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Developing and Implementing Tools for Prevention and Early Intervention

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Abstract

Mental ill-health poses the greatest threat worldwide to the survival, fulfillment, and productivity of young people. Implementation of prevention and early intervention services during adolescence and youth offers the best opportunity for health and productivity gains, as 75% of all mental and substance use disorders emerge before the age of 25 years. Our vision is that all young people will be better protected from the major risk factors that threaten their mental health and well-being so that they will be able to access freely, without stigma, mental health care that is as expert and evidence-based as possible—care that is continuously shaped by new research knowledge as well as perspectives and needs of young people, their families, and their communities.

Case History of Optimal Care

Daniel, 19, a first-year university student, has been struggling with his studies since commencing an economics degree at a major university. He had moved away from home and was in unfamiliar surroundings, though some of his high school friends were attending the same university. They noticed he had become increasingly withdrawn and irritable and was using cannabis in greater amounts. One of his friends, Michelle, reached out to him and carefully explored what he

Group photos (top left to bottom right) John Torous, Andrew Chanen, Eric Chen, Merete Nordentoft, Bob Heinssen, Swapna Verma, Pat McGorry, Kim Do, Vinod Srihari, Andrew Chanen, Eric Chen, Michael Schoenbaum, Pat McGorry, John Torous, Kim Do, Swapna Verma, Merete Nordentoft, Vinod Srihari, Pat McGorry, Bob Heinssen, Michael Schoenbaum

was experiencing. Daniel was guarded at first but Michelle persisted, and he was able to confide that he was feeling very anxious and low in mood and energy. He also said he did not feel safe going out and was unable to sleep well. After a few conversations, he agreed to accompany Michelle and talk to the local integrated youth health service, which operated a suite of services on campus. The open plan design and informal, welcoming attitude of the reception/concierge staff put him at ease, and he was able to share his story with Amy, a clinician at the service. Further sessions led to a shared understanding that Daniel had developed relatively severe depression complicated by warning signs of psychosis. A holistic recovery plan was devised, involving cessation of cannabis use, sensitive support from Amy and one other male friend, liaison with his course coordinator regarding course pressures, and involvement of Daniel's parents, who visited and received support and information with Daniel's permission. While antidepressants were not prescribed initially, pending a trial of psychotherapy (cognitive behavioral therapy, CBT), they were added after several weeks as Daniel had not responded quickly enough to the other interventions. Despite subthreshold psychotic symptoms, antipsychotic medication was not necessary and the former faded away as Daniel slowly improved. Within a few months he had recovered fully and was able to complete his first year of university successfully, albeit with somewhat lower grades than he would otherwise have expected. His friendships strengthened and his relationship with his parents improved. His teachers also gained a better understanding of how to support students impacted by mental ill-health.

Case History of Modal or Suboptimal Care or Failure of Care

Jodie, 17, experienced a steady increase of problems at school. She was in conflict with teachers and her peer relationships were unstable and short-lived. Having been bullied earlier in high school, she was often low in mood with episodes of explosive anger. She also suffered from anxiety and, more recently, panic attacks. Her parents were extremely worried, especially by recent episodes of self-harm during which she inflicted cuts on her forearms. Jodie went to see the local doctor who, after 7 mins of strained discussion, prescribed antidepressants and arranged to see her again in 3 weeks. He did not contact her parents due to privacy issues. Several days later, Jodie made a series of deep cuts to her left thigh and was taken by ambulance to the local emergency department. There she was met with a deeply unsympathetic response and informed that she was wasting the time of the staff, who needed to attend to "real" medical problems. One staff member even said not to come back unless she was "serious" about killing herself. She was discharged without a follow-up appointment. Her parents sought to make an appointment with the local specialist mental health service but were told that she "did not meet the criteria" for serious mental illness and would not be offered a service. She was

referred back to her local doctor. Private psychiatric help was only available at high cost in a different part of the city. Jodie became more angry, hopeless, and disengaged. Six months later she threw herself in front of a train at her local station.

Realizing The Vision for Optimal Care

To ensure that the type of care represented in the first case history is available to all, a paradigm shift is needed—one marked by innovation and change on three levels (Figure 13.1) that interact and synergize each other:

1. *Diagnosis with utility*: Utility for early intervention and youth mental health means harnessing the principles of staging and precision medicine in mental health care across all stages of illness to guide treatment and discovery.
2. *Mechanisms of risk and protection*: Discovery and deeper understanding are needed of the malleable neurobiological mechanisms involved in the emergence, persistence, recurrence, and progression of mental ill-health in youth. Similarly, we need to characterize the developmental trajectories during transition to adulthood as well as the risk and protective factors that influence the emergence of ill-health, caseness, and need for care. Ideally this will enable interventions (biological or psychosocial) to be synchronized with both developmental and clinical stages.
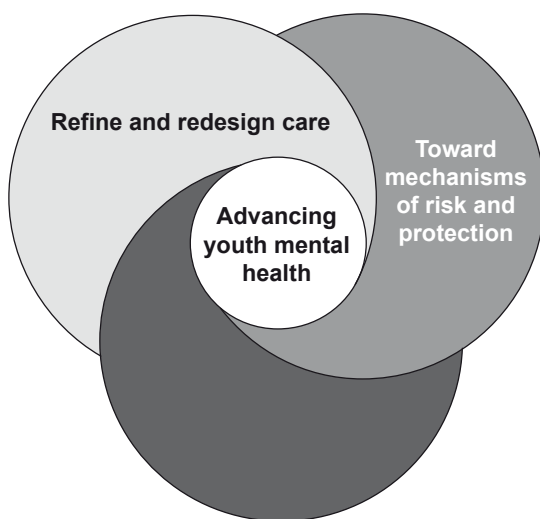

Figure 13.1   Elements of a paradigm change envisioned to advance youth mental health.

3. *Refine and redesign*: Existing evidence needs to be translated and effective models scaled up into routine care that aims for universal access and optimal quality. Design and construction of models of care need to ensure early diagnosis and sustained intervention for as long as required.

Over the past two decades, genuine progress in early intervention has been made. This began with early psychosis and has now expanded to a wider range of mental disorders. New models of care that place a premium on early diagnosis, hope, and recovery have been developed and are being expanded (Hetrick et al. 2017; Kane et al. 2016; Malla et al. 2017; McGorry 2015; McGorry et al. 2014a). Substantial progress has been made and principles clarified. However, adaptation is required for various levels of resourcing and different cultures, and there is a need to integrate primary care with specialized care to manage complexity, acuity, and persistence.

The Target Population in Youth Mental Health: Refine versus Redefine

The move toward a transdiagnostic and dimensional conceptualization of severe mental illnesses offers the opportunity to advance a framework that facilities a more unified model of prevention and early intervention. Evidence that many, although not all, mental disorders emerge post puberty (Merikangas et al. 2009) indicates that there is a critical time in development to which efforts should be targeted. However, the actual delineation of this critical period—that is, defining the specific time frame when the brain is maturing and most susceptible to risk of developing mental health conditions, and likewise most receptive to preventive efforts—has proven difficult. As a result, poor, variable, and often arbitrary definitions are used in the youth mental health field, resulting in unique challenges to the design of neurodevelopmentally appropriate prevention and (neuro)scientifically informed interventions, as well as in the delivery of high-quality continuous care.

Any discussion that aims to frame youth mental health must acknowledge the challenges posed by the cultural, biological, and societal heterogeneity that is embedded in concepts such as *adolescence* and *youth*. Even a seemingly straightforward definition of youth—the period of time between sexual maturation and the assumption of adult roles and responsibilities conferred by culture—underscores the challenges of drawing boundaries. The absence of an operational definition for youth sets up real barriers to prevention and intervention efforts, as it creates an overreliance on current definitions, which are largely based on chronological age.

The most commonly utilized standard for defining youth mental health, chronological age, imposes artificial boundaries on clinical care during critical

periods of brain development. Across the world, different definitions of youth are used: 12–18 years of age is frequently utilized for administrative and service delivery purposes. There is some merit to this definition, as it is widely recognized that many mental illnesses first manifest during the sensitive period of brain development surrounding puberty (see Allen, this volume). Thus, puberty provides a common starting point for many mental illnesses and often falls within the 12- to 18-year range. However, overwhelming evidence and consensus among all authors of this chapter hold that this definition is wrong. In particular, we are most concerned with the upper age cutoff point. Given the convenience of chronological age, we believe that there is a need to create more epidemiological and neurodevelopmentally appropriate definitions of scope.

While there is no simple solution to help define the scope of youth mental health, recognizing the challenge is a practical first step. From a neurological perspective, the age of 18 years is not an appropriate cutoff point, given the overwhelming evidence of continued brain maturation and onset of new illnesses (Kessler et al. 2007) like schizophrenia, bipolar disorders, and alcohol use disorders, as of this point in life. Yet while 18 years is too early, it is not clear what should constitute a more appropriate upper limit, as there remains a lack of strong evidence of an individual biomarker that would signify the end of adolescence on personal, social, and brain development. Neuroimaging-based definitions of brain development offer some clues but currently do not provide a practical or scalable solution. This, in part, explains the continuing reliance on chronological age as a default: there is simply no other alternative. Recognizing that chronological age will continue to be utilized, if only for administrative reasons, we suggest that it is more appropriate to set the upper limit at age 25 years. This better reflects the underlying neurodevelopmental risk period for youth mental health and, as will be outlined below, confers additional benefits through the creation of new opportunities in support of primary as well as secondary prevention efforts.

The direct harm that results from current definitions of scope are exemplified in challenges encountered by some early intervention service programs. For example, despite robust evidence that cost savings occur when prevention and early intervention programs are in place, the very structure of mental health services causes ineligibility for care once an individual surpasses the system's age limit. As of age 18, for instance, an individual is no longer part of child/adolescent services and is covered only by adult services. While there must be a transition, the age of 18 is less than optimal. Forced termination of coverage by adolescent services often precludes optimal implementation of much-needed care, such that individuals no longer receive the longitudinal care they need toward recovery and society is unable to benefit from the projected cost savings commitment with delivery of that care. Compounding the issue, limiting the scope of youth mental health to

18 years creates a loophole for insurance companies, which may opt not to provide "adult" mental health patients over the age of 18 with access to early intervention services.

Thus, a more ideal definition of the scope of youth mental health will not reflect chronological age, but rather be framed in the context of clinical services designed to meet the needs of the population at risk and which require interventions. This includes creating services that integrate mental, physical, and sexual health with alcohol and other drugs expertise, vocational interventions, and online/digital health platforms (McGorry et al. 2014a; Rickwood et al. 2019). This functional definition moves discussion away from chronological age and more toward service delivery. It also raises important questions for consideration: What service delivery model should now be used to define youth mental health? Is it necessary to create a new model or clinical specialty?

One example of a clinical service-based definition that offers opportunity for improvement is to link youth mental health to child and adolescent psychiatry. For many patients, the transition from child/adolescent/youth to adult services creates an abrupt transition of care, commensurate with loss of strong therapeutic relationships and access to specialized care. For example, in the same clinic, the needs of a 19-year-old with recent onset of psychosis in an adult clinic are radically different than those of a 45-year-old with chronic schizophrenia, in terms of required psychosocial support, medical needs, employment assistance, and more. This raises the potential need for a new branch of mental health services—one that extends across the current boundary imposed by age (18 years) and connects the child/adolescent/youth psychiatry and adult psychiatry systems, with a flexible boundary between each system to enable seamless care across the lifespan. The concept of less rigid borders is already accepted in mental health service delivery, as the transition between geriatric and adult psychiatry is often fluid, based on the needs of the patient at hand. Yet even if a new youth mental health specialty were to be created, it is unclear how "appropriate transitions" would be defined. For this, we need a research agenda focused on two broad domains (see, e.g., Shah et al. as well as Bitanihirwe and Woo, this volume): biomarkers and clinical decision making. Until research is able to provide guidance on the optimal time for transitions to adult services, a focus prioritizing continuity of care is most appropriate. This functional definition allows consideration for local resources and cultural practices while aiming to support optimal care for youth mental health.

Even without a more concrete definition, it is still critical to plan for and conceptualize the scope of youth mental health in terms of evolving care systems. Such plans create the foundation upon which further support can be solidified, research efforts can be directed, and around which communities can unite and direct their efforts. Conceptualizing youth mental health as prevention for the general population as well as an early intervention mechanism for

those with acute needs offers a practical starting point to frame future steps. This definition also broadens the scope of youth mental health: it acknowledges that to reach the general population as well as serve those in need, youth mental health services must operate beyond the clinic and become embedded in the community, marked by strong collaborations with the educational, judicial, and social services where at-risk youth may first present.

How Can Knowledge Exchange Improve
Both Science and Clinical Care?

The bench to bedside mantra is a staple of biomedical research. In youth mental health, can this bidirectional exchange be accelerated to effect much-needed solutions in both prevention and early intervention? Can we employ the rigor and methods of scientific research in clinical care and use the priorities of patients to drive the research agenda?

To account for the unique aspects of youth mental health, we propose that the bidirectional knowledge exchange be reframed as a three-way interaction between researchers, clinicians, and patients/families. Targets for this tridirectional knowledge exchange would include the discovery of risk factors, mechanisms, and clinical responses to existing interventions in youth mental health. These multiple stakeholders and targets must also be considered within the context of prevention, early intervention, and ongoing care. Further, new strategies must be framed from the perspective of brain development so that interventions can take place at the right time during the right stage of neurological maturation. Given the complexity of multiple stakeholders, targets, domains, and time frames, it is easy to understand why unified research has progressed slowly, despite a number of pioneering advances in individual areas of research. Equally, however, there is great potential embedded within this complexity. To harness it, we propose a learning health-care system for youth mental health (see Figure 13.2).

The Institute of Medicine (IOM) has presented a vision for twenty-first century health care based on the principles of efficacy, safety, and equity. Accordingly, characteristics of an ideal health system include science-based intervention, easy and timely access to services, and person-centered care. Measurement-based treatment plays a key role in assuring the quality, effectiveness, and responsiveness of therapies provided to individual patients. Medical informatics and data science specialties provide powerful tools for aggregating and mining clinical data, which in turn can be used to discern lessons about current practice, areas of uncertainty, and opportunities for new research. The learning health-care system envisioned by IOM is an ideal platform for practice-based studies in youth mental health, aimed at improving patient care and driving the process of scientific discovery.

Developing a common framework for data collection, analysis, and reporting is a necessary step. Key global initiatives to facilitate this process have already been formed. The International Youth Mental Health Research Network (IYMHRN), currently represented by over 30 academic and other organizations involved in youth mental health research, has produced a set of research priorities for youth mental health, in consultation with funding bodies (C. Mei et al., in prep.). These priorities include developing a global standardized toolkit of assessment and outcome measures for youth mental health that can be used to evaluate and compare services and identify effective service features. Further proposed activities of the IYMHRN include linking clinical research with data analysts to support the utilization and interpretation of large data sets. Overall, the priorities developed by IYMHRN aim to provide a youth-specific framework to enable a systematic and global strategy for new and innovative research as well as the translation and implementation of existing evidence, in collaboration with key stakeholders, including young people and their families, mental health clinicians and service providers, and policy makers. This is facilitated by IYMHRN's strong links with other youth-focused initiatives such as Frayme, a Canadian-based international knowledge translation platform. A key focus of Frayme is to synthesize evidence, translate knowledge, and support the global implementation of integrated youth services (Halsall et al. 2019). These recent initiatives are supported by a range of established platforms, including the International Association for Youth Mental Health, IEPA Early Intervention in Mental Health, and the journal, *Early Intervention in Psychiatry*, which supports evidence-based practice in youth mental health as well as research innovation and translation.

With a specific focus on the early psychosis spectrum, the National Institute of Mental Health (NIMH) has expressed strong interest in a subset of measures that could bridge clinical and academic programs, thereby supporting implementation, quality improvement, health services, and translational research. The immediate goal of this multisite research approach, the Early Psychosis Intervention Network (EPINET), is to improve early identification, diagnosis, clinical assessment, intervention effectiveness, service delivery, and health outcomes in clinics that offer evidence-based specialty care to persons in the early stages of psychotic illness. EPINET will link community clinics and academic research programs through core measures of clinical phenotypes, service delivery, and functional outcomes as well as a uniform informatics approach for aggregating and analyzing pooled data. Data analytics will allow individual clinics to monitor treatment fidelity, quality, and outcome metrics in real time, and to compare local performance to results obtained across all network sites. With standard clinical measures as its *lingua franca,* EPINET will facilitate communication and collaboration among participating clinicians, academic researchers, and early psychosis service users, thus setting the stage for a large practice-based research program aimed at establishing new standards for care

Table 13.1 Interactions in the Early Psychosis Intervention Network (EPINET), a learning health-care model for youth mental health. Discovery in basic sciences can inform translational research and, in turn, clinical service delivery, which then can inform the agenda for basic discovery science

	Clinical Service Delivery System	**Translational Research Clinics**	**Discovery Science Research Centers**
Conceptual Framework	Measurement-based treatment	Experimental therapeutics	Neuroscience molecular biology genomics
Methodology	Clinical staging, treatment to target, step-wise care	Experimental manipulation of putative mechanism	Network, circuitry, morphological, and functional profiling in experimental models with genetic or environmental risks
Principal Responsibilities	Implement, refine, and optimize evidence-based interventions	Establish target engagement and treatment efficacy	Identify disorder mechanisms and therapeutic targets

and accelerating studies of psychosis risk factors, biomarkers of illness, and preemptive intervention. Table 13.1 illustrates "upstream" interactions among discovery science centers and research-oriented clinical programs. Standard measures of these dimensions will create a "data bridge" across research and clinical settings:

1. Common data elements will be used to identify potential research participants among those enrolled in early psychosis programs.
2. Using these common measures as end points in diverse studies, translation and implementation of findings will be accelerated into clinical practice settings.

EPINET will create a national laboratory to address important practice issues as well as emerging scientific questions. EPINET stakeholders anticipate a national forum to promote active sharing of experience, data, and new ideas about the nature and optimal treatment of early psychosis. Expertise within the network will accelerate progress in several areas, including practice innovations for reducing the duration of untreated psychosis, mitigating medical comorbidities in first-episode psychosis, and optimizing the effectiveness of existing treatments. Scientifically, EPINET will support a range of precision medicine approaches to early psychosis, including observational and experimental studies of underlying mechanisms and novel interventions. Working in collaboration with national partners and international colleagues, such as the Australian Early Psychosis Research Network, NIMH imagines a new era of

early psychosis treatment that fully realizes the IOM vision of effective, continuously improving, and science-driven health care for the future.

Building a Tridirectional Partnership

The success of any learning health-care system will be reliant on an effective exchange of knowledge, within and between stakeholder groups, as well as on fruitful collaborations and cooperation. We hold that the unique aspects of youth mental health require a partnership between three general groups of stakeholders: researchers, clinicians, as well as patients and their families. Notwithstanding the presence of various hurdles within each stakeholder group, which must be addressed and overcome, multiple factors will hinder effective collaboration between the groups. Here we highlight challenges as well as opportunities for synergy within and between each stakeholder group.

Within the research community, there is an overall need for more transdisciplinary collaborations. Emergent knowledge from multiple disciplines (e.g., molecular, genetic, social, and behavioral science) is required to understand the complexities involved in youth mental health. Within each research domain, well-honed specialization is needed, yet this in itself can create barriers to experts from other domains, thus pointing to the need for effective cross-disciplinary communication.

Effective communication and collaboration must also be secured between the research and clinical communities (bench to bedside and back again). Figure 13.2 illustrates a fully integrated translational approach that links clinical and discovery science in accordance to the learning health-care model proposed above. Interactions between clinical and preclinical research—at various levels of investigation (genetic, molecular, cellular, circuitry, psychic, cognitive, and behavioral phenotyping), performed with state-of-the-art methodologies—are applicable to both patients and animal models. At various stages of disease, patient assessments together with epidemiological, ecological momentary investigations lead to the development of preclinical models that are closely linked to the pathophysiology of the disease. To test the interaction between genetic and environmental risk factors during the critical period of peripuberty/adolescence, insults derived from epidemiological studies could be applied in appropriate animal models at various periods of brain development. Wherever possible, assessment end points of preclinical models should be aligned with the ones used in clinical studies. Besides demonstrating new pathological mechanisms involved in the progression and modification of disease, this integrated translational approach should lead to the identification of sensitive and accurate biomarker profiles that are essential for early diagnostics, for monitoring therapeutic efficacy, as well as for potential drug targets, to be tested and validated in clinical settings.
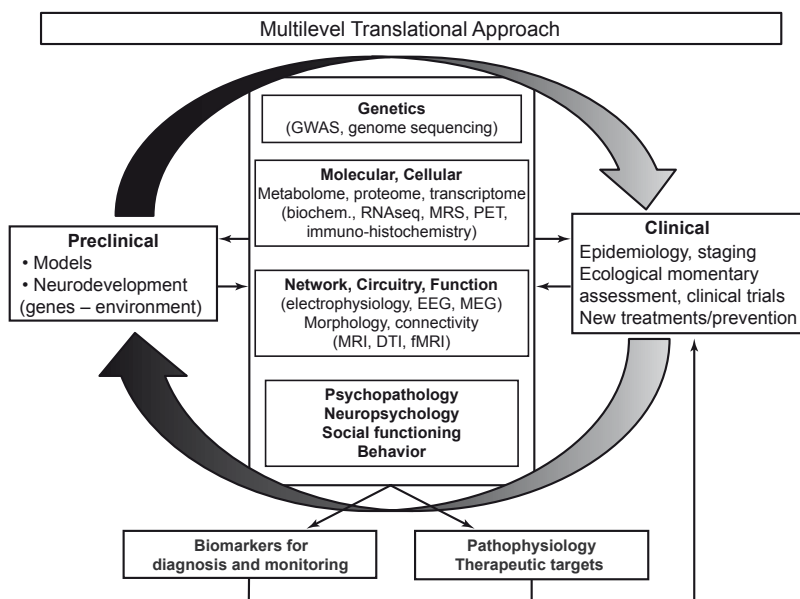
Figure 13.2 Framework by which mechanisms suggested by clinical observations can be tested and preclinical models in patients validated. Risk assessments gained from genome-wide association studies (GWAS) and whole genome sequencing are used to generate novel experimental models. Biochemical and RNA deep sequencing methodologies establish profiles (metabolomic, proteomic, and transcriptomic) on specific biological materials (blood, fibroblasts, olfactory tissue, stem cells, nervous tissues). Noninvasive brain magnetic resonance spectroscopy (MRS) and positron emission tomography (PET) are methods of choice for translation to assess molecular and cellular alterations in specific structures in both patients and models. Histochemistry (immuno-labeling, *in situ* hybridization) applied to patients' postmortem brain and nervous tissue allows specific altered cell types to be identified. At the circuitry and network connectivity levels, electroencephalography (EEG), magnetic encephalography (MEG), and functional and diffusion magnetic resonance imaging (fMRI, DTI)—combined with classical electrophysiology—enable specific dysfunctions to be characterized at high time and spatial resolutions. Finally, psychopathology profiling and cognitive/affective and social impairments can be studied in both patients and experimental models.

Applying such a translational approach within early intervention programs, researchers have demonstrated that effective links could be established between clinical and discovery science (Baumann et al. 2013; Föcking et al. 2016). For instance, the role of a glutathione brain deficit in schizophrenia pathophysiology, first observed in patients (Do et al. 2000; Gysin et al. 2007; Tosic et al. 2006; Xin et al. 2016), was investigated in rodent models to allow characterization of its role in inducing numerous relevant schizophrenia phenotypes, such as inflammation, NMDA receptor hypofunction, and dopamine

dysregulation (Dwir et al. 2016; Hardingham and Do 2016; Steullet et al. 2016). Interestingly, the experimental model of gene–environment interactions showed that additional insults at peripuberty, but not in adulthood, led to permanent excitatory-inhibitory cortical imbalance, which is known to underlie cognitive deficits (Cabungcal et al. 2013a). This finding highlights childhood and peripuberty as critical periods of high vulnerability for environmental adverse insults, and has led to the study of the differential impact of traumatic early- versus late-life events in patients (Alameda et al. 2016) and the contribution of redox imbalance (Alameda et al. 2018).

The same complexity that can isolate researchers from each other, however, can also occur with clinicians as well as patients and families. For clinicians, co-designing research platforms within clinical services, joint journal clubs, and joint meetings offer possible solutions. For patients and families, synergistic collaborations offer opportunities to better characterize the phenomenology of youth mental health and build support for the research agenda among a more cognizant general public.

Apart from translational neuroscientific approaches, an important knowledge domain in youth mental health is descriptive psychopathology. Current initiatives for early detection are limited by a lack of psychopathological knowledge for the early evolution of symptoms. Existing psychopathological knowledge is mostly based on patients with established illnesses. Efforts to extend this knowledge base have thus far come from two approaches: (a) simple epidemiological tools (such as self-administered questionnaires), developed for large population surveys with acknowledged limitations for capturing subtle early psychopathology, and (b) methods extending from established illnesses (such as the CAARMS). Neither method addresses the possibility of new complexities and forms of experiences, which may not simply be diluted forms of psychopathological experiences from established illnesses. Recent research has emphasized external empirical brain measurements and tended to under-recognize the value of information provided by subjective experiences. Yet in general, symptoms still contribute most of the predictive powers in outcome determination. To what extent a refined psychopathological information may help to provide diagnostic and prognostic information to guide treatment is an empirical question that will only be answered once we have the right approaches and tools—such as those offered by the learning health-care model for youth mental health.

Ignoring patients and families from the knowledge exchange network would be a critical oversight. Traditionally there have been many heterogeneous voices from the patient/family communities, and at times critical voices from those who may have had poor experiences with the current system. However, supporting those who have had good experiences and coalescing their voice through youth research councils or leadership roles in mental health service organizations can help ensure that their voice is better recognized—and that

we learn from it. As youth are increasingly being approached by researchers, especially in an era of digital and technology-based monitoring, it is important that they be allowed the opportunity to set their agenda and demand that research suit their personal and ethical considerations. The initial challenges of the first wave of digital interventions may be related to poorly developed collaborations (Torous et al. 2019). Finally, the evidence for youth mental health prevention increasingly suggests the necessary role of families and environments in promoting mental wellness. Patient/family synergies with clinicians to develop more comprehensive treatment plans that deliver clinical services where needed but also engage the family unit and local community offer high potential for improved youth mental health outcomes.

Neuroscience research can also directly inform novel interventions for youth mental health and learn from what they seek. Patient interest in biofeedback offers one example of a bridge between neuroscience and care that has great potential. For instance, understanding how functional connectivity between the prefrontal cortex and amygdala supports (as well as disrupts, in several conditions) cognitive control offers the potential of neurocircuit-specific interventions (e.g., biofeedback and CBT) optimized to these targets. However, to date such specific efforts directed toward youth mental health are scarce and should be prioritized in the research agenda.

To advance this tridirectional knowledge exchange requires removing barriers and gathering of new support. One primary barrier that currently impacts all stakeholders is the chronological age determination used in child and adolescent services. As discussed, chronological age determination often removes patients and families at a time when their involvement is most crucial. In terms of support, specific funds for intergroup collaborations (e.g., clinicians who wish to pursue research) are often limited in resources-limited mental health settings.

How Can Effective Prevention and Early Intervention Efforts Be Refined or Redesigned?

Delivering effective preventions and interventions for youth mental health requires a synthesis between scientific and care delivery systems. Primary prevention remains the goal and a research priority, although currently there is more actionable evidence for secondary and tertiary prevention efforts. Lack of primary prevention, however, curtails our ability to act. Priority needs to be given to activate the support necessary to advance research and engage the family unit, public policy, and clinical systems, not merely to support but also to implement preventive efforts.

One immediate challenge is the blurring of current definitions of prevention and intervention in youth mental health. Because risk factors, triggers,

onset, and course of many youth mental health conditions are the focus of active research, prevention programs themselves are still evolving. Current prevention efforts target mainly nonspecific risk factors, and quantifying their success remains a challenge as this must occur over the course of years to even decades. In addition, many current prevention strategies do not take into account considerations of the temporal development and progression of risk across different neurodevelopmental stages unique to youth mental health conditions. However, as discussed below, clinical staging has emerged as a promising framework to guide service delivery and research given its focus on the continuum of mental disorders from asymptomatic to chronic illness and its conceptualization of the transdiagnostic trajectories of mental disorders. This focus facilitates the selection of interventions that are proportionate to need and risk of illness progression and provides a framework for evaluating the pathophysiology and biomarkers for each illness stage that can then inform innovative neurobiological and psychosocial interventions (McGorry and Hickie 2019). The universal, selective, and indicated preventive mental health framework reviewed by Arango et al. (2018) offers a series of strategies aimed toward prevention (Figure 13.3).

We wish to point out, however, that disagreement (both local and global) exists as to what constitutes a triad of universal, selective, and indicated strategies as well as when and where it should actually be implemented. A further challenge to implementing prevention programs relates to the epidemiological uncertainty of how many youths are actually at risk of developing mental health conditions, let alone understanding their degree of risk. Without better quantification of risk, it is difficult to plan or promote funds for the appropriate scale and scope of required services.

Likewise, interventions today are limited by an evolving understanding of youth mental disorders and often do not take into account considerations of the temporal development and progression of these conditions related to underlying brain changes. Some youth mental health interventions, like the Recovery After an Initial Schizophrenia Episode (RAISE) program at NIMH, do offer
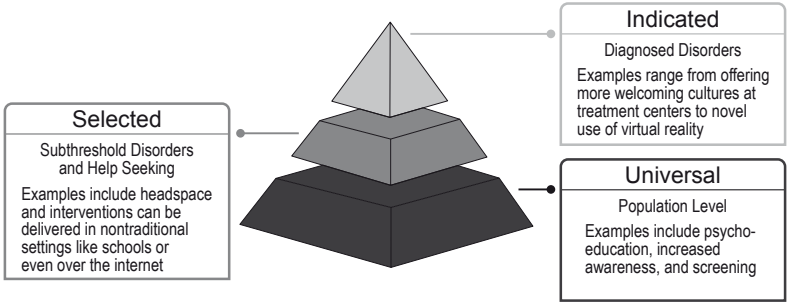

Figure 13.3 Selected, universal, and indicated strategies for a preventive youth mental health framework.

a more neurodevelopmentally informed approach toward intervention, in this case for schizophrenia. One potential reason may be that the relatively low prevalence of schizophrenia compared to other youth mental health disorders, such as depression, makes early intervention efforts for schizophrenia feasible to fund and support. Programs that target young people with early phases of psychosis include OPUS in Denmark, EPPIC in Australia, PIANO in Italy, and PEPP in Canada.

More broadly, a number of youth mental health services that target a range of mental disorders have emerged over the last decade, initiating in Australia through the development of headspace and flowing to other parts of the globe (McGorry and Mei 2018). These integrated models of care have shown positive outcomes across access to care, symptomatic and functional recovery, and client satisfaction (Fusar-Poli 2019; Hetrick et al. 2017). Available services span the United Kingdom (Youthspace), Ireland (Jigsaw), Canada (Foundry, ACCESS Open Minds), the United States (allcove), the Middle East (headspace in Israel), and Europe (headspace in Denmark and Iceland; @ease in The Netherlands). Youth mental health services, such as headspace in Australia, deliver treatment within a preventive framework that provides evidence-informed stepped care guided by risk-benefit considerations and shared decision making (McGorry et al. 2014a). A key component of the headspace model is ensuring that the delivery of evidence-based treatment is matched to the patient's current need as well as the risk of illness persistence and progression. This preventive focus is essential given that the majority of headspace clients present during the early stages of illness and often experience risk of self-harm and suicidal ideation, significant distress, functional impairment, and substance abuse (Rickwood et al. 2014, 2015; Scott et al. 2012b). Simple and brief psychosocial interventions are typically offered as first-line treatments, with pharmaceutical approaches provided to those who do not benefit from initial psychosocial interventions or who present with increased severity or risk (McGorry et al. 2014a). This is in line with the clinical staging model (McGorry et al. 2006).

Across the diagnostic spectrum, clinical staging offers a way forward to bridge current gaps in linking diagnostic models to more personalized and effective intervention, prognosis, neurobiological markers, and psychosocial outcomes (McGorry and Hickie 2019). The clinical staging model currently provides a useful heuristic transdiagnostic framework to guide early intervention and prevention. To achieve its full potential, the model aims to evolve into an evidence-based clinicopathological framework, whereby each stage is linked to neurobiological, psychological, and clinical phenotyping (McGorry et al. 2014b). To date, a number of neurobiological markers have been linked to stage of illness, with findings indicating that established mental disorders are associated with more severe neurobiological and neurocognitive markers compared to attenuated syndromes (Bartholomeusz et al. 2017; Hermens et al. 2013; Lagopoulos et al. 2012; Naismith et al. 2012). This aligns with the

potential progression of mental illness proposed by the clinical staging model and supports the applicability of staging to prognosis, early intervention, and prevention, particularly in the context of youth mental health.

Meeting the need for a more transdiagnostic framework—one that offers appropriate intervention and prevention strategies—is further impaired by a lack of disease-specific staging with which these strategies could be coupled. Concern for nonspecificity and a lack of validity with current diagnostic schemes, represented often by the DSM or ICD, have recently given rise to efforts that seek to reconceptualize or reclassify mental illnesses. Resulting efforts (e.g., clinical staging, RDoC, or HITOP) reflect research-directed projects to increase the validity of diagnostics. Whether these and other efforts will transfer well into pathways of care, and how they may be able to guide appropriate service delivery, remains a research priority; currently, clinical staging offers greater clinical utility, particularly in guiding treatment selection and models of care (McGorry and Hickie 2019). Closing the treatment gap through better implementation and utilization of today's service and interventions constitutes another.

This discussion on radical changes to nosology presents a broader question of whether the underlying youth mental health system itself must radically change. Can progress toward effective prevention and early intervention be obtained through incremental improvement, refinement, and a more radical redesign of how we scientifically study and clinically approach youth mental health? One argument for refinement is that current patients need ongoing services and support. Since many evidence-based practices, especially around access to services and screening, are not always implemented in youth mental health, actualizing current knowledge and interventions appropriately may be a way to effect rapid improvement. A redesign argument considers the current unmet need, paired with today's poor clinical outcomes in youth mental health, and suggests that new approaches are necessary. Further, it suggests that the structure, funding, and support of today's youth mental health services, as well as current model of illnesses, may impede adoption of evidence-based practices today as well as the development of new ones tomorrow. One advantage of redesigned systems is that they provide an opportunity for low- and middle-income countries to develop initial youth mental health systems that are adaptive and often better received by patients.

It is clear that the process of redesign must be accomplished together with young people (Rickwood et al. 2019). Feedback from youth shows that they want mental health clinics to be different: open during hours that suit their lifestyle and a better setting, one that is more welcoming and less clinical. The headspace program in Australia, which has been scaled up to 110 national centers and replicated internationally, suggests that simply lowering the barriers to entry, to simply the need to talk, creates a better, stigma-free entry point for youth to access mental health services. This has been confirmed by an independent evaluation of headspace, which revealed improved access to care for

young people with high levels of satisfaction (Hilferty et al. 2015). It also suggests the potential of positioning mental health services in less traditional environments, such as shopping malls, schools, or community centers. Likewise, there is support for increasing the appeal of youth mental health services when they are co-located within primary care/general practices or pediatric clinics. Neuroscience-focused language can be employed to frame the biological basis of youth mental health to patients/families; this can help reduce stigma and enable patients/families to better understand the nature of these conditions. In addition, minimizing the use of mental health diagnoses and instead explaining conditions in terms of features may help youth better accept and engage with services. The role of online/mobile technology and smartphones will be critical in the redesign of programs, as seen already through headspace's online service (eheadspace), which offers access to information, support, and mental health care for young people, including those who might otherwise not access professional help (Rickwood et al. 2016). The current success of suicide text messages services (e.g., CrisisTextLine in the United States) likely foreshadows a new way to deliver mental health services.

Normal neurodevelopmental progression associated with stages of youth (e.g., exploration, risk taking, peer approval, and autonomy) provides a context to increase the acceptability, uptake, and support for youth mental health services by patients. For example, matching the desire for peer support with peer-led treatments (e.g., peer support services offered at headspace, ACCESS Open Minds, Foundry, and the Wellness Recovery Action Planning in schizophrenia) offers potential. Although more evidence exists for adults than youth (Cook et al. 2012), peer support is a key component of youth mental health services that is acceptable to young people and potentially cost-effective (Hamilton et al. 2017). Some interventions which have been validated in adults (e.g., use of peer interpersonal contact to decrease stigma) may not be as effective when applied to youth. To inform applicability of existing services and guide the development of novel prevention and intervention strategies focused on youth mental health, a research agenda that accounts for normal developmental as well as dynamic pathological processes is necessary.

What Principles Might Guide the Development and Accelerate Clinical Deployment of Digital Technologies in Youth Mental Health?

The recent rise in interest in digital mental health technologies (e.g., smartphone apps and virtual reality) represents an evolving frontier for youth mental health. With direct applicability to prevention and interventions efforts, digital mental health offers a relevant example that can be explored to highlight

current successes as well as failures in a vision for the field, refining versus redesigning care, implementing learning health-care systems to support tridirectional knowledge exchange, and creating the support to overcome barriers.

A useful starting point is to consider both the benefits and risks of new digital technologies, along with their unique relevance to youth mental health. Potential benefits include scalability, novel monitoring, real-time interventions, and new investment:

1. Because prevalence of ownership and access to smartphones and computers is high in youth, a foundation for scalability of any digital mental health program is already given.
2. A myriad of sensors on today's smartphones (e.g., GPS, accelerometer, gyroscope, microphone, screen touch, proximity, Bluetooth, wifi, and more) offers a window into real time and often functional outcomes (Torous et al. 2016). A patient's phone, for instance, can record how many hours a person slept, exercised, or spent calling peers. Real-time collection of smartphone signals requires no active engagement from an individual and is often labeled passive data. Active data refers to more traditional ecological momentary assessment, or surveys, which can also be offered via a smartphone. Together, active and passive smartphone data, as well as a host of wearable sensors (e.g., smartwatches), provide an opportunity to collect low-cost longitudinal data at a previously unprecedented level of detail.
3. Digital technologies like smartphones and sensors not only collect data, they can process it, implement decision support algorithms, and provide real-time interventions via app-based exercises, peer support, and connection to care. Virtual reality headsets already possess a strong evidence base for delivering effective exposure therapy and are well accepted among youth.
4. Because of broad support for digital mental health, new funding resources, from both philanthropy and pharmaceuticals, can be used to advance the field.

However, the unique advantages of digital mental health must also be considered in light of several, also unique, risks:

1. Clinical evidence for the efficacy of digital mental health tools (e.g., smartphone apps) is currently minimal, although there is a growing wealth of feasibility studies. A recent systematic review of mental health apps targeting preadolescent and adolescent mental health identified 24 studies, of which only 7% featured patients with a mental health diagnosis (Grist et al. 2017).
2. Real-time monitoring raises privacy and ethical concerns.

3.   There is growing concern that few mental health patients actually adhere to smartphone apps and may instead use them only for a limited time before deleting.

4.   There is risk that digital mental health tools may fragment youth mental health if data is not appropriately shared with clinical systems, thus isolating mental health from general health.

The unique elements of digital mental health offer numerous visions for the future of youth mental health. From a practical standpoint, digital tools fulfill two roles: (a) to augment and integrate with care systems and (b) to push toward more self-care. Currently, there is a plethora of mental health apps that promote a self-responsibility and self-care vision for the field (Parker et al. 2018). They also provide a novel approach for peer support and create easily accessible networks for youth trained to support each other. Digital health tools can be designed to offer youth a customized treatment delivery platform that can be adapted to their unique needs. On a design level, the user interface, user experience, social experience, and external reinforcements can be co-designed by youth to drive engagement with care. While currently under-researched, there is a need to understand how certain deficits in diseases such as schizophrenia (e.g., working memory or attention) may need to be offset in the design of these digital tools.

The issue of refining versus redesigning care also emerges in digital mental health. In lower- and middle-income countries, where minimal investment is often allocated to basic health-care services, can digital technologies jumpstart efforts and deliver new models of digital psychiatry that are effective and accessible? In all areas of the world, can digital mental health tools be used to quantify a patient's environment and then use that data to recommend appropriate interventions (e.g., sleep, exercise, diet)?

The redesign of the approval process by the U.S. Food and Drug Administration (FDA) for medical software (covering apps and virtual reality) represents a radical departure from the past. On the youth mental health side, digital tools have not yet forced the issue of refining versus redefining care, although the issue will be accelerated with the pending (as of 2019) FDA approval of the first video game for attention deficit hyperactivity disorder. Although telemedicine has not caused a redesign of youth mental health, increased access and expansion of the digital age through mobile technology now needs to be addressed. We need to reconsider how to assess the efficacy of these new digital tools. Randomized controlled trials do offer benefits, and will be necessary, but they may not necessarily capture the potential of these technologies to offer individual and personalized interventions. More importantly, digital technologies will require continual improvement and iterations that evolve both with technology and user demand. Evaluation models, such as A/B design, and partnerships with experts in the game industry may offer

a novel way to isolate the currently elusive active ingredient in digital mental health tools.

The necessity of a learning health-care system to support tridirectional knowledge exchange is also relevant in digital mental health. Many existing evidenced-based CBT apps, supported by on-demand clinicians or coaches, have failed because they did not consider patient/family perspectives. Increasingly, research has shown that apps designed without the input of users suffer from poor engagement (Torous et al. 2019). Patient/family viewpoints need to be considered through the co-design of apps and informed consent. However, little evidence exists on the co-design of apps for youth with mental health needs, and even less about what is needed to build trust and deliver informed consent. Privacy issues remain a top concern when surveying users about smartphone apps. If a smartphone, for example, can capture a digital signature of an underlying endophenotype, it may be possible to design studies to assess both longitudinal outcomes as well as causal inference. Theories such as how the adolescent brain is cued to respond to social reward could then be tested at scale across multiple countries in a uniform manner. Whether digital phenotyping will prove capable of predicting clinical outcomes or identifying risky behavioral patterns, amidst digital noise and the natural variation in human behavior, remains an open research question.

Finally, as with other aspects of youth mental health, creating the support to overcome barriers remains an important focal point for discussion. Little is known about how digital psychiatry should interface with the technology industry in terms of partnerships, privacy, cost models, data ownership, data access, and ethics. While there is no simple solution, there is an urgent need for increased transparency. For example, the privacy policies of many mental health smartphone apps require a college level education for comprehension, which not all youth with mental health issues possess (Powell et al. 2018). Increasingly, patients are turning to clinicians to ask whether technology itself poses a risk to youth mental health through internet addiction. The current lack of knowledge on the topic and need for an informed response is a pressing issue, as are questions regarding legal access to youth mental health data: When should parents, police, and clinicians be able to obtain legally the digital data collected on an individual? Data from digital devices will clearly offer an important new tool in the future of youth mental health, but addressing these ethical and legal questions around its use must be a first priority.

How Can We Build Support and Overcome Barriers to Ensure Successful Implementation of Youth Mental Health Services?

All mental health systems across the globe are under-resourced. Lack of adequate resources is especially true for youth mental health services, which further is impacted by the arbitrary definitions that often remove support for

necessary services when a person reaches the age of 18. In campaigns to increase support, prior efforts have framed deficits in youth mental health as a human rights violation or called for cost redistribution of resources within health-care systems. Neither approach has yielded substantial results. Thus, to increase support and overcome barriers in youth mental health, we advocate pursuing a new vision, approach, and societal investment strategy.

Focusing on support, we present the "model, mobilize, and momentum" mantra as a scaffold for the field to optimize opportunities. One way to build support is to model youth mental health services in a particular area around successful examples from other regions or countries. Careful comparison to successful models can create a convincing argument for support at home. In addition, it is important to mobilize evidence and build youth mental services on solid scientific backing. Seizing momentum, it may be beneficial to expand a certain domain or service when the opportunity arises, rather than wait for broad scope funding to improve all aspects of care. Together the "model, mobilize, and momentum" mantra allows youth mental health services to be poised to act and advocate for support at the right moment.

Opportunities for support are more likely to emerge when stakeholders are well aligned. This includes improving relationships within as well as outside of the mental health field. Within the mental health field, there is a need for continual education and training around youth mental health interventions (e.g., headspace model, individual placement and support, RAISE, EPPIC, OPUS, and PIANO). Medical students and mental health clinicians need to read about youth mental health interventions and service models (e.g., headspace, RAISE) in textbooks, lectures, and clinical guidelines because without exposure, they will never turn to or demand more research on these evidence-based programs. Outside of the mental health field, better alignment is needed (e.g., with NGOs) to ensure that the perspectives of all patients (not just those who are engaged) are heard. In Denmark, for example, the organization PsykiatriAlliancen (psychiatry alliance), comprised of 33 organizations, has developed a core program to promote mental health services and to campaign for and present a unified voice, similar to current efforts in cancer advocacy. Acknowledging that some individuals may have a negative experience with the current youth mental health system, it is important to also ensure that the vast majority who do have good experiences are also heard.

In addition, it is important to mobilize individuals as well as entire communities. Outreach must go beyond families and political leaders: engaging police departments, schools, and social services can build powerful partnerships that are often overlooked. Framing youth mental health as a net gain at the community level, by explaining long-term health and cost savings and focusing on high prevalence disorders (e.g., depression), can garner broad support. However, unifying community support around more prevalent conditions carries the risk of reducing support for serious mental illnesses, thus creating

inadvertent competition for support between different illnesses. One potential solution is to utilize a hybrid approach—one that offers both primary and specialist mental health care in a single package.

Even when community support is optimal, the youth mental health field itself can cause barriers if services or programs are not designed properly or adequately funded to meet the scale of need (McGorry et al. 2019). The key to any successful program is to ensure access and efficacy of an intervention, so that functional outcomes can be delivered to all stakeholders. When there is a bottleneck in access or efficacy, the probability of failure increases greatly. Another common stumbling block occurs when the field is held to an unduly high standard for evidence; in reality, a plethora of evidence-based interventions already exist just waiting for implementation, such as around access to services and screening. Furthermore, ensuring that an intervention delivers functional outcomes (e.g., increased employment or social skills), as opposed to a mere change in symptom measures, is important for creating the necessary impact to build continued support. Primary prevention efforts in the community, modeled after successful efforts in the cancer and cardiology communities, offer a practical starting point. It is important to set realistic expectations, realizing that a successful youth mental health intervention will require many years of follow-up. While early returns on investments, such as in RAISE, OPUS, and youth mental health care more broadly are possible, this should not be seen as the norm.

Finally, the design of services in conjunction with users provides another means to reduce barriers and garner support. Here, digital mental health offers a tremendous opportunity for collaboration. Utilizing the digital expertise of youth mental health patients offers potential for co-design of new online and connected tools.

Conclusion

The youth mental health field has many advantages working in its favor, as nearly all societies offer broad support for youth. Harnessing that support into (a) diagnosis with utility, (b) mechanisms of risk and protection, and (c) the refinement and redesign of care models will advance the field and improve lifelong outcomes. New tools from genetics to digital phenotyping and advanced models of partnerships from learning health-care systems to community collaborations will help. What is lacking, however, is an effective research agenda to address many of the unanswered questions that remain:

- How should the youth mental health field best communicate with the public?
- How can effective interventions be implemented and scaled up?
- What standards for evidence are needed?
- How can the co-design of effective interventions be optimized?

- What is the best way to identify the functional outcomes that matter most to stakeholders?
- Which research and clinical priorities need to be addressed to maximize clinical impact?

Our vision is for all young people to be better protected from the major risk factors that threaten their mental health and well-being, so that they can freely access, without stigma, mental health care that is as expert and evidence-based as possible. Achieving this vision will require a massive focus on research focused on

- identifying targets for early prevention and longitudinal data on trajectories of illness,
- establishing nationwide programs that ensure early access to care,
- implementing today's important evidence-based interventions,
- furthering efforts to bridge basic science and clinical practices, and
- activating communities.