



Building a National Clinical Trials Network in child and youth mental health: Growing Minds Australia

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Abstract

Many fields of medicine have benefited from the formation of clinical trials networks (CTNs), whereby researchers come together on a large scale to identify high-priority questions and implement coordinated clinical trials. CTNs in the field of mental health, however, have been rare and largely absent from the Australian context. Here we present an overview of the newly formed Growing Minds Australia Clinical Trials Network (GMA-CTN), which represents the first comprehensive CTN in child and youth mental health in Australia. The 60 principal members of the GMA-CTN represent teams across 19 diverse areas related to specific forms of psychopathology (e.g., internalising, externalising, neurodevelopmental disorders, early psychosis, substance use), specific research methods and processes (e.g., health economics, e-Health, implementation science), and specialised areas of practice (e.g., school-based systems, parenting interventions, Indigenous mental health, refugee families). Core functions of the GMA-CTN include collaborative trial protocol development; peer review, prioritisation, and endorsement of proposed trials; training; development of clinical guidelines; and consumer representation. The research by the CTN will encompass the populations typically accessing youth mental health services, while placing a key emphasis on the early periods of life, and the role of parents and caregivers as critical partners in the co-design of research and the delivery of intervention and prevention strategies. The structures and processes built into the network are designed to coordinate collaboration between diverse stakeholders and ensure that provisions for translation are integrated into research from the outset. In this paper we examine the potential for a dedicated CTN to initiate fundamental improvement in child and youth mental health systems, and discuss the unique and complex challenges associated with establishing such an initiative.

Keywords: Child Mental Health; Clinical Trials; Early Intervention; Implementation Science.

Building a National Clinical Trials Network in Child and Youth Mental Health: Growing Minds Australia

The emergence of clinical trials networks (CTNs) can be considered among the most significant shifts in the landscape of health research in recent years. These networks comprise large numbers of researchers and stakeholders (e.g., practitioners, consumers), who collaborate to improve the quality and impact of clinical trials in a defined field. Core to this approach is an emphasis on improving consumer outcomes by implementing evidence-based interventions from trials aligned with the best interests of all stakeholders, and a commitment to enhancing the efficiency of research through the coordination of potentially competing trials, prioritisation of research questions, and methodological practices such as common outcome measures (ACTA, 2015). In addition to utilising shared infrastructure for trial development and implementation, CTNs typically operate through formal governance structures (e.g., steering committees, scientific advisory committees), and procedures for mutually beneficial activities such as the collaborative development of trial protocols, shared participant recruitment, and trial endorsement. This endorsement indicates that a trial has undergone peer-review by a CTN and may increase the potential to gain funding and disseminate findings based on recognition of the CTN's 'brand'.

The Need for New Approaches to Child and Youth Mental Health

Australia and New Zealand have around 35 established national CTNs, prime examples of which include the Australasian Kidney Trials Network (Morrish et al., 2013), and the Australia and New Zealand Musculoskeletal Clinical Trials Network (Buchbinder et al., 2020). Some research areas have proven to be highly fertile ground for CTNs, with at least 13 of these in oncology alone. CTNs in mental health, however, have been conspicuously absent. The decision by the Australian Federal Government to fund two CTNs

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3 in mental health through the Million Minds Medical Research Future Fund in 2020 marked a
4 major turning point. This spawned one CTN in adult mental health and one in child and youth
5 mental health (CYMH). Such investment seems well justified. According to the Productivity
6 Commission's (2020) Mental Health report, "the mental health of children and families
7 should be a priority, starting from help for new parents and continuing through a child's life"
8 (Productivity Commission, 2020, p. 2). Nonetheless, the mental health needs of children and
9 adolescents in Australia often go unmet due to poor availability and access to evidence-based
10 treatments, long waiting times, high costs, and poor recognition and understanding of CYMH
11 in the community (Boulter & Rickwood, 2013; Johnson et al., 2018; Tully et al., 2019). In
12 this paper we provide an overview of the CTN awarded in CYMH, known as the Growing
13 Minds Australia Clinical Trials Network (GMA-CTN).
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28 In many ways, the field of CYMH is unique. Child mental health is understood to be
29 highly embedded in the multiple contexts or systems (e.g., family, school, peers) nested
30 within the broader ecology of the developing child. Mental health outcomes often reflect
31 complex interactions and transactions between these contexts and individual differences at
32 the child-level, and social relationship mechanisms within these contexts are particularly
33 proximal to problem maintenance. For interventions to produce clinically significant and
34 durable gains, it is therefore often necessary to focus not only on the referred child, but
35 parents/caregivers and other agents of change across multiple contexts. Further complexity is
36 introduced by the developmental dimension of psychopathology. The risk mechanisms that
37 contribute to poor mental health are transformed significantly across development, and the
38 same disorder may necessitate markedly distinct management among children and
39 adolescents of different ages. Developmentally-specific protective factors may likewise
40 require prevention strategies to be adapted based on age (Cicchetti & Toth, 2018).
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Australia has long been home to innovation in CYMH, which in recent years has included world-leading translational research in neurodevelopmental disorders and novel models for early intervention in psychosis. At the same time, clinical services are spread across disparate and disconnected providers, spanning government CYMH services, school counsellors, general practitioners, private psychologists, psychiatrists, paediatricians, alternative health practitioners, and increasingly, online (eHealth) programs. Moreover, child mental health science and practice is often divided into disconnected silos that correspond to artificial diagnostic categories, despite evidence that most children have problems that cut across such boundaries (Astle et al., 2021; Dadds & Frick, 2019). Progress in the development of novel evidence-based treatments is often painstakingly slow due to the complexity of logistical issues such as participant recruitment. Change in the CYMH workforce is also slow and gradual due to the mechanisms on which it currently relies (e.g., university-based programs for new practitioners; continuing education workshops for existing practitioners), and the outputs of clinical trials are often not adopted in real-world settings. We would thus argue that no significant improvement in CYMH is likely without fundamental changes to the coordination of services and new approaches to research, training, and implementation science.

Toward a Learning Healthcare System in CYMH

The prospect of a CTN in CYMH is highly appealing due to its potential to promote what has come to be known as a Learning Healthcare System (LHS). A LHS is characterised by the continuous generation and implementation of knowledge from clinical research embedded within healthcare delivery (Olsen et al., 2007). As articulated in its original description, a LHS facilitates knowledge translation in order to empower a culture of shared responsibility, and engages all stakeholders in the production and dissemination of clinical

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3 evidence. This system was proposed as a means to overcome the limitations associated with
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5 traditional approaches to evidence-based medicine, such as the lengthy time-lags in
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7 translational research (Morris et al., 2011). A recent systematic review of literature
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9 concerning the adoption of a LHS in a range of fields identified 32 papers, including 13
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11 empirical studies (Budrionis & Bellika, 2016). This review indicated that mental health has
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13 rarely been an explicit focus of such work, with the exception of select areas of adult mental
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15 health, such as depression in older adults (Azar et al., 2015), and severe mental illness such as
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17 schizophrenia (Gremyr et al., 2019). The field of CYMH stands to benefit greatly from the
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19 cultivation of a LHS, and in our view the most significant benefits are likely to come from
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21 one encompassing the common forms of child and adolescent psychopathology that often
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23 first present early in development.
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31 *The Growing Minds Australia CTN*

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33 A CTN in CYMH could potentially take many forms. It has been proposed that
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35 various features of CTNs are particularly key in contributing to a LHS and therefore have
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37 important implications for the success or failure of such a network (ACTA, 2019). These
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39 features include: (1) the scope of the CTN in terms of membership and representation; (2) the
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41 capacity of the CTN to identify research questions of importance to practitioners and
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43 consumers; (3) the peer review process used for trial development; (4) the trial infrastructure
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45 established by the CTN; (5) practices to facilitate translation into healthcare; and (6) the
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47 training of the workforce involved in translating knowledge into practice. These features
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49 were therefore key considerations in the development of the GMA-CTN, as outlined in the
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51 following sections.
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56 *1. CTN membership.* The membership of a CTN, including its size, breadth, and
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58 diversity, will determine the scope of the expertise available to inform trial development and
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3 implementation. This also has practical implications for research functions such as the
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5 efficient recruitment of participant samples from appropriate clinical populations and is
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7 therefore key to conducting sufficiently statistically powered trials. The representation of a
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9 field as broad and diverse as CYMH presents a significant challenge in its own right.
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11 Transformative change in CYMH services is most likely to come from a CTN that is
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13 comprehensive, both in terms of the disorders that are targeted, as well as the age groups and
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15 populations represented. Accordingly, the GMA-CTN spans research including the most
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17 common forms of internalising and externalising psychopathology that emerge across
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19 childhood and adolescence, disorders that emerge very early in development (e.g.,
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21 neurodevelopmental disorders, fetal alcohol spectrum disorder), and more severe disorders
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23 associated with a later onset in adolescence (e.g., psychosis, substance use).
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29 The expertise represented across specific age groups and populations is also
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31 particularly broad and extends to perinatal interventions, parenting interventions, school-
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33 based and peer (e.g., bullying) interventions, rural and remote populations, Indigenous and
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35 marginalised groups, and refugee populations. Moreover, such research may necessitate
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37 expertise beyond the traditional bounds of the health sector, including that of educational,
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39 developmental, and social researchers. Such representation will remain a key consideration as
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41 the membership of the GMA-CTN expands beyond its principal members in the coming
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43 years. Notwithstanding the Australian focus, the CTN currently includes international
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45 partners in the UK, and it is expected that further international collaborations will enhance
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47 our capacity to address key aims, including cross-cultural research questions.
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51 *2. Identification of clinically meaningful research questions.* For a CTN to identify
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53 research questions that are meaningful to real-world practice, the contributions of diverse
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55 practitioners and consumers with lived experience are vital. In CYMH, stakeholders include
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57 not only referred children and youth, but also their parents and caregivers, who often play
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3 active roles in many evidence-based treatments (Allen, Hawes, & Essau, 2021). Moreover,
4 the challenges experienced by CYMH practitioners and consumers within various social
5 contexts (e.g., Indigenous communities, refugees) are at times highly unique. The
6 engagement of these stakeholders is potentially complex, and within the GMA-CTN is
7 approached through strategic partnerships and affiliations with a range of peak professional
8 bodies, colleges, and research associations (e.g., Australian Association for Infant Mental
9 Health; Australian Clinical Trials Alliance; Australian Psychological Society; National
10 Mental Health Commission; Parenting and Family Research Alliance; Royal Australian and
11 New Zealand College of Psychiatrists). Research questions will be generated by members
12 submitting proposals for trials and providing input on trial prioritisation. The CTN further
13 incorporates a Community Engagement Advisory Committee, comprising diverse parents,
14 caregivers, and young people with relevant lived experience. In addition to playing an active
15 role in the co-design of trials, these consumers are represented on the steering committee
16 responsible for overall governance of the CTN, and on the scientific advisory committee that
17 votes on trial prioritisation and endorsement. This will enable stakeholders to have early input
18 into research decision-making and maximise future clinical implementation.

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3. *Peer review processes.* Peer review processes serve numerous important functions within a CTN, related to the endorsement of trials and the development of high quality trial protocols. In the GMA-CTN, these processes will be overseen by a Scientific Advisory Committee representing diverse expertise across CYMH disorders, thereby facilitating opportunities for transdiagnostic research. The coordination of sophisticated and synergistic research methods across such a network (e.g., consistent approaches to economic cost/benefit measurement and modelling) nonetheless poses a particular challenge. Accordingly, trial protocol development will be supported by teams referred to as the GMA Core Methods groups, comprising expertise in methods including informatics, trial design, statistics, health

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3 economics; and that related to health systems, online resources, and eHealth. In addition to
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5 advising on these aspects of specific trials, a key aim is for all trials in the CTN to adopt
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7 similar best practice methods in order to maximise quality and synergy, and the Core
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9 Methods groups provide strategic input into this.
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12 *4. Trial infrastructure.* The core activities of a CTN rely in part on establishing a
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14 shared and reusable clinical trial infrastructure. The GMA-CTN was conceived as a
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16 facilitating network rather than a coordinating network, meaning that it is focused on
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18 activities that support collaborative development, funding, and execution of trials (e.g.,
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20 advocacy and industry/consumer liaison; collaborative study protocol development; scientific
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22 meetings; clinical guideline development), but not direct project management of trials (e.g.,
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24 data management, regulatory affairs, trial monitoring). This is reflected in the core
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26 infrastructure of the CTN, which includes a purpose-built website to facilitate member
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28 engagement and disseminate methodological and clinical resources related to trial
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30 development and implementation, and the appointment of an Executive Officer responsible
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32 for day-to-day operational processes. The policies and procedures established for peer review
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34 and trial endorsement by the GMA-CTN, and related branding, also form part of this core
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36 infrastructure. Although CTNs in oncology have been known to have ongoing funding
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38 sources for some CTN infrastructure, such support has typically not been available to other
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40 fields (ACTA, 2019). The sustainability of such infrastructure is therefore a key challenge for
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42 a CTN in CYMH, and may rely on actions such as fundraising and philanthropy, as planned
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44 for the GMA-CTN.
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51 *5. Translation into healthcare practice and systems.* For a CTN to lead to a LHS, it is
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53 important that the trials it supports are cost-effective and utilise relevant endpoints to
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55 facilitate translation of results into policy and practice. Such translation carries its own
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57 complex challenges, including the need to consider current and emerging workforce skills,
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3 community mental health literacy, and clinical workflows. A GMA Core Methods group
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5 focused on translation to mental health services and policy has been established for these
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7 reasons. Moreover, this focus will extend beyond the existing healthcare system to include
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9 translation into novel service models. A key example of this is the GMA Check-Up, one of
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11 the flagship trials planned for the CTN, testing an online screening and referral pathway. The
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13 design of the GMA Check-Up is based on a stepped care approach to early identification and
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15 intervention, whereby families complete an online assessment and are provided with non-
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17 stigmatising feedback and triage. This will enable families to access evidence-based
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19 treatment options, including eHealth and prevention-focused programs, suited to their current
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21 needs. This trial addresses critical gaps in traditional CYMH services concerning early
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23 intervention and prevention, which will be an ongoing focus of future trials. Other structures
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25 within the CTN, including the Community Engagement Advisory Committee, will help to
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27 ensure that the endpoints of GMA-CTN trials are meaningful to the parents/caregivers and
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29 children/youth accessing mental health services in Australia, and relate to problems
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31 commonly encountered in clinical care.
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38 6. *Workforce training.* The GMA-CTN will enhance the immediate and long-term
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40 impact of CYMH knowledge translation through education and training opportunities for
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42 both practitioners and researchers. Using a coordinated approach at the national level,
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44 workshops and resources will be delivered to up-skill CYMH practitioners in the evidence-
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46 based interventions developed by members. The training of researchers carries distinct
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48 challenges, and the need to support career progression among early- and mid-career
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50 researchers (EMCRs) in CYMH is particularly noteworthy. These EMCRs were a key
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52 consideration in the initial design of the GMA-CTN and will be the focus of some targeted
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54 initiatives. Roughly one-third of the 60 principal members of the GMA-CTN are EMCRs,
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56 represented across the various groups and committees of the network. These researchers will
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3 benefit from formal mentoring by experienced CYMH researchers in the CTN and their
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5 training will be prioritised through dedicated funds. These GMA Research Fellowships will
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7 support doctoral and postdoctoral activities across key investigator groups and will enable
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9 this next generation of researchers to develop the skills needed to contribute to a LHS.
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14 *Conclusions*

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17 Australia has much to gain from CTNs in CYMH, and the GMA-CTN offers a novel
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19 model for such a network at the national level. This initiative has the potential to facilitate the
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21 continuous generation and implementation of knowledge from CYMH research embedded
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23 within traditional and non-traditional services, and to engage all stakeholders in a culture of
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25 shared responsibility. The building of such a network presents major challenges, many of
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27 which relate to the complexities of representing a field as broad and diverse as CYMH, and
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29 the demands of coordinating sophisticated and synergistic research practices on such a scale.
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31 This includes the need to ensure that provisions for translation are meaningfully integrated
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33 into research from the outset.
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38 It is hoped that other Australian funding agencies will follow MRFF in supporting the
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40 growth of CTNs in mental health. Most apparent is the need for funding schemes that help
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42 maintain existing CTNs and promote collaboration between new and existing CTNs in the
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44 future. Our aim is to build a CYMH network that is collaborative, productive, and
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46 sustainable, and the collective support of Australian researchers, practitioners, and policy
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48 makers, will be critical to achieving this. As a team, we have an opportunity to transform
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50 CYMH in Australia and improve equitable access to evidence-based care, and will be
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52 reaching out to all stakeholders to join us.
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