benefit to human health. Laboratory discoveries are not typically made in a form ready for adoption by the clinician to treat patients, and research doesn’t end with the discovery in the laboratory—it is the first step on the development pathway leading to creating a treatment suitable for humans.

The Centers for Disease Control and the National Institutes of Health in the US draw a distinction between “translation research” and “translational research”. *Translation* research is the process or the sequence of events by which a proven scientific discovery is successfully integrated into established practice and policy. It does not include pure biomedical or basic science research, nor conducting an initial intervention efficacy or effectiveness trial. In this definition, translation research takes existing effectiveness studies and tries to understand the process that moves discoveries to sustained adoption. The many components of translation research comprise dissemination research, implementation research, and diffusion research—the study of how best to transfer evidence-based knowledge into routine or representative practice—and by definition it requires involvement and input of the end-user. This is not the same as the more broadly used “*translational* research”, the continuum from upstream bench science to effectiveness research (Schillinger 2010).

The NIH recognises that there is a lack of clarity in the literature among science writers about where the translational research spectrum ends and translation research work begins; and indeed much of the journal literature uses “translational research” for both processes.

The National Cancer Institute of Canada defines “knowledge translation” as a dynamic and iterative process that includes synthesis, dissemination, exchange and ethically-sound application of knowledge to improve health, provide more effective health services and products and strengthen the health care system. This process happens in a complex system of interactions between researchers and knowledge users which may vary in intensity, complexity and level of engagement depending on the nature of the research and the findings and the needs of the user of the knowledge (Best et al 2006; Canadian Institutes of Health Research n.d.).

Mold et al (2008) describe translational research as “research that seeks to characterise the sequence of events through which a scientific discovery moves between basic scientists, clinical researchers, practitioners, and consumers, and to find more effective ways to facilitate this process.” They say it can be further specified by identifying three translational phases:

- Phase 1 is basic science to human research or human research to basic science;
- Phase 2 is human research to practice-based and community-based research or practice-based and community-based research to human research;
- Phase 3 is practice-based research to practice and community or practice and community to practice-based research (often further divided into dissemination research, implementation research, and diffusion research).

For many people, Woolf (2008) says, translational research means the “bench-to-bedside” enterprise of harnessing knowledge from basic sciences to produce new drugs, devices, and treatment options for patients. For this area of research, the end point is a promising new treatment that can be used clinically. For others—especially health services providers who focus on health as the primary outcome—translational research means translating research into practice, ensuring that new treatments and research knowledge actually reach the patients or populations for whom they are intended and are implemented correctly. The end point for “bench-to-bedside” translational research is only the starting point for this second area of translational research which seeks to close the gap and improve quality by improving access, coordinating systems of care, helping clinicians and patients change behaviours and make more informed choices, providing point-of-care decision support tools, and strengthening the patient-clinician relationship.

Frameworks for translational research

In 2010, a translational research working party of the US National Cancer Institute proposed this framework of initiatives for “transforming translation”:

Coordinated management

- Establish a coordinated Institute-wide organisational approach to manage the diverse early translational research portfolio, reduce fragmentation and redundancy, and ensure that resources are focused on the most important and promising opportunities.
- Designate a specific portion of budget for early translational research to facilitate coordinated management, long-term planning, and prioritisation among opportunities and approaches as well as to demonstrate the Institute’s commitment to translational research.
- Develop a set of award codes that accurately captures the nature and scope of the early translational research portfolio to enable a complete, shared understanding of total investment, help identify gaps and opportunities, and demonstrate the extent of translational activity to the public.
- Create a transparent, inclusive prioritisation process to identify the most promising early translational research opportunities based on scientific quality, technical feasibility, and expected clinical or public health impact.

Tailored funding programs

- Modify guidelines for multiproject collaborative early translational research awards to focus research on advancing specific opportunities along a developmental pathway toward patient benefit, and to reward collaborative team science.
- Improve processes and mechanisms for review and funding of investigator-initiated early translational research to incentivise researchers to propose such studies.
- Establish a special funding program to advance a select number of especially promising early translational research opportunities identified through the newly created prioritisation process.

- Establish a program for joint centre/industry funding of collaborative early translational research projects that integrate the complementary strengths of both parties to pursue opportunities that are more attractive as a combined effort.
- Integrate access to laboratory, manufacturing and other preclinical development services more effectively with high-priority, milestone-driven early translational research projects to better address this often rate-limiting step in moving a product forward to early human testing.

Operational effectiveness

- Build a project management system involving staff both at NCI and at extramural institutions to facilitate coordination, communication, resource identification and access, and management of milestone-based progress for multidisciplinary, early translational research projects.
- Coordinate core services essential for early translational research to reduce duplication and ensure that high quality services are readily accessible to all projects and investigators.
- Improve standardisation, quality control and accessibility of annotated biospecimen repositories and their associated analytic methods to strengthen this key translational resource.
- Develop enhanced approaches for negotiation of intellectual property agreements and agent access to promote collaborations among industry, academia, Institute, and foundations.
- Increase Institute interaction and collaboration with foundations and advocacy groups to capitalise on their complementary skills and resources for advancing early translational research.
- Enhance training programs and career incentives to develop and maintain a committed early translational research workforce.

In Europe, the Stockholm Declaration of 2008 committed oncologists throughout the European Union to a consensus based framework for translational cancer research. The Declaration said:

“Oncology is a unique discipline which is increasingly depending on multi-disciplinarity. The concept was progressively defined during the 20th century and developed around clinical considerations in order to have surgeons, radiologists, pathologists, radiation and medical oncologists working together in concord. The current explosion of new concepts and technologies emerging from molecular and cellular biology has made it necessary to bridge the gap between the various fields of basic, epidemiological and clinical research. ...The translational cancer research continuum, in which the patients are always in focus, stands at the heart of a Comprehensive Cancer Center [CCC] where all components of the research process, from basic to clinical to outcome research are fully integrated with each other.” (Ringborg 2008).

The result was an intense 18-month collaborative effort to reach consensus on an agreed excellence framework (Rajan et al 2013). It used these methods: a systematic review of existing translational research models appraised for suitability in performance assessment of cancer centres; a survey of European researchers, clinicians, patient representatives and managers to score potential excellence criteria; a focus group to review and rescore the excellence criteria; an expert group to refine the list; an open validation round with stakeholders; and a critical review of the emerging framework by an independent body.

The resulting framework has 18 criteria categorised in six themes, each with its own set of agreed criteria:

- Theme 1. Organisational policies and strategies: evidence for integration of basic, translational, and clinical research with excellence in all areas
- Theme 2. People management: clear recruiting strategy to promote excellence
- Theme 3. Research infrastructure/competencies: centre has internationally competitive facilities and proven forefront expertise in a substantial number of key areas.
- Theme 4. Clinical trial management: clinical trials are well designed, with innovative aspects
- Theme 5. Internationally recognised excellence: research has resulted in changes in clinical thinking and practice
- Theme 6. Financial expertise: efficient financial management and support

The consensus building exercise found clearly that assessing excellence in translational research should be based on qualitative rather than quantitative criteria. Participants felt that while state-of-the-art infrastructure was important for excellent translational research, the assessment of excellence itself should focus more on how efficiently the results are being used and the quality of their outputs.

The European excellence framework is now being piloted (Rajan et al 2013).

Models

A group of academic evaluators charged with assessing translational efforts (Trochim, Kane, Graham & Pincus (2011) described four widely recognised models of translational research – Sung (2003); Westfall, Mold & Fagnan 2007); Dougherty & Conway 2008; and Khouri et al 2007).

Sung (2003) described translational research as two-phase framework of “blocks” in the process of moving from basic research to improved health. They called the first phase ‘T1’ and the second ‘T2’.

“The first translational block involves the transfer of new understandings of disease mechanisms gained in the laboratory into the development of new methods for diagnosis, therapy, and prevention and their first testing in humans. The second translational block affects the translation of results from clinical studies into everyday clinical practice and health decision making.”

The model of translational research offered by Westfall et al (2007) is similar but divides the process into three phases. Phase T1 goes from basic scientific research to human clinical research (early phase clinical trials in humans). Phases T2 and T3 comprise practice-based research, dividing Sung’s phase T2 into two distinct phases. In T2, knowledge is moved from the early clinical trials with patients into guideline development, meta-analyses, and systematic reviews. T3 is translation to practice, and covers dissemination and implementation research. The Westfall model says that the T2 and T3 phases are a two-directional process where practice influences research and research influences practice.

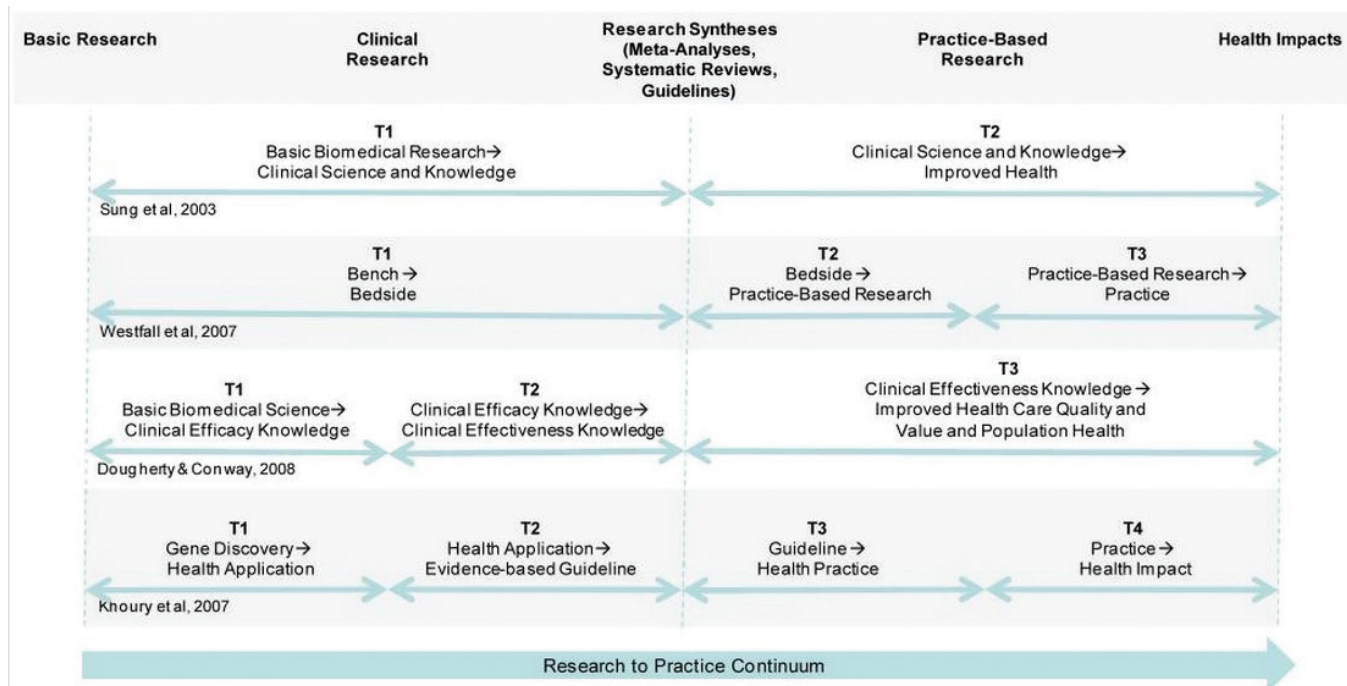
Dougherty and Conway (2008) also adopt a three-phase model, T1 from basic biomedical science to clinical efficacy knowledge, T2 to clinical effectiveness trials and development of practice guidelines and tools for patients, clinicians and policy makers, and T3 to improved health quality and population health. Each step moves to progressively broader settings over time. They also describe the bidirectional nature of the process.

Khouri et al (2007) present a four-phase model. The first two phases T1 and T2 distinguish efficacy from effectiveness studies in clinical research. Phase T3 encompasses dissemination, implementation, and diffusion research. They describe the additional T4 as “outcomes research,” which they define as:

“research that describes, interprets and predicts the impact of various influences, especially (but not exclusively) interventions on ‘final’ endpoints that matter to decision makers. Decision makers include patients, families, individuals at risk, provider, private and public payers, and so forth”

Trochim, Graham & Pincus (2011) offer a diagram (Figure 1) combining the differing phases in these four models, in an attempt to array the interactions throughout the research-practice continuum to show how translational research interacts throughout, not as a series of potentially distinct sequential phases. Translational research is seen as a continuous effort, and does not have distinct translational phases between clinical and practice research.

Fig 1 | Combining differing phases of translation across four widely recognised models of translational research (Trochim et al, 2011)



The science of science management – evaluation

Trochim and his colleagues (2011) contend that the phased model of translational research described above has been confusing, and in particular that it is unsuitable as a basis for evaluation.

“We offer an alternative to the dominant contemporary tendency to define translational research in terms of a series of discrete ‘phases’ ... We assume that translational research has potential relevance at many points along this continuum and we depict translational research as a meta-arching endeavour.”

They say that evaluation will be essential for managing translational research, learning what works and what does not, and being accountable for investments, but the current state of conceptual models and definitions poses significant challenges to the ability to evaluate. There is disagreement about where the start and endpoints are; what is being translated; whether it is a bridging or a continuous process, and the demarcation points of phases of the research.

Instead, the authors advocate identification of key operational and measurable process markers along the pathway from research to practice as the basis for evaluation of translational research.

The generic process in a research study is typically:

Application → Funding → Implementation → Publication → Replication → Synthesis → Action

At each point there are specific observable dates, events or actions that could be used as process markers, and help assess efforts to reduce the time it takes move research into practice and health impacts (Trochim et al 2011).

There has been growing recent discussion of the science of science management. As Pincus and his colleagues (2012) say: “The science of science management aims to instil empirical and methodological rigor in the decision making behind research investments.” It includes the essential role of evaluation, and the appropriate nature and methods of evaluation. The December 2013 issue of the journal *Evaluation & the Health Professions* (36: 4) is devoted to applying that discussion to translational research.

The context for much US discussion of translational research is the “roadmap” program launched in 2002 by the National Institutes of Health. Its translational research initiative is centred on the Clinical and Translational Science Awards (CTSA), a multibillion dollar program to help improve the quality, efficiency, and effectiveness of translational health sciences research. Although the NIH explicitly requires internal evaluation, institutions receiving the awards are given wide latitude to choose the structure and methods for evaluating their local program (Kane et al 2013). The initiative became a rallying point for many scientific discussions and after nearly a decade remains popular, but Balas and Elkin (2013) say that “many evaluations of its actual impact are inconclusive.”

Tillman et al (2013) have documented policies and activities of 53 US funded research programs. They find that the evidence to support the effectiveness of the programs is weak. Evaluators are challenged not only to produce better quality evaluative research, but also to develop new tools for detecting causal linkages among and between education, training, and other research support services and effective translational research.

In an editorial article for the December 2013 issue of *Evaluation & the Health Professions*, Harold Pincus and his colleagues ask: “Who needs to know what in order to answer which questions?” They write translational research in the supported institutions is evaluated in a very complex scientific, political, and social ecology. Evaluators have to negotiate different interests, understand multiple power relationships, and identify key priorities. They face multiple markets, each of which has different roles in the research enterprise, and each has different challenges. Key questions need answers, and evaluation is expected to provide the answers.

Evaluators therefore need to frame their task around the fundamental question: “*who* needs to know *what*, in order to answer *which* critical management questions?” and weigh the needs of the multiple participants – institutional stakeholders (researchers, trainees, department chairs, managers), and also national stakeholders (overseeing bodies, funders, governments and the public) who address issues that include:

“... challenges associated with first-in-human studies; limited recruitment and retention in clinical trials; the identification and measurement of health outcomes to assess intervention effectiveness; barriers to increasing awareness about research resources and potential research partnerships at the investigator and community levels; lack of incentives for team-based science; policy and regulatory challenges in developing full and substantive collaborations with industry and other partners; and ethical concerns (including related regulatory requirements) associated with the interplay between clinical research and practice.” (Pincus et al 2013, p. 45).

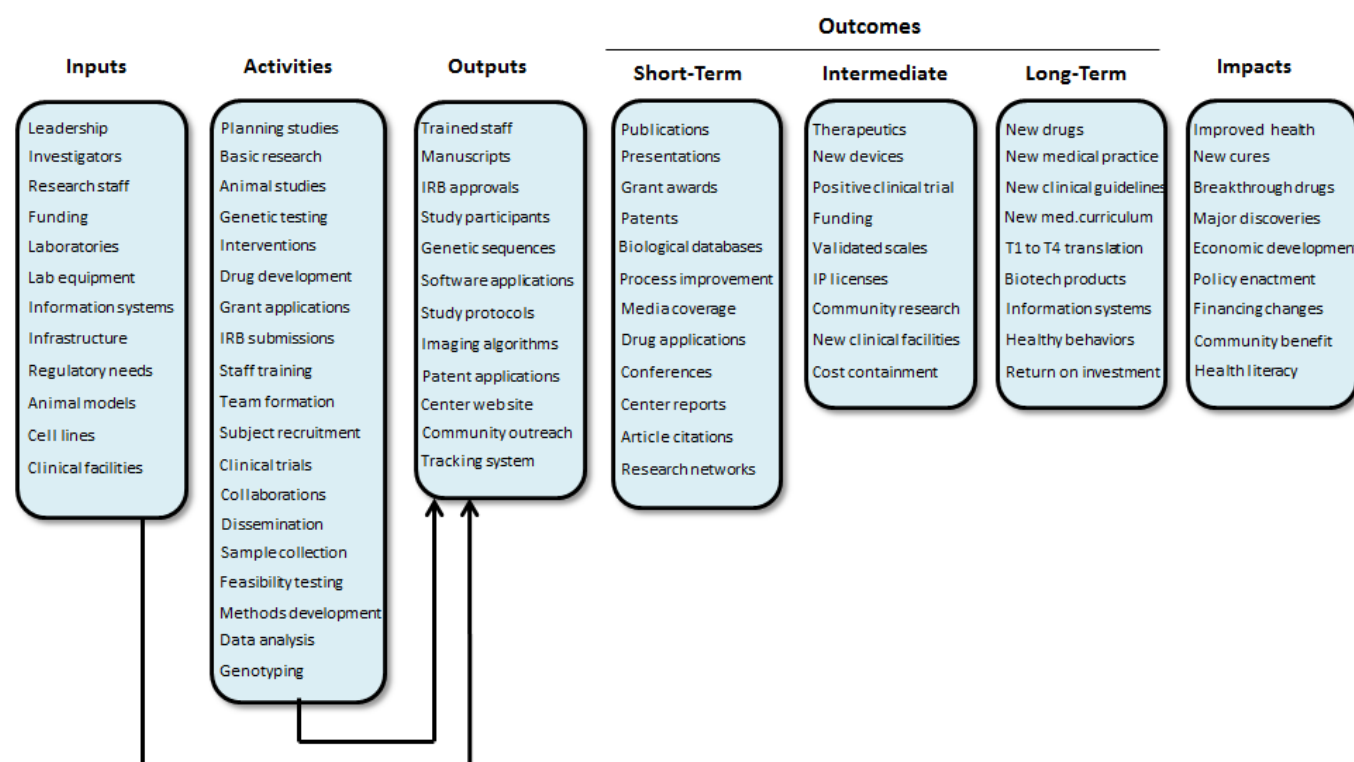
Many authors propose models and tools to facilitate evaluation of aspects of translational research, or describe evaluative processes they have used, and believe them to have wider application.

An increase in cross-disciplinary, collaborative team science initiatives over the last few decades has spurred interest by multiple stakeholder groups in empirical research on scientific teams, giving rise to an emergent field referred to as the science of team science (Falk Krzesinski et al 2011). It is not yet empirically clear exactly how and when collaborative efforts actually enhance the scientific enterprise, but working collectively poses important challenges that more solitary science avoids. The findings from this concept-mapping project constitute a prompt for advancing the science of team science at theoretical, empirical, and translational levels.

Initial progress has been made on developing a Translational Research Impact Scale, a standardised tool for identifying and measuring impacts across translational research sites for medical practice and population health (Dembe et al 2013). Many traditional measures of research impact, such as publication rates, impact factors, and patent awards, are relatively narrow in scope, and do not adequately measure the

intermediate or long-term outcomes of the research enterprise, such as adoption of new diagnostic or therapeutic practices, changes in public policy, or improvements in population health. The Scale uses a set of 72 impact indicators arranged in three broad research impact domains and nine subdomains. The Logic Model is available at http://cph.osu.edu/sites/default/files/docs/TRIS_Logic_Model.pdf

Fig 2 | Logic model determinants and outcomes of translational research



A committee of the US CTSA Consortium is developing common metrics (measures such as size, capacity, quantity, duration or frequency) to assess the efficiency of clinical research processes and outcomes, and encourage use of these metrics in data collection. It has also developed a standardised protocol to define, pilot test, refine, and implement the metrics. The ultimate goal is to learn critical lessons about how to evaluate the processes and outcomes of clinical and translational research (Rubio et al 2013).

Scott et al (2013) add questions from WHO's Health Services Program Evaluation Model to more traditionally used metrics: "The WHO approach ...focuses more on eight evaluative focal points including: relevance, efficiency, adequacy, effectiveness, process, impact, equity and sustainability." These questions, they say, can generate user judgments about how well the efforts of the research centre are progressing.

Creating and sustaining the next generation of clinical and translational research, researchers, and practitioners within a culture of innovation and excellence requires thoughtful and fair allocation of resources (Grazier et al 2013). They discuss approaches to assessing return on investment in the clinical research unit. Not only the classic indicators of economic return (such as additional grants, publications, patents), but outputs in productivity, creativity, efficiency, and better health status should also be measured. Their approach includes "identifying types of costs, impacts and values (external, internal, financial, social); creating alternative conceptual frameworks to estimate the impacts and value of translational research on individual researchers, the research enterprise, consumers of research and clinical care, and the public; surveying ... available sources and formats of economic and social impact data; determining costs of collecting and analysing financial data; testing usability of each framework and efficacy of resulting metrics; and creating protocols for use".

Dilts (2013) offers a "Three-Plus-One" evaluation model – three local levels and one global level. The primary level for evaluation is the *study* or *process* level. The *aggregate* level assesses management of the portfolio of current trials. The third, which Dilts says is often overlooked in evaluation, is the strategic level, asking whether the right trials are being conducted. Dilts'

"*plus-one*" level moves beyond the single research centre to multicenter trials and the needs of a network.

Case studies that show how successful researchers have used the translation science infrastructure allow evaluators to understand what factors lead to success, and identify patterns in complex research infrastructure in order to achieve service improvement (Hogle et al 2013).

A case report illustrates how multidisciplinary translational teams can be assessed using outcome, process, and developmental types of evaluation using a mixed-methods approach (Wooten et al 2013). Types of evaluation appropriate for teams include relevant research questions and assessment methods. Logic models are applied to both scientific projects and team development. The use of expert panels is explored.

Dilts, Cheng et al (2010) comment on the length, variability, and low accrual results of clinical trial development in cancer research, and the need for the clinical trials system to be reengineered. They identify what they call "chutes and ladders" (after the board game) – that is, points where the trial process may be expedited because the work has already been done in other research, or where gaps in knowledge appear that must be addressed before the trial can continue. They consider that improvements in clinical trials in oncology have of only limited effect if done in isolation, and there is a need for collaboration to create an efficient and effective system.

Clinical and translational research is a multidisciplinary, collaborative team process. To evaluate this process, Dozier et al (2013) developed a method to document emerging research networks and collaborations to describe their productivity and viability over time. They used an e-mail survey sent to 1,620 clinical and basic science faculty members, inviting respondents to identify their research collaborators. This low-burden approach yielded a rich dataset useful for evaluation to assess networks at individual, social, organisational leadership, physical proximity and links with other sources of data.

Collaboration

Bahr and Cohen (2008) observe that translational biomedical research involves translating scientific discoveries into new clinical diagnostics, and using the outcomes to guide further research. This often requires the expertise of researchers from a diverse range of disciplines. A key requirement to constructing multidisciplinary groups is to ensure that members have different but complementary skills. As an example, they consider the differences between a pairing of two cancer biologists, and a pairing between a biologist and clinician. The two biologists, they suggest, might discover a cure for treating a mouse model of cancer and publish their work, but this is not likely to lead directly to clinical applications. On the other hand, collaboration between the biologist and a clinician would focus on a means of applying the discovery to patients, and presents a better opportunity to develop quicker clinical applications of bench-side research. (They ask if it would be feasible to foster such collaborations by tracing co-authorship or common citations in published sources.)

The Institute for Clinical & Translational Science at the University of California Irvine is “committed to transforming ideas into medical reality.” To achieve this goal, it hosts an annual clinical translational research day to identify resources and build collaborations between researchers and community organisations involved with public health—“to break out of our silos, network, and build new and fruitful collaborations” (UCIrvine 2013)

Emmons et al (2008) says that transdisciplinary collaboration has great potential to speed the rate of adoption of evidence-based practices, and give examples of transdisciplinary collaborations in American academic and community settings, and factors that may influence the long-term outcomes of transdisciplinary efforts. As we shall see later, commentators perceive the difficulty of creating such collaborations as a significant barrier to forming translational research partnerships.

Cunningham et al (2011) found that effective, collaboratively oriented healthcare required not only efficient transmission of information, but also social and professional interaction within and across networks. Success factors to understand a network’s characteristics, attend to its functioning, and invest in facilitating improvement.

A recent field experiment in the Harvard Medical School system of hospitals and research centres tried to understand how co-location affected the likelihood of scientific collaboration (Boudreau et al 2012). While the baseline likelihood of any two researchers collaborating was small, random co-location significantly increased the likelihood of joint research grant applications by almost 70%. The results suggested that matching between scientists could produce considerable friction even among people in the same organisation and relatively close proximity and system, but even brief and focused face-to-face interactions could affect formation of scientific collaborations.

Similarly, a recent Australian study paper examined collaboration in a complex translational cancer research network of hospital-based clinicians and university-based researchers (Long et al 2014). It found that proximity and past working relationships both had significant effects on the choice of current collaboration partners. Professional grouping, a significant barrier discussed in the translational research literature, influenced past collaborations but not current or future collaborations. Since geographic proximity influenced the choice of collaborators in a dispersed network, enhancing cross site interactions by improving virtual communication technology, increasing social interactions, and maximising opportunities to meet members from other sites should be considered. Key network players had an important role to play in facilitating links between groups.

The same researchers (Long et al 2013) commented that little had been given to the importance of leadership of translational research networks in taking discoveries made ‘at the bench’ and translating them into practices used ‘at the bedside.’ Their study explored three questions: did the leaders of a TRN hold key positions of centrality or brokerage in the informal social network of collaborative ties? If so, did they recognise the leadership opportunities positions afforded them? What activities did they believe would maximise a networks success? Social network analysis found that governing body members had high brokerage potential in the informal network of work-related ties, in the face of challenges such as ‘silos’ and the mismatch between academic and clinical goals of research. Their leadership roles included expert advice necessary to coordinate effort across domains; representing a specialty, campus or research group; and mentoring and resolving conflicts within project teams. Understanding these leadership roles was a key to successful translational research networks.

Dissemination

There are repeated references in the literature to the “gap” between research and practice (e.g. Glasgow 2003; Marincola 2003; Kerner 2005; Ringborg 2008; Woolf 2008; Wallerstein 2010). “One of the most consistent findings from clinical and health services research is the failure to translate research into practice and policy” (Grimshaw et al (2012).

In a 2003 study of the quality of health care delivered to adults in the US, McGlynn and colleagues estimated that, on average, Americans received about half the medical care processes recommended. They say the substantial gap between what is known to work and what is actually done demands attention (McGlynn et al 2003).

Glasgow et al (2003) say one of the underlying reasons for this well documented gap is the assumption that effectiveness research naturally and logically follows from successful efficacy research. But these two research traditions evolved different methods and values, and as a result there are inherent differences between the characteristics of a successful efficacy intervention and an effectiveness intervention. Moderating factors that limit robustness across settings, populations, and intervention staff need to be addressed in efficacy studies, as well as in effectiveness trials. Greater attention needs to be paid to documenting intervention reach, adoption, implementation, and maintenance, to help close the gap between efficacy and effectiveness research and to guide evaluation and possible adoption of new programs. They outline the distinctive characteristics of efficacy and effectiveness intervention studies in this table (Glasgow et al 2003):

Issue	Efficacy Studies	Effectiveness Studies
Reach	<i>Homogeneous, highly motivated sample, exclude those with complications, other comorbid problems</i>	<i>Broad, heterogeneous, representative sample, often use a defined population</i>
Efficacy or effectiveness	<i>Intensive, specialised interventions that attempt to maximise effect size; very standardised; randomised designs</i>	<i>Brief, feasible interventions not requiring great expertise; adaptable to setting; randomised, time series, or quasi-experimental designs</i>
Adoption	<i>Usually 1 setting to reduce variability; settings with many resources and expert staff</i>	<i>Appeal to and work in multiple settings; able to be adapted to fit setting</i>
Implementation	<i>Implemented by research staff closely; following specific protocol</i>	<i>Implemented by variety of different staff with competing demands, using adapted protocol</i>
Maintenance and cost	<i>Few or no issues; focus on individual level</i>	<i>issues; setting-level maintenance is as important as individual-level maintenance</i>

This is a position vigorously argued in the resource manual on effectiveness, dissemination and implementation research published by the Clinical & Translational Science Institute of the University of California San Francisco (Schillinger 2010).

It says that many of the problems associated with dissemination and implementation result from the practice of sacrificing external validity in the hope of maximising the internal validity of research findings, which is the hallmark of efficacy rather than effectiveness. That is, in many studies and research designs, there may be a trade-off between internal validity (*"Did the treatment cause the effect?"*) and external validity (*"Can you generalise the results?"*). Most interventions that are assessed as efficacious tend to be intensive and demanding of both staff and participants, but these measures may also limit the generalisability of the findings. Some threshold level of intensity of intervention is probably necessary, but program designers should be developing programs of the minimal intensity needed for change, rather than maximum intensity (Schillinger 2010).

Glasgow and Emmons (2007) argue that "to enhance integration of research and practice, we need to change how we perform research program development, evaluation, and reporting. It will be much easier for local practitioners and policymakers to judge program relevance if researchers (a) pay greater attention to context and external validity and (b) partner with relevant decision makers and target audiences at the outset. This is only one of many strategies needed to increase translation of evidence-based interventions, but it is a critical component and excellent starting point." They make these summary recommendations:

- anticipate and address likely barriers to dissemination
- appreciate and integrate multiple types of evidence
- adopt research designs, such as practical clinical and behavioural trials across settings, that address concerns of clinicians and policymakers
- conduct broader evaluations that include multiple outcomes, address generalisability, and report on contextual factors
- do not expect a program to work perfectly initially, but plan for adaptation and refinement to fit local conditions and emerging issues shape the literature on what constitutes effective interventions.

They say: "What is discovered today can have a positive impact on what funders and what organisations serving your population will do tomorrow" (Glasgow & Emmons (2007).

More recently, Grimshaw, Eccles & Lavis (2012) write that one of the most consistent findings from clinical and health services research is the failure to translate research into practice and policy. As a result, patients fail to benefit from advances in healthcare, may be subject to iatrogenic risk, and healthcare systems are exposed to unnecessary expenditure. Over the last decade, they say, there has been increasing international policy and research attention on how to reduce the evidence, practice and policy gap. They summarise current concepts and evidence to guide knowledge translation activities, defined as T2 research (the translation of new clinical knowledge into improved health). They address five key questions:

- what should be transferred;
- to whom should research knowledge be transferred;
- by whom should research knowledge be transferred;
- how should research knowledge be transferred; and,
- with what effect should research knowledge be transferred?

In 2005, Ellis and colleagues set out to find what strategies to disseminate cancer control interventions that promoted the uptake of behaviour change had been evaluated. They conducted a systematic review of primary studies evaluating dissemination of five cancer control interventions: smoking cessation, healthy diet, mammography, cervical cancer screening, and control of cancer pain. They found 31 studies were identified that evaluated dissemination strategies in these five areas, and concluded there was no strong current evidence to recommend any one dissemination strategy as effective in promoting the uptake of cancer control interventions. The authors concluded that there was a strong need for more research into dissemination of cancer control interventions, and future research should consider issues such as appropriate study design and the outcomes to be evaluated (Ellis et al 2005).

Also in 2005, Kerner, Rimer and Emmons said one of the greatest challenges facing health promotion and disease prevention was translating research findings into evidence-based public health and clinical practices that are actively disseminated and widely adopted. Despite the tremendous strides made in developing effective disease prevention and control programs, there was little study of effective dissemination of evidence-based programs to and adoption by community, public health, and clinical practice settings (Kerner 2005).

In 2012, Grimshaw and colleagues suggest that the basic unit of knowledge translation should usually be up-to-date systematic reviews or other syntheses of research findings. Knowledge translators need to identify the key messages for different target audiences and fashion them in language and translation products that are easily assimilated by different audiences. There are a large number of planned knowledge translation models aimed at healthcare professionals and consumers (patients, family members, and informal carers). The evidence on the effects of different knowledge translation approaches targeting health policy makers and senior managers is much weaker, but there is a profusion of innovative approaches that warrant further evaluation (Grimshaw et al 2012).

At a basic level of dissemination, there are journals and websites devoted to publishing current papers on translation and translational research for the use of other researchers. We describe one such American collaborative venture as an example of a growing enterprise.

The US Association of Independent Research Institutes annually publishes a list of what it calls “success stories ... examples of basic research successfully moved toward translation,” with summaries of translational research by its member institutes in all fields of health, including cancer – for example, these cases from its 2011 report: tumour paint; melanoma immunotherapy; assay for lung cancer patients; a molecular test for predicting response to radiation therapy; new cancer treatments, including treatment for late-stage melanoma, and a “one-two punch” for lethal cancer; therapy for metastatic renal cell carcinoma; monitoring pancreatic cancer; a potential diagnostic tool to determine risk of ovarian cancer; and identification of carcinogenic chemicals in drinking water (AIRA 2011).

Barriers

In 2001, Pober et al asked why the boom in biomedical research discoveries, and the broad consensus within academic medical centres that a primary mission is to move scientific discoveries into meaningful clinical outcomes, had not been successfully exploited for improving medical therapy or diagnosis. They attributed the limited success of translation to various factors, chief of which is that translation was rarely straightforward and required continuing research in both the clinic and the laboratory. In addition, translational research was hindered by insufficient targeted resources, a shortage of qualified

investigators, an academic culture that hindered collaboration between clinical and laboratory-based investigators, a traditional structure that favoured departmental efforts over interdisciplinary programs, and an increasing regulatory burden.

Four years later, Mankoff et al (2004) suggested that obstacles to effective translational medicine included that fact that the available standard therapies for most common diseases were less efficacious than they are believed to be and proportionately little is spent to identify truly effective therapies. They say it may be a mistake to think that basic science, without observations in the clinic and possible associations between different noxes and disease, will efficiently produce novel therapies to test. Coordinated efforts by advocacy groups, academia and industry to educate the public of the need for translational medicine could result in novel and effective therapies.

Most of the billions dollars the US National Institutes of Health spend annually on biomedical research, Westfall, Mold and Fagnan say, is spent on basic research that aims to understand how living organisms work. A relatively smaller amount is spent on clinical studies involving people. A new initiative, the NIH Roadmap, focussed increased attention on the need to translate basic research more quickly into human studies and then, hopefully, into tests and treatments that can improve clinical practice for the benefit of patients. Inventing a new medicine or treatment is only the starting point for improving the health of an individual patient. The magnitude and nature of the work required to translate findings from human medical research into valid and effective clinical practice have been underestimated. The vast majority of patients receive medical care in the ambulatory primary care setting, yet the majority of clinical research happens in an academic clinical setting. It takes an estimated average of 17 years for only 14% of new scientific discoveries to enter day-to-day clinical practice (Westfall et al 2007).

In response to these barriers, the then Director of the NIH, Dr Elais Verhouni, said it was the responsibility of those involved in today’s biomedical research enterprise to translate the remarkable scientific innovations into health gains for the nation:

“In order to address this imperative, we at the National Institutes of Health (NIH) asked ourselves: What novel approaches can be developed that have the potential to be truly transforming for human health?” (Zerhouni 2005)

There are also intrinsic and interacting reasons for the general failure for health research to translate into practice, including economic and social policy, as well as scientific factors. Schillinger (2010) focuses on those elements of the scientific process that can present barriers to dissemination and implementation. They include characteristics of the intervention studied, the target settings, the research/evaluation design, and interactions of these three issues. As we saw above, Schillinger associates many of these problems with the practice of sacrificing external validity in the hope of maximising internal validity. Two additional barriers, he says, are that programs are not packaged so that they are straightforward to implement, and implementation materials do not permit any deviation from the original efficacy study protocol or do not describe permissible modifications.

Other elements of the research design can limit translation, Schillinger says. Small and unrepresentative samples of patients and staff cannot be generalised. Attention should be focused on inclusion of more typical settings and intervention personnel. Studies only rarely address outcomes important to

policymakers, such as cost-effectiveness or other economic outcomes. This mismatch between a research design on the one hand and the realities in the target practice setting leads to low adoption and implementation. Community-based participatory research, methods and practical clinical trials each offer means of enhancing the relevance and effectiveness of public health interventions.

A transformative research paradigm that bridges the gap between science and practice through community engagement and social action to increase health equity can help overcome these barriers, say Wallerstein and Duran (2010). Community-based participatory research (CBPR) has emerged in the last decades. As CBPR expands, so does the potential for the translational sciences to develop, implement, and disseminate effective interventions across diverse communities through strategies to redress power imbalances; facilitate mutual benefit among community and academic partners; and promote reciprocal knowledge translation, incorporating community theories into the research.

Engagement

Introducing the first edition of the *Journal of Translational Medicine*, Marincola (2003) says the purpose of translational research is to test in humans novel therapeutic strategies developed through experimentation. Translational research should be regarded as a two-way road: *bench to bedside* and *bedside to bench*. He regrets that *bedside to bench* efforts have been limited because full time clinicians have poorly understood the scientific aspects, and basic scientists have poorly appreciated the difficulty of dealing with humans. Translational research would be most useful to the scientific community at large if journals fostered specific interest in publishing *ex vivo* human observation. Peer reviewers for such articles should be clinical scientists competent not only in the intricacies of molecular or cell biology, but also intimate with the reality of ethics committees, regulatory agencies, and (most importantly) with the humane aspects of dealing with sick individuals and their families. Marincola hopes this approach may focus both basic scientists and clinicians and those struggling to fill the gap between them on the effective treatment of diseases affecting women, men and children, and make translational research more than an interesting concept.

The translational process has generally been viewed as complex and protracted, lacking clearly defined start and end points. Historically, it was represented by a single step on a linear path between scientific discovery and its clinical application (often a very long step – for example, in the case of penicillin, nearly twenty years). Today, however, translation is no longer linear or unidirectional. Translation can now happen

from both bench to bedside and bedside to bench, often with many journeys in both directions. Venters' view of translational research is of research that facilitates or enables the faster or more effective transition of basic research towards large scale evaluation to validate use for humans (Venters 2010).

Westfall and his colleagues cite Dr Kerr White as saying that one of the major problems with clinical research in the US was using tertiary academic medical centres as the chief location of research ideas and recruitment of subjects: the vast majority of research was conducted on the 0.1 % of the population who were cared for in an academic tertiary hospital. This problem was compounded by an approach that did clinical research on subjects, ignoring their unique cultural, ethnic, and geographic identities, and that focused primarily on the researchers' interests. As a result, much of the research did not readily translate into practice, nor reflect the clinical problems experienced in other healthcare settings. Many researchers have responded by moving their research efforts into the community, directly engaging the community in their research. Practice-based research mixes scientific inquiry and community engagement. However, practice-based research has faced growing confusion about the terms 'community' and 'engagement'. Participatory research is not simply about using a group of neighbourhoods or community members to pursue a particular research agenda – it is really about an attitude to research that embraces sharing power. At its core, participatory research is about conducting research **with** a group, rather than conducting research **on** a group, and **with** a community rather than simply **in** a community or **for** a community (Westfall et al 2009).

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Australian Technology Park
Level 9, 8 Central Avenue
Eveleigh NSW 2015

PO Box 41
Alexandria NSW 1435

Tel: 02 8374 5600

Fax: 02 8374 3600

Email: information@cancerinstitute.org.au

www.cancerinstitute.org.au