EARLY INTERVENTION IN PSYCHIATRY FROM EARLY PSYCHOSIS TO A TRANSDIAGNOSTIC STAGING APPROACH

Patrick McGorry MD PhD

DISCLOSURE SLIDE

NONE


AUSTRALIA

OUTLINE

- EARLY INTERVENTION:

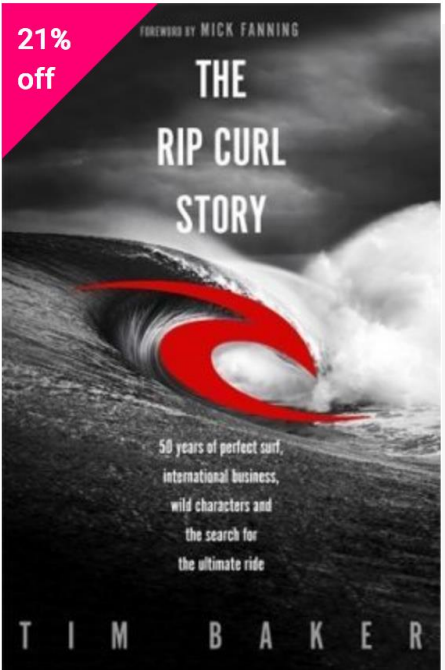
“The crisis consists precisely in the fact that the old is dying and the new cannot be born.”

Antonio Gramsci

- At Risk Mental State (ARMS) Ultra High Risk (UHR) or Clinical High Risk (CHR)
- Duration of Untreated Psychosis (DUP)
- EARLY PSYCHOSIS CARE
- TRANSDIAGNOSTIC EI AND YOUTH MENTAL HEALTH

THE IDEA

THE SEARCH



1992

The History of The Search

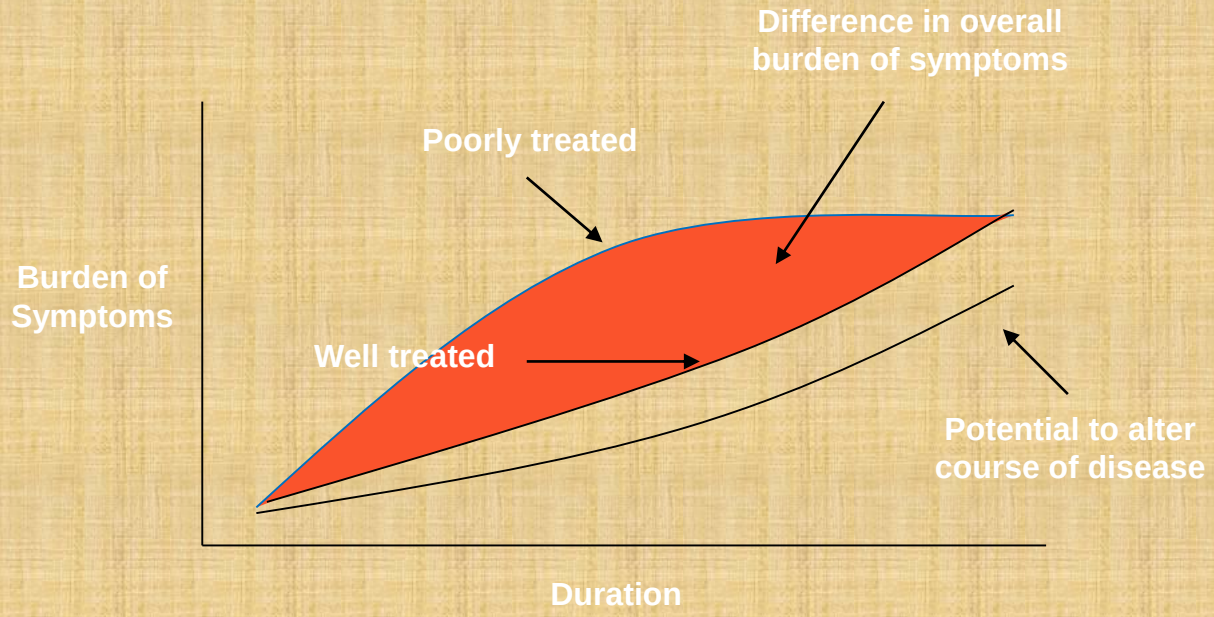
In the late '80s, and with a vision for the company well established, Brian and Claw were trying to articulate what it meant to be part of Rip Curl.

LAST EPISODE PSYCHOSIS

“An air of desolation more calculated to fix than to remove”

Emil Kraepelin

BURDEN OF DISEASE



THE CONCEPT OF RECOVERY AND SECONDARY PREVENTION IN PSYCHOTIC DISORDERS

Patrick D. McGorry

The concept of recovery is embedded in the current classification of functional psychosis, an unfortunate fact which has obscured important therapeutic and preventive opportunities for patients and their relatives. A range of theoretical perspectives is reviewed which could be drawn upon to extend research, and develop and evaluate new forms of intervention in this area. The major tasks facing patients and their families at different stages of illness are described, and a series of principles is then proposed to guide the clinical care of recovering psychotic patients.

Australian and New Zealand Journal of Psychiatry 1992; 26:3-17


Aubrey Lewis Unit

VOL. 22, NO. 2, 1996

EPPIC: An Evolving System of Early Detection and Optimal Management

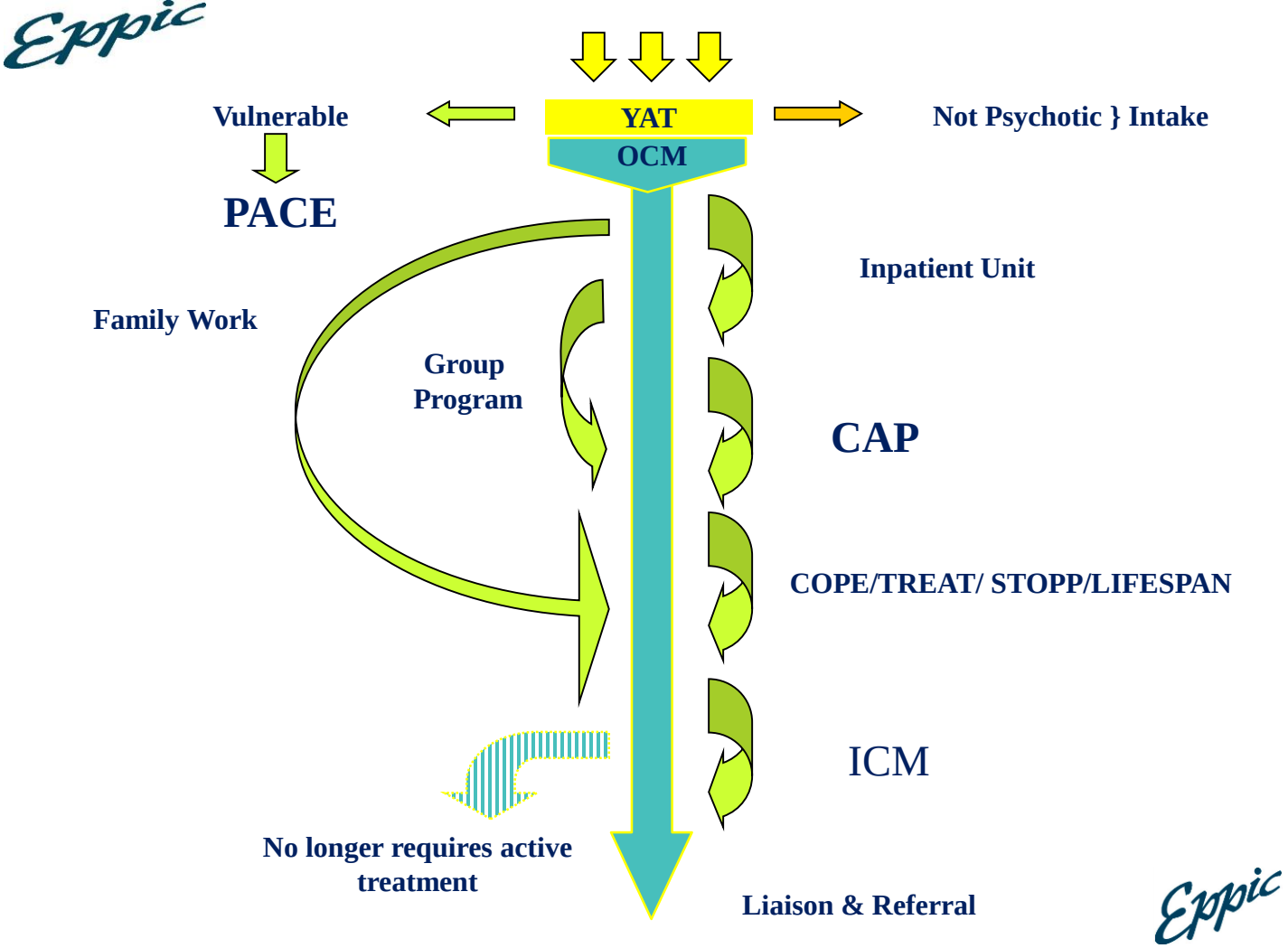
by Patrick D. McGorry, Jane Edwards, Cathrine Mihalopoulos, Susan M. Harrigan, and Henry J. Jackson

Abstract

Early intervention at the onset of psychotic disorders is a highly attractive theoretical notion that is receiving increasing international interest. In practical terms, it amounts to first deciding when a psychotic disorder can be said to have commenced and then offering potentially effective model is contrasted with the first. The implications of these findings and future developments are discussed.

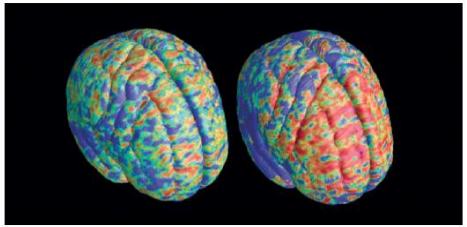
Schizophrenia Bulletin, 22(2):305–326, 1996.

Very early schizophrenia still constitutes a relatively unexplored territory. Entry into this territory calls for new ideas on


Eppic
Vulnerable
YAT
OCM
Not Psychotic } Intake
PACE
Inpatient Unit
Family Work
Group
Program
CAP
COPE/TREAT/ STOPP/LIFESPAN
ICM
No longer requires active
treatment
Liaison & Referral
Eppic


William Buckland House
centre for adolescent health
2

OUTLOOK SCHIZOPHRENIA



ELSEVIER SCIENCE PUBLISHING/TYRONE CANNON

The brain of someone developing schizophrenia (right) typically shrinks more rapidly than normal (red colours indicate the highest rates of contraction).

PREVENTION

Before the break

Paying attention to risk factors and warning signs could avert some cases of schizophrenia — or at least better prepare people for what's to come.

'Born at risk'). Even when schizophrenia has taken hold, early treatment after the first episode of psychosis can limit the severity of the illness and increase the chances of recovery.

McGorry and others have taken the idea of early treatment further, proposing to intervene at the first suggestive signs of psychosis. A person might become suspicious, or start to hear a voice, but still recognize that these things are not tethered to reality. They may withdraw from friends and family, or have trouble focusing at school or work. The criteria for this 'at risk' category differ slightly between researchers, but they all require that a person is sufficiently distressed by their symptoms to seek help.

About one-third of people in this at-risk category develop psychosis within three years, and most are diagnosed with schizophrenia. A version of this at-risk category, called attenuated psychosis syndrome (APS), was considered for inclusion as a new diagnosis in the recent fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-5*), one of the most widely used inventories of mental illnesses. But most people with APS do not actually develop full-blown psychosis, so after much discussion the syndrome was not included in *DSM-5*.

WE CAN PREDICT *AND* EVEN DELAY THE ONSET OF PSYCHOSIS….

META-ANALYSIS

Predicting Psychosis

Meta-analysis of Transition Outcomes in Individuals at High Clinical Risk

Paolo Fusar-Poli, MD, PhD; Ilaria Bonoldi, MD; Alison R. Yung, PhD; Stefan Borgwardt, PhD; Matthew J. Kempton, PhD; Lucia Valmaggia, PhD; Francesco Barale, PhD; Edgardo Caverzasi, PhD; Philip McGuire, PhD

Context: A substantial proportion of people at clinical high risk of psychosis will develop a psychotic disorder over time. However, the risk of transition to psychosis varies between centers, and some recent work suggests that the risk of transition may be declining.

Objective: To quantitatively examine the literature to date reporting the transition risk to psychosis in subjects at clinical high risk.

Data Sources: The electronic databases were searched until January 2011. All studies reporting transition risks in patients at clinical high risk were retrieved.

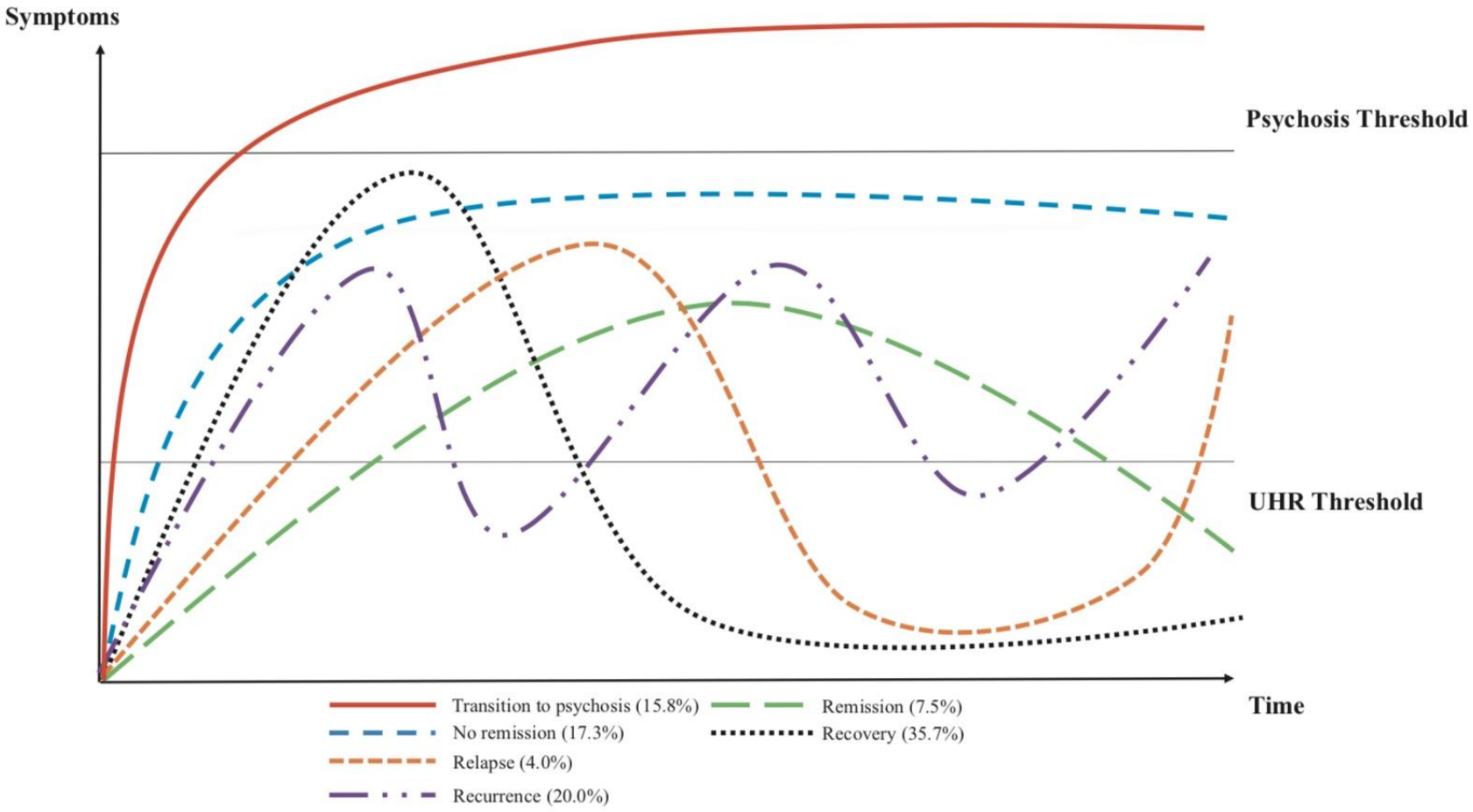
Study Selection: Twenty-seven studies met the inclusion criteria, comprising a total of 2502 patients.

Data Extraction: Transition risks, as well as demographic, clinical, and methodologic variables, were extracted from each publication or obtained directly from its authors.

Data Synth [illegible] transition risk, indepen[illegible] of the psychometric instru[illegible]ts used, of 18% af[illegible] 6 months of follow-up, 22% after [illegible]ear, 29% after 2 [illegible]rs, and 36% after 3 years. Signifi[illegible]t moderators acco[illegible]ing for heterogeneity acros[illegible]udies and influencing the [illegible] the age of participants, publication year, treatments received, and diagnostic criteria used. There was no publication bias, and a sensitivity analysis confirmed the robustness of the core findings.

Conclusions: The state of clinical high risk is associated with a very high risk of developing psychosis within the first 3 years of clinical presentation, and the risk progressively increases across this period. The transition risk varies with the age of the patient, the nature of the treatment provided, and the way the syndrome and transition to psychosis are defined.

Arch Gen Psychiatry. 2012;69(3):220-229


Symptoms
Psychosis Threshold
UHR Threshold
Time
Transition to psychosis (15.8%)
Remission (7.5%)
No remission (17.3%)
Recovery (35.7%)
Relapse (4.0%)
Recurrence (20.0%)

Psychological Medicine

cambridge.org/psm

Editorial

Cite this article: Ajnakina O, David AS, Murray RM (2018). 'At risk mental state' clinics for psychosis – an idea whose time has come – and gone!. *Psychological Medicine* 1–6. https://doi.org/10.1017/S0033291718003859

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Key words:
At risk mental state; pathways to care; psychosis; schizophrenia; transition.

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'At risk mental state' clinics for psychosis – an idea whose time has come – and gone!

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Abstract

At Risk Mental State (ARMS) clinics are specialised mental health services for young, help-seeking people, thought to be at ultra-high risk of developing psychosis. Their stated purpose is to reduce transitions from the ARMS state to clinical psychotic disorder. Reports of ARMS clinics provide 'evidence-based recommendations' or 'guidance' for the treatment of such individuals, and claim that such clinics prevent the development of psychosis. However, we note that in an area with a very well-developed ARMS clinic (South London), only a very small proportion (4%) of patients with first episode psychosis had previously been seen at this clinic with symptoms of the ARMS. We conclude that the task of reaching sufficient people to make a major contribution to the prevention of psychosis is beyond the power of ARMS clinics. Following the preventative approaches used for many medical disorders (e.g. lung cancer, coronary artery disease), we consider that a more effective way of preventing psychosis will be to adopt a public health approach; this should attempt to decrease exposure to environmental factors such as cannabis use which are known to increase risk of the disorder.

O’DONOGHUE ET AL (IN PREP)

1138 young people

13.7% first attended an ARMS clinic

A further 7.6% attended other youth mental health services.

Individuals who first presented at an early intervention clinic were more likely to be female and younger, and less likely to be migrants or have substance abuse.

Rates of hospital admissions, including involuntary admissions, for young people who transitioned from the ARMS clinic, headspace, or the other youth mental health services were significantly reduced compared to those who presented directly with a FEP.

Psychological Medicine

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Invited Review

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Key words:
Anxiety; at-risk mental state; clinical high risk; depression; psychosis; transdiagnostic; ultra-high risk

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Breaking the web: life beyond the at-risk mental state for psychosis

Jesus Perez[1,2,3] and Peter B. Jones[1,2]

[1]Department of Psychiatry, University of Cambridge, Cambridge, CB2 0SZ, UK; [2]CAMEO, Cambridgeshire and Peterborough NHS Foundation Trust, Elizabeth House, Fulbourn, CB21 5EF, UK and [3]Norwich Medical School, University of East Anglia (UEA), Norwich, NR4 7TJ, UK

Abstract

Psychiatry's most recent foray into the area of risk and prevention has been spear-headed by work on at-risk mental states for psychotic disorders. Twenty-five years' research and clinical application have led us to reformulate the clinical evolution of these syndromes, blurred unhelpful conceptual boundaries between childhood and adult life by adopting a developmental view and has changed the shape of many mental health services as part of a global movement to increase quality. But there are problems: fragmentary psychotic experiences are common in young people but transition from risk-state to full syndrome is uncommon away from specialist clinics with rarefied referrals and can, anyway, be subtle; diagnostic over-shadowing by the prospect of schizophrenia and other psychotic disorders may divert clinical attention from the kaleidoscopic and disabling range of probably treatable psychopathology with which people with risk syndromes present. We use a 19th Century lyric poem, The Lady of Shallot, as an allegory for Psychiatry warning us against regarding these mental states only as pointers towards diagnoses that probably will not occur. Viewed from the fresh perspective of common mental disorders they tell us a great deal about the psychopathological crucible of the second and third decades, the nature of diagnosis, and point towards new treatment paradigms.

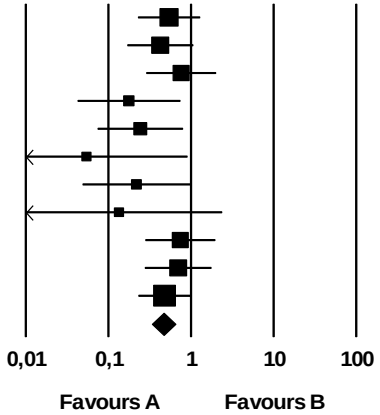
VAN DER GAAG ET AL (2013)

Forest plot of Risk Ratios at 12 months

Study name	Risk ratio	Lower limit	Upper limit	Z-Value	p-Value
McGorry, 2002	0,542	0,226	1,298	-1,374	0,169
McGlashan, 2006	0,425	0,168	1,076	-1,806	0,071
Yung, 2012	0,760	0,285	2,026	-0,549	0,583
Amminger, 2008	0,177	0,042	0,750	-2,350	0,019
Nordentoft, 2006	0,243	0,073	0,805	-2,315	0,021
Bechdolf, 2012	0,054	0,003	0,913	-2,023	0,043
Morrison, 2004	0,219	0,048	0,993	-1,969	0,049
Addington, 2011	0,134	0,008	2,404	-1,364	0,173
Yung, 2012	0,742	0,278	1,982	-0,594	0,552
Morrison, 2012	0,700	0,274	1,788	-0,745	0,456
Van der Gaag, 2012	0,478	0,229	0,998	-1,966	0,049
	0,462	0,334	0,641	-4,635	0,000

Statistics for each study

Risk ratio and 95% CI



Meta Analysis

RESEARCH REPORT

Lack of evidence to favor specific preventive interventions in psychosis: a network meta-analysis

Cathy Davies[1], Andrea Cipriani[2], John P.A. Ioannidis[3-7], Joaquim Radua[1,8,9], Daniel Stahl[10], Umberto Provenzani[1,11], Philip McGuire[12,13], Paolo Fusar-Poli[1,11,13,14]

[1]Early Psychosis: Interventions & Clinical-detection (EPIC) Lab, Department of Psychosis Studies, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK; [2]Department of Psychiatry, University of Oxford, and Oxford Health NHS Foundation Trust, Oxford, UK; [3]Department of Medicine, Stanford Prevention Research Center, Stanford, CA, USA; [4]Department of Health Research and Policy, Stanford University School of Medicine, Stanford, CA, USA; [5]Department of Biomedical Data Science, Stanford University School of Medicine, Stanford, CA, USA; [6]Meta-Research Innovation Center at Stanford, Stanford University, Stanford, CA, USA; [7]Department of Statistics, Stanford University School of Humanities and Sciences, Stanford, CA, USA; [8]FIDMAG Germanes Hospitalàries, CIBERSAM, Sant Boi de Llobregat, Spain; [9]Department of Clinical Neuroscience, Centre for Psychiatry Research, Karolinska Institutet, Stockholm, Sweden; [10]Biostatistics Department, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK; [11]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy; [12]Department of Psychosis Studies, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK; [13]National Institute for Health Research (NIHR) Maudsley Biomedical Research Centre, London, UK; [14]OASIS Service, South London and Maudsley NHS Foundation Trust, London, UK

Preventing psychosis in patients at clinical high risk may be a promising avenue for pre-emptively ameliorating outcomes of the most severe psychiatric disorder. However, information on how each preventive intervention fares against other currently available treatment options remains unavailable. The aim of the current study was to quantify the consistency and magnitude of effects of specific preventive interventions for psychosis, comparing different treatments in a network meta-analysis. PsycINFO, Web of Science, Cochrane Central Register of Controlled Trials, and unpublished/grey literature were searched up to July 18, 2017, to identify randomized controlled trials conducted in individuals at clinical high risk for psychosis, comparing different types of intervention and reporting transition to psychosis. Two reviewers independently extracted data. Data were synthesized using network meta-analyses. The primary outcome was transition to psychosis at different time points and the secondary outcome was treatment acceptability (dropout due to any cause). Effect sizes were reported as odds ratios and 95% confidence intervals (CIs). Sixteen studies (2,035 patients, 57% male, mean age 20.1 years) reported on risk of transition. The treatments tested were needs-based interventions (NBI); omega-3 + NBI; ziprasidone + NBI; olanzapine + NBI; aripiprazole + NBI; integrated psychological interventions; family therapy + NBI; D-serine + NBI; cognitive behavioural therapy, French & Morrison protocol (CBT-F) + NBI; CBT-F + risperidone + NBI; and cognitive behavioural therapy, van der Gaag protocol (CBT-V) + CBT-F + NBI. The network meta-analysis showed no evidence of significantly superior efficacy of any one intervention over the others at 6 and 12 months (insufficient data were available after 12 months). Similarly, there was no evidence for intervention differences in acceptability at either time point. Tests for inconsistency were non-significant and sensitivity analyses controlling for different clustering of interventions and biases did not materially affect the interpretation of the results. In summary, this study indicates that, to date, there is no evidence that any specific intervention is particularly effective over the others in preventing transition to psychosis. Further experimental research is needed.

Key words: Psychosis, risk, prevention, needs-based interventions, cognitive behavioural therapy, antipsychotics, omega-3, integrated psychological interventions, family therapy, network meta-analysis, guidelines

(World Psychiatry 2018;17:196–209)

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[Intervention Review]

Interventions for prodromal stage of psychosis

Dina Bosnjak Kuharic[1], Ivana Kekin[2], Joanne Hew[3], Martina Rojnic Kuzman[2], Livia Puljak[4]

[1]University Psychiatric Hospital Vrapče, Zagreb, Croatia. [2]Department of Psychiatry, Clinical Hospital Centre Zagreb, Zagreb, Croatia. [3]Department of Acute Care Psychiatry, South London and Maudsley NHS Foundation Trust, London, UK. [4]Center for Evidence-Based Medicine and Health Care, Catholic University of Croatia, Zagreb, Croatia

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*BARNABY NELSON, GÜNTER P AMMINGER, ANDREAS BECHDOLF, PAUL FRENCH, ASHOK MALLA, ANTHONY P MORRISON, STEFANIE J SCHMIDT, JAI L SHAH, ANDREW THOMPSON, MARK VAN DER GAAG, STEPHEN J WOOD, SCOTT W WOODS, ALISON R YUNG, PATRICK D MCGORRY

Doctopic: Analysis and Interpretation
19TLP1017_Nelson
[PII]

Comment

Evidence for preventive treatments in young patients at clinical high risk of psychosis: the need for context

Cochrane reviews, as rigorous evaluations of evidence in health care, have a substantial effect on clinical and policy decision-making; however, their findings and methods need to be contextualised. These reviews are done by groups of academics who might or might not have adequate expertise or clinical experience in the field they examine, and the methods are indeterminate and conservative.

The recent Cochrane review[1] of intervention trials for patients at clinical high risk of psychosis concluded that, despite the considerable research effort in this area, the evidence base was weak and firm conclusions could not yet be drawn. The authors noted that the "strongest trials (RCTs) with control conditions.[1] Although this method is arguably a better approach than network meta-analyses, it meant that the critical issue of whether, when all pooled together, specific targeted interventions were superior to standard treatment was left unaddressed. When this issue has been addressed, the onset of psychosis in the clinical high risk population could at least be delayed through specific targeted treatments, with a 50% risk reduction over 12 months.[5,6]

The Cochrane review did show the benefits of cognitive behavioural therapy (CBT) over supportive therapy, with a number needed to treat (NNT) of 13 over 1 year and a relative risk of 0·45 (about 8% *vs* 16%

IM Vanney/Science Photo Library

EDITORIAL

Clinical High Risk for Psychosis—Not Seeing the Trees for the Wood

Patrick D. McGorry, MD, PhD; Barnaby Nelson, PhD

"It's not the tools that you have faith in: tools are just tools. They work, or they don't work. It's people you have faith in or not."
Steve Jobs

Three decades ago, the schizophrenia field finally began to challenge the intrinsic pessimism that had inhibited preventive approaches for a century. Early detection and specialized early treatment models for first-episode psychosis have since become the global standard of care, producing better outcomes that "bend the curve" of the early course of illness[1] and have opened the door to the prevention or delay of the first episode of psychosis. The development of operational criteria (the "ultra" or "clinical" high risk [CHR] criteria) for identifying what we originally termed the *at-risk mental state* meant that an even earlier stage of illness could be identified prospectively and studied for its heuristic and therapeutic potential.

Related article

els of premorbid risk factors and are highly symptomatic with substantial comorbidity, substance use, suicidal behavior, and functional impairment. They not only demonstrate a clear-cut need for care, despite being subthreshold for first-episode psychosis, but also a range of neurobiologic disturbances, including structural brain changes, neurocognitive impairment, and blood biomarker changes. Some authors have alleged that this cohort of help-seeking patients are within the normative range and to offer care might be harmful through labeling or overtreatment.[5] The Fusar-Poli et al review[2] clearly validates their morbidity and risk. The question then arises of how to find and engage the people with a genuine need for care enriched for risk of psychosis and other potentially poor outcomes and how to intervene safely to reduce these risks and improve outcomes. Another challenge is to engage more than a minority of such patients[3] for whom solutions have been developed.[4]

The meta-analytic approach, especially at the umbrella level, fails to fully capture the cutting edge of knowledge and

EVIDENCE IS LIKE BEAUTY - IN THE EYE OF THE BEHOLDER

Doctopic: Analysis and Interpretation
19TLP1017_Nelson
[PII]

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Related article

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Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Intervention strategies for ultra-high risk for psychosis: Progress in delaying the onset and reducing the impact of first-episode psychosis

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ABSTRACT

Over a quarter of a century ago, the formulation of the "at risk mental state" and operational criteria to prospectively identify individuals at "clinical" or "ultra-high risk" (UHR) for psychosis created a global wave of research momentum aimed at predicting and preventing first-episode psychosis. A substantial number of randomized controlled trials (RCTs) were conducted to determine if transition to psychosis could be delayed or even prevented. The efficacy of a range of interventions was examined, with standard meta-analyses clearly indicating that these could at least delay transition for 1–2 years and that outcomes improve. Recently, network meta-analyses have attempted to identify the most effective intervention. These highlighted the fact that no one form of intervention is superior to the rest, a finding interpreted in such a way as to create doubts concerning the value of intervening. These doubts have been reinforced by a subsequent Cochrane review which judged the quality of the evidence as low or very low. Here, we report a narrative review of findings from RCTs and meta-analyses on the efficacy of interventions in UHR. We also critique the network meta-analyses and the

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Review

Preventive interventions for individuals at ultra high risk for psychosis: An updated and extended meta-analysis

Cristina Mei [a,b,1], Mark van der Gaag [c,d,**,1], Barnaby Nelson [a,b], Filip Smit [c,e,f], Hok Pan Yuen [a,b], Maximus Berger [a,b], Marija Krcmar [a,b], Paul French [g], G. Paul Amminger [a,b], Andreas Bechdolf [h,i], Pim Cuijpers [c], Alison R. Yung [a,b,g], Patrick D. McGorry [a,b,*]

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Psychosis

ABSTRACT

Intervention at the earliest illness stage, in ultra or clinical high-risk individuals, or indicated prevention, currently represents the most promising strategy to ameliorate, delay or prevent psychosis. We review the

Lack of robust meta-analytic evidence to favour cognitive behavioural therapy for prevention of psychosis

While achievements in detection and prognostic assessment of young people at clinical high risk for psychosis (CHR-P) have been recently consolidated, the efficacy of preventive interventions remains unclear[1].

Cognitive behavioural therapy (CBT) is the currently recommended preventive intervention, but the most updated network meta-analysis[2] found no robust evidence to favour it (and any of the other indicated interventions) compared to the control condition (i.e., needs-based interventions). A subsequent independent pairwise meta-analysis by the Cochrane group[3] confirmed these findings, concluding that there was "no convincing unbiased, high-quality evidence" that any type of intervention is more effective than needs-based interventions (another pairwise meta-analysis was subsequently published[4], but used older data). A further umbrella review showed no evidence that CBT impacts other clinical outcomes such as acceptability of treatments, severity of attenuated positive/negative psychotic symptoms, depression, symptom-related distress, social functioning, general functioning, and quality of life[5]. These studies high-

Indeed, the authors of the meta-analysis acknowledged that only one missing trial would be needed to render their end-of-treatment results non-significant[6]. To empirically test this, we have updated that meta-analysis by removing the low-quality small trial[7] and adding the large PREVENT trial. The updated risk ratio for CBT vs. control interventions to prevent transition to psychosis at 12 months was 0.631 (95% CI: 0.388-1.028, p=0.064), which shows no significant meta-analytic evidence that CBT can robustly prevent transition to psychosis.

Third, the authors' conclusion that CBT can robustly improve attenuated psychotic symptoms conflicts with the very small effect size, approaching the non-significance level (standardized mean difference = –0.15; 95% CI: –0.28 to –0.01)[6], which is unlikely to be associated with clinically meaningful benefits in the real-world.

Finally, the meta-analysis in question may be affected by reporting biases, which increased the likelihood of the results being significant in favour of CBT. For example, additional transitions to psychosis beyond those originally reported were included as "the most accurate data on transition rates"[6]. These data have never

SYNOPSIS: CLINICAL HIGH RISK PSYCHOSIS

–We can identify a clinical phenotype with a “need for care” which has a substantial risk of transition to psychosis

–Prediction can be sharpened but with falling transition rates “enrichment” is an issue

–We can reduce this risk through the provision of relatively specialised psychosocial care – CBT influenced…

–There are other comorbid or emerging/incident syndromes which means that there is valence for other exit syndromes and a range of outcomes including persistence or recurrence of the UHR stage and poor functioning

–Needs to be the target of new intervention strategies

–We need to clarify the sequence of optimal treatment for UHR stage

–Ideally this needs to be done in parallel with the prediction and treatment of other syndromes

–And guided by a parsing of heterogeneity (need to consider transdiagnostic perspective)

–$82m AMP Project

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ORIGINAL ARTICLE

WILEY

Baseline data of a sequential multiple assignment randomized trial (STEP study)

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Abstract

Aim: Research has shown that preventative intervention in individuals at ultra-high risk of psychosis (UHR) improves symptomatic and functional outcomes. The staged treatment in early psychosis (STEP) trial aims to determine the most effective type, timing and sequence of interventions in the UHR population by sequentially studying the effectiveness of (1) support and problem solving, (2) cognitive-behavioural case management and (3) antidepressant medication with an embedded fast-fail option of (4) omega-3 fatty acids or low-dose antipsychotic medication. This paper presents the recruitment flow and baseline clinical characteristics of the sample.

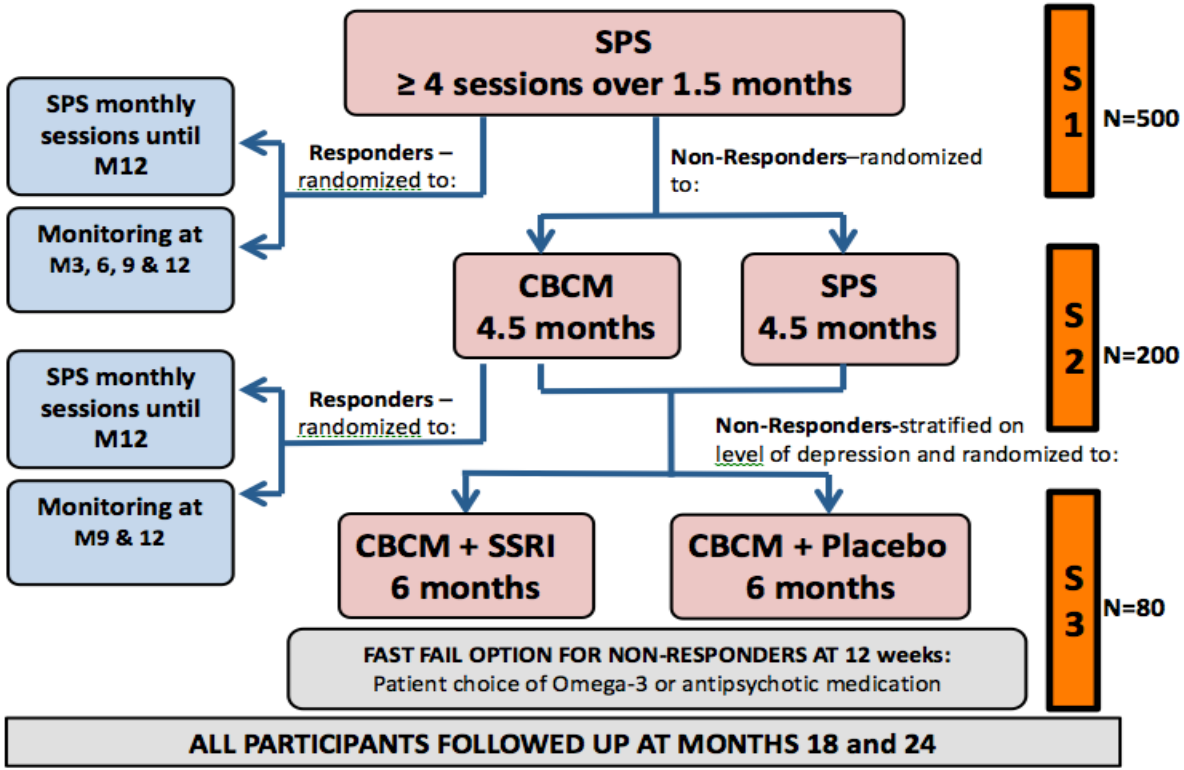
Methods: STEP is a sequential multiple assignment randomized trial. We present the baseline demographics, clinical characteristics and acceptability and feasibility of this treatment approach as indicated by the flow of participants from first contact up until enrolment into the trial. Recruitment took place between April 2016 and January 2019.

Results: Of 1343, help-seeking young people who were considered for participation, 402 participants were not eligible and 599 declined/disengaged, resulting in a total of 342 participants enrolled in the study. The most common reason for exclusion was an active prescription of antidepressant medication. Eighty-five percent of the enrolled sample had a non-psychotic DSM-5 diagnosis and symptomatic/functional measures showed a moderate level of clinical severity and functional impairment.

Discussion: The present study demonstrates the acceptability and participant's general positive appraisal of sequential treatment. It also shows, in line with other trials in UHR individuals, a significant level of psychiatric morbidity and impairment, demonstrating the clear need for care in this group and that treatment is appropriate.

KEYWORDS
antidepressant medication, clinical trial, prodrome, psychosis, ultra-high risk

TRIAL DESIGN



JAMA Psychiatry | Original Investigation

A Sequential Adaptive Intervention Strategy Targeting Remission and Functional Recovery in Young People at Ultrahigh Risk of Psychosis

The Staged Treatment in Early Psychosis (STEP) Sequential Multiple Assignment Randomized Trial

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IMPORTANCE Clinical trials have not established the optimal type, sequence, and duration of interventions for people at ultrahigh risk of psychosis.

OBJECTIVE To determine the effectiveness of a sequential and adaptive intervention strategy for individuals at ultrahigh risk of psychosis.

DESIGN, SETTING, AND PARTICIPANTS The Staged Treatment in Early Psychosis (STEP) sequential multiple assignment randomized trial took place within the clinical program at Orygen, Melbourne, Australia. Individuals aged 12 to 25 years who were seeking treatment and met criteria for ultrahigh risk of psychosis according to the Comprehensive Assessment of At-Risk Mental States were recruited between April 2016 and January 2019. Of 1343 individuals considered, 342 were recruited.

INTERVENTIONS Step 1: 6 weeks of support and problem solving (SPS); step 2: 20 weeks of cognitive-behavioral case management (CBCM) vs SPS; and step 3: 26 weeks of CBCM with fluoxetine vs CBCM with placebo with an embedded fast-fail option of ω-3 fatty acids or low-dose antipsychotic medication. Individuals who did not remit progressed through these steps; those who remitted received SPS or monitoring for up to 12 months.

MAIN OUTCOMES AND MEASURES Global Functioning: Social and Role scales (primary outcome), Brief Psychiatric Rating Scale, Scale for the Assessment of Negative Symptoms, Montgomery-Åsberg Depression Rating Scale, quality of life, transition to psychosis, and remission and relapse rates.

RESULTS The sample comprised 342 participants (198 female; mean [SD] age, 17.7 [3.1] years). Remission rates, reflecting sustained symptomatic and functional improvement, were 8.5%, 10.3%, and 11.4% at steps 1, 2, and 3, respectively. A total of 27.2% met remission criteria at any step. Relapse rates among those who remitted did not significantly differ between SPS and monitoring (step 1: 65.1% vs 58.3%; step 2: 37.7% vs 47.5%). There was no significant difference in functioning, symptoms, and transition rates between SPS and CBCM and between CBCM with fluoxetine and CBCM with placebo. Twelve-month transition rates to psychosis were 13.5% (entire sample), 3.3% (those who ever remitted), and 17.4% (those with no remission).

CONCLUSIONS AND RELEVANCE In this sequential multiple assignment randomized trial, transition rates to psychosis were moderate, and remission rates were lower than expected, partly reflecting the ambitious criteria set and challenges with real-world treatment fidelity and adherence. While all groups showed mild to moderate functional and symptomatic improvement, this was typically short of remission. While further adaptive trials that address these challenges are needed, findings confirm substantial and sustained morbidity and reveal relatively poor responsiveness to existing treatments.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT02751632

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Multimedia

Supplemental content

Author Affiliations: Author affiliations are listed at the end of this article.

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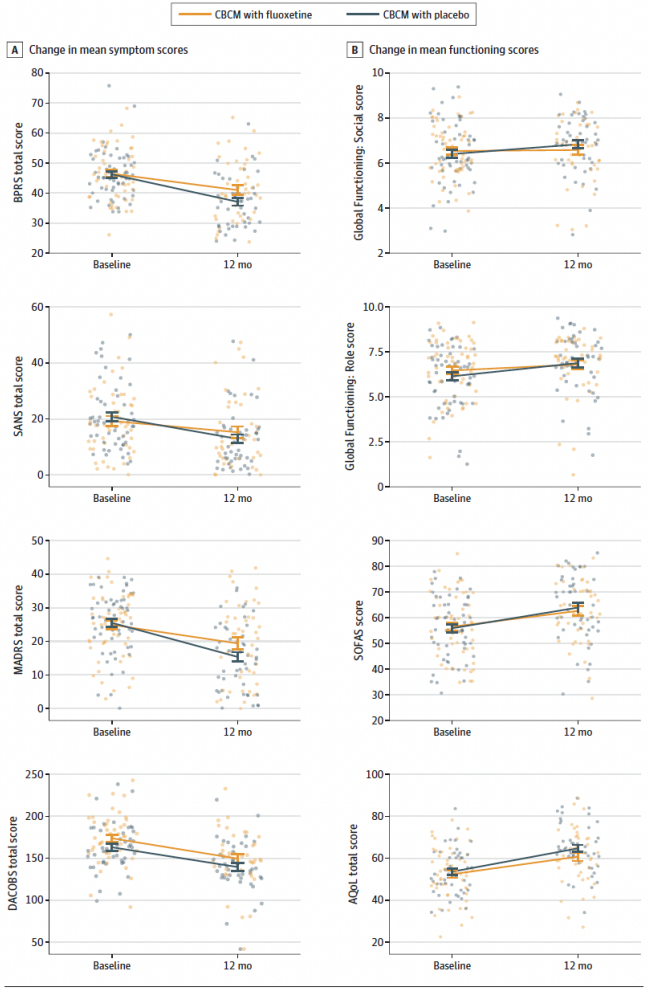
Key Points

Question What are the optimal type, timing, and sequence of interventions for individuals at ultrahigh risk of psychosis?

Findings In this sequential multiple assignment randomized trial including 342 individuals, a specialized psychological intervention (cognitive-behavioral case management [CBCM]) and a psychopharmacological intervention (CBCM and antidepressant medication) were not more efficacious than control conditions in improving remission and functional recovery. Relapse rates among individuals who remitted were high.

Meaning The findings of this study show that addition of sequentially more specialized psychosocial and antidepressant treatment for individuals who did not remit did not lead to superior outcomes, underscoring the need for further adaptive trials, treatment innovation, and an extended duration of care for relapse prevention.

Figure 2. Changes in Mean Symptom and Functioning Scores From Baseline to the End of Step 3



Circles represent individual participant data. Fluoxetine or placebo commenced at 6 months (start of step 3). AQoL indicates assessment of quality of life; BPRS, Brief Psychiatric Rating Scale; CBCM, cognitive-behavioral case management; DACOBS, Davos Assessment of Cognitive Biases Scale; MADRS, Montgomery-Åsberg Depression Rating Scale; SANS, Scale for the Assessment of Negative Symptoms; SOFAS, Social and Occupational Functioning Assessment Scale.

DISCUSSION

While the sample overall showed modest functional and symptomatic improvement over 12 months, remission rates were lower than expected, the transition rate was slightly higher than anticipated, and there was no significant difference between groups on the secondary outcomes.

Even when remission was achieved, it was difficult to maintain and continuing supportive therapy did not reduce relapse rates compared to monitoring.

DISCUSSION

The findings suggest that enhancing the intensity of treatment with psychological interventions (CBCM) or antidepressant medication in real-world youth mental health services does not produce benefit over continuing simpler care for longer. However, some caution is needed given the following caveats.

First, **the bar for remission was high**, though appropriate, requiring sustained symptomatic *and* functional improvement. If remission had been based on symptomatic improvement only, the overall remission rate would have increased to 41.2% (compared to 27.2%).

Second, the rate of **treatment discontinuation was substantial** (18%, Step 1; 48%, Step 2; 38%, Step 3) but comparable to the seminal STAR*D trial,[34] albeit with a different population focus.

Third, **adherence** to CBCM and to SSRI was **suboptimal** as with many of these trials to date. **Fidelity to CBCM was only modest** and therapists were primary care clinicians.

While some caution is warranted, and **needs-based care should continue to be provided to all UHR patients**, the findings indicate the need for further sequential RCTs examining existing treatments with improved adherence and fidelity, and for the development of innovative, more effective treatments and enhanced modes of delivery.

This could include **virtual reality, neuro-feedback, higher-fidelity CBT, individual placement and support, biotherapies (e.g., cannabidiol, anti-inflammatories, pomaglumetad methionil), neuroprotective agents including low-dose lithium, and reconsideration of low-dose antipsychotic medication for non-remitters to psychosocial interventions**.

Attempts to develop new treatments are underway, however we also need to better understand the **'active ingredients'** of existing treatments, particularly from a transdiagnostic perspective and **better define heterogeneity** within and across current syndromes and stages.

Enhancing the intensity of treatment with psychological interventions or medications was challenging to implement with fidelity and adherence in this largely primary care-based sample but nevertheless could not be demonstrated to produce any benefit over and above continuing a simpler form of care.

Low remission and high relapse rates confirm the sustained vulnerability and substantial morbidity of the UHR population and highlight the need to conduct further adaptive trials, develop new treatments, provide sustained specialist care, and identify subgroups for whom treatments can be tailored.

"What do you mean 'Your guess is as good as mine'?
My guess is a hell of a lot <u>better</u> than your guess!"

DYNAMIC PREDICTION

INTERNATIONAL JOURNAL OF METHODS IN PSYCHIATRIC RESEARCH Open Access

ORIGINAL ARTICLE | Free Access

A new method for analysing transition to psychosis: Joint modelling of time-to-event outcome with time-dependent predictors

Hok Pan Yuen ✉, Andrew Mackinnon, Barnaby Nelson

First published: 24 September 2017 | https://doi.org/10.1002/mpr.1588 | Citations: 11

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Development and Validation of a Dynamic Risk Prediction Model to Forecast Psychosis Onset in Patients at Clinical High Risk

Erich Studerus ✉, Katharina Beck, Paolo Fusar-Poli, Anita Riecher-Rössler

Schizophrenia Bulletin, Volume 46, Issue 2, March 2020, Pages 252–260, https://doi.org/10.1093/schbul/sbz059

Published: 29 July 2019

JAMA Psychiatry | Original Investigation

Multimodal Machine Learning Workflows for Prediction of Psychosis in Patients With Clinical High-Risk Syndromes and Recent-Onset Depression

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IMPORTANCE Diverse models have been developed to predict psychosis in patients with clinical high-risk (CHR) states. Whether prediction can be improved by efficiently combining clinical and biological models and by broadening the risk spectrum to young patients with depressive syndromes remains unclear.

OBJECTIVES To evaluate whether psychosis transition can be predicted in patients with CHR or recent-onset depression (ROD) using multimodal machine learning that optimally integrates clinical and neurocognitive data, structural magnetic resonance imaging (sMRI), and polygenic risk scores (PRS) for schizophrenia; to assess models' geographic generalizability; to test and integrate clinicians' predictions; and to maximize clinical utility by building a sequential prognostic system.

DESIGN, SETTING, AND PARTICIPANTS This multisite, longitudinal prognostic study performed in 7 academic early recognition services in 5 European countries followed up patients with CHR syndromes or ROD and healthy volunteers. The referred sample of 167 patients with CHR syndromes and 167 with ROD was recruited from February 1, 2014, to May 31, 2017, of whom 26 (23 with CHR syndromes and 3 with ROD) developed psychosis. Patients with 18-month follow-up (n = 246) were used for model training and leave-one-site-out cross-validation. The remaining 88 patients with nontransition served as the validation of model specificity. Three hundred thirty-four healthy volunteers provided a normative sample for prognostic signature evaluation. Three independent Swiss projects contributed a further 45 cases with psychosis transition and 600 with nontransition for the external validation of clinical-neurocognitive, sMRI-based, and combined models. Data were analyzed from January 1, 2019, to March 31, 2020.

MAIN OUTCOMES AND MEASURES Accuracy and generalizability of prognostic systems.

RESULTS A total of 668 individuals (334 patients and 334 controls) were included in the analysis (mean [SD] age, 25.1 [5.8] years; 354 [53.0%] female and 314 [47.0%] male). Clinicians attained a balanced accuracy of 73.2% by effectively ruling out (specificity, 84.9%) but ineffectively ruling in (sensitivity, 61.5%) psychosis transition. In contrast, algorithms showed high sensitivity (76.0%-88.0%) but low specificity (53.5%-66.8%). A cybernetic risk calculator combining all algorithmic and human components predicted psychosis with a balanced accuracy of 85.5% (sensitivity, 84.6%; specificity, 86.4%). In comparison, an optimal prognostic workflow produced a balanced accuracy of 85.9% (sensitivity, 84.6%; specificity, 87.3%) at a much lower diagnostic burden by sequentially integrating clinical-neurocognitive, expert-based, PRS-based, and sMRI-based risk estimates as needed for the given patient. Findings were supported by good external validation results.

CONCLUSIONS AND RELEVANCE These findings suggest that psychosis transition can be predicted in a broader risk spectrum by sequentially integrating algorithms' and clinicians' risk estimates. For clinical translation, the proposed workflow should undergo large-scale international validation.

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Published online December 2, 2020.

Supplemental content

Author Affiliations: Author affiliations are listed at the end of this article.

Group Information: A complete list of the PRONIA (Personalised Prognostic Tools for Early Psychosis Management) Consortium members appears at the end of article.

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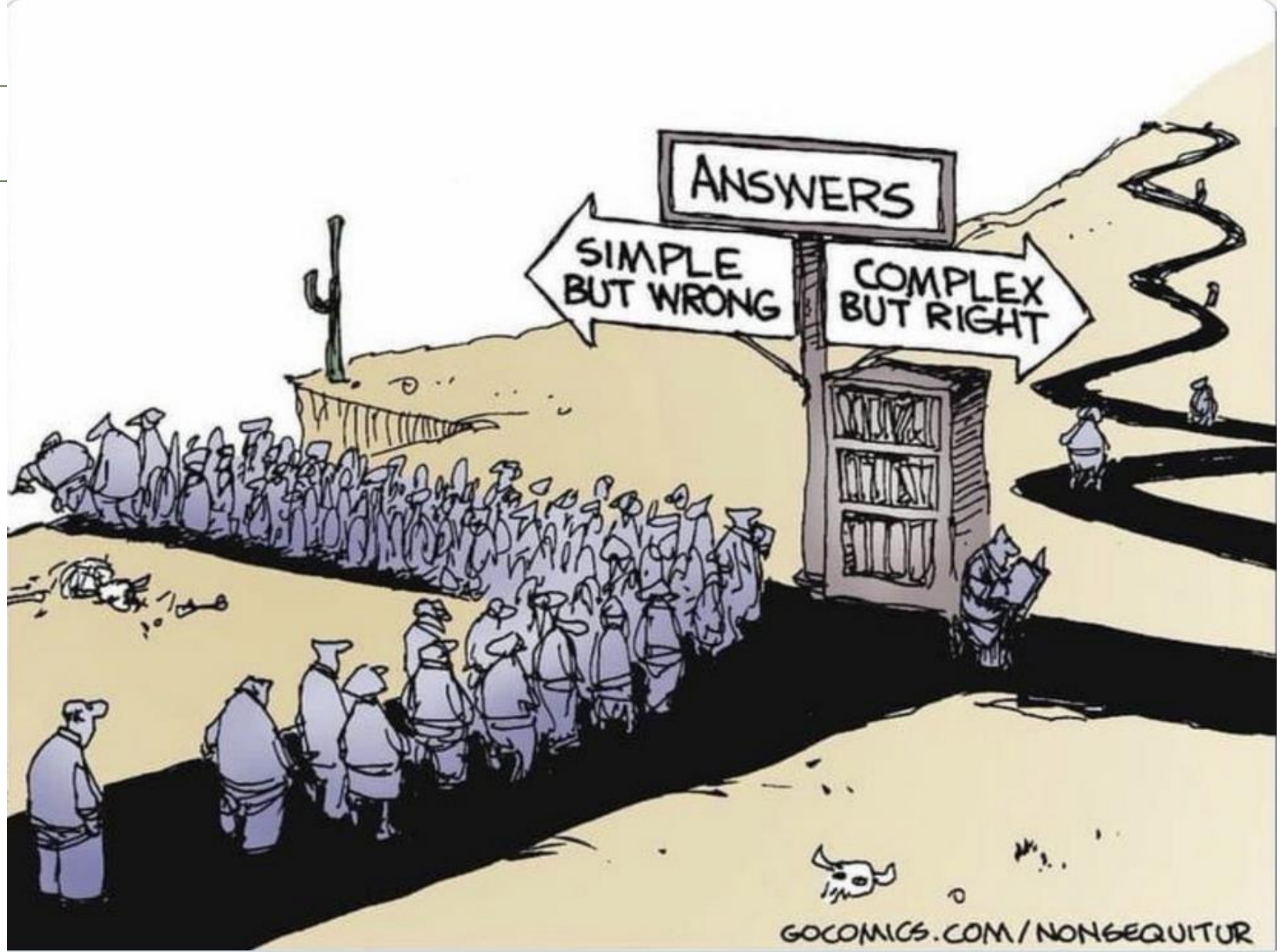
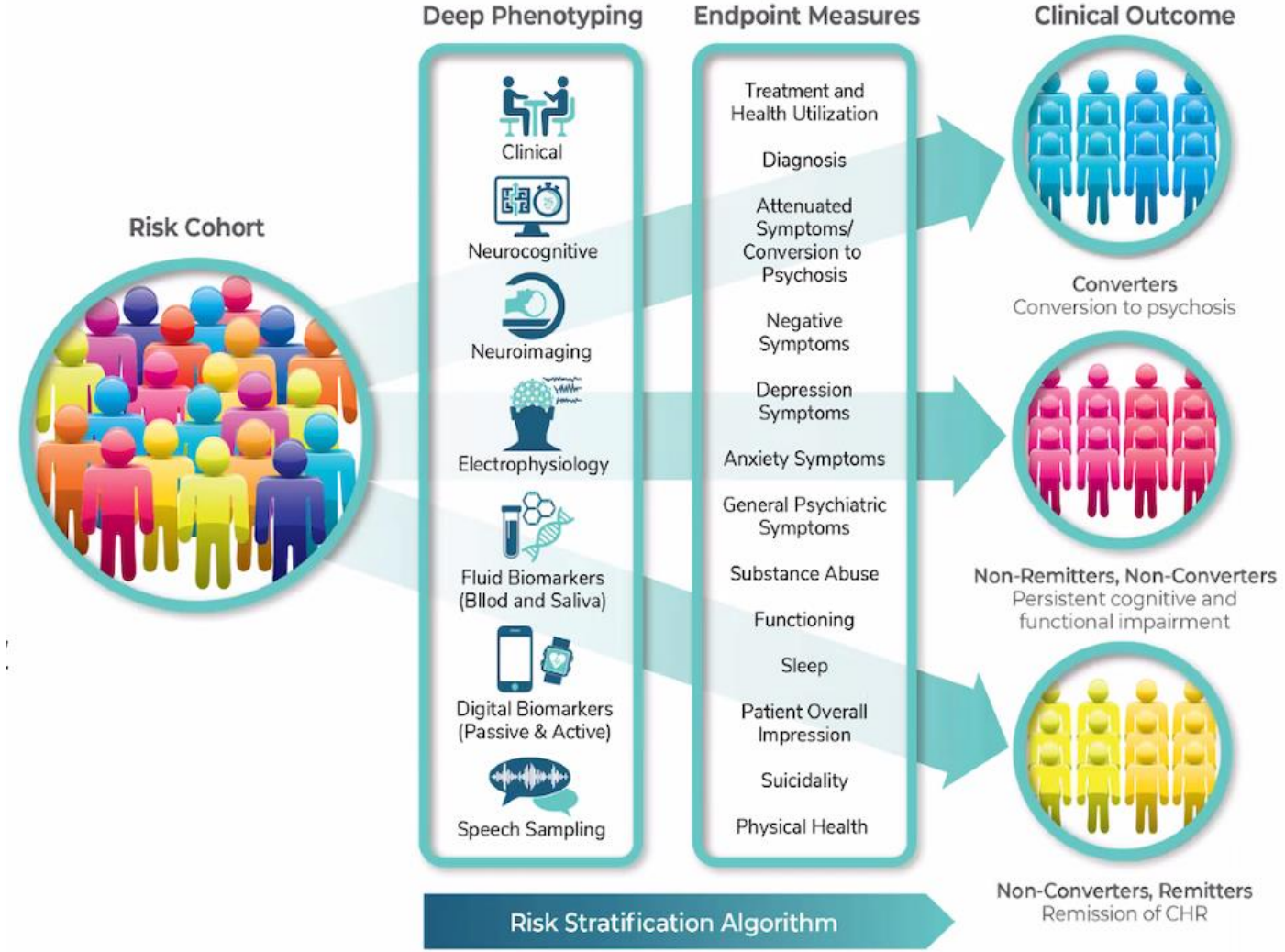

ANSWERS
SIMPLE BUT WRONG
COMPLEX BUT RIGHT
GOCOMICS.COM/NONSEQUITUR

TRAJECTORIES AND PREDICTORS IN THE CLINICAL HIGH RISK FOR PSYCHOSIS POPULATION:
PREDICTION SCIENTIFIC GLOBAL CONSORTIUM (PRESCIENT)

THE UNIVERSITY OF MELBOURNE

AMP SCZ
Early Intervention

orygen


Deep Phenotyping
Endpoint Measures
Clinical Outcome
Risk Cohort
Clinical
Neurocognitive
Neuroimaging
Electrophysiology
Fluid Biomarkers (Bllod and Saliva)
Digital Biomarkers (Passive & Active)
Speech Sampling
Treatment and Health Utilization
Diagnosis
Attenuated Symptoms/ Conversion to Psychosis
Negative Symptoms
Depression Symptoms
Anxiety Symptoms
General Psychiatric Symptoms
Substance Abuse
Functioning
Sleep
Patient Overall Impression
Suicidality
Physical Health
Converters
Conversion to psychosis
Non-Remitters, Non-Converters
Persistent cognitive and functional impairment
Non-Converters, Remitters
Remission of CHR
Risk Stratification Algorithm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THE UNIVERSITY of ADELAIDE
oxygen

AMP SCZ has established a Harmonized Research Network and Data Processing, Analysis, and Coordination Center

Recruitment to begin Q4 2021

- CHR participants: 1,937
- Healthy control participants: ≥ 555

ProNET: Psychosis-Risk Outcomes Network

Scott Woods
Yale University

Carrie Bearden
University of California, Los Angeles

John Kane
Northwell Health

PREDICT: Psychosis Risk Evaluation, Data Integration, and Computational Technologies

Martha Shenton
Harvard University

René Kahn
Icahn School of Medicine at Mount Sinai

PRESCIENT: Trajectories and Predictors in the Clinical High-Risk for Psychosis Population

Barnaby Nelson
University of Melbourne

Patrick McGorry
University of Melbourne

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FNIH

Article

Outcomes of Nontransitioned Cases in a Sample at Ultra-High Risk for Psychosis

Ashleigh Lin, Ph.D.

Stephen J. Wood, Ph.D.

Barnaby Nelson, Ph.D.

Amanda Beavan, B.Sc.

Patrick McGorry, M.D., Ph.D., F.R.A.N.Z.C.P.

Alison R. Yung, M.D., F.R.A.N.Z.C.P.

Objective: Two-thirds of individuals identified as at ultra-high risk for psychosis do not develop psychotic disorder over the medium term. The authors examined outcomes in a group of such patients.

Method: Participants were help-seeking individuals identified as being at ultra-high risk for psychosis 2–14 years previously. The 226 participants (125 female, 101 male) completed a follow-up assessment and had not developed psychosis. Their mean age at follow-up was 25.5 years (SD=4.8).

Results: At follow-up, 28% of the participants reported attenuated psychotic symptoms. Over the follow-up period, 68% experienced nonpsychotic disorders: mood disorder in 49%, anxiety disorder in 35%, and substance use disorder in 29%. For the majority (90%), nonpsychotic disorder was present at baseline, and it persisted for 52% of them. During follow-up, 26% of the cohort had remission of a disorder, but 38% developed a new disorder. Only 7% did not experience any disorder at baseline or during follow up. The incidence of nonpsychotic disorder was associated with more negative symptoms at baseline. Female participants experienced higher rates of persistent or recurrent disorder. Meeting criteria for brief limited intermittent psychotic symptoms at intake was associated with lower risk for persistent or recurrent disorder.

Conclusions: Individuals at ultra-high risk for psychosis who do not transition to psychosis are at significant risk for continued attenuated psychotic symptoms, persistent or recurrent disorders, and incident disorders. Findings have implications for ongoing clinical care.

Am J Psychiatry Lin et al.; AiA:1–10

Schizophrenia Bulletin
doi:10.1093/schbul/sbx173

Can We Predict Psychosis Outside the Clinical High-Risk State? A Systematic Review of Non-Psychotic Risk Syndromes for Mental Disorders

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SPECIAL ARTICLE

Beyond the "at risk mental state" concept: transitioning to transdiagnostic psychiatry

Patrick D. McGorry, Jessica A. Hartmann, Rachael Spooner, Barnaby Nelson

Orygen, The National Centre of Excellence in Youth Mental Health, and Centre for Youth Mental Health, University of Melbourne, Parkville, Australia

The "at risk mental state" for psychosis approach has been a catalytic, highly productive research paradigm over the last 25 years. In this paper we review that paradigm and summarize its key lessons, which include the valence of this phenotype for future psychosis outcomes, but also for comorbid, persistent or incident non-psychotic disorders; and the evidence that onset of psychotic disorder can at least be delayed in ultra high risk (UHR) patients, and that some full-threshold psychotic disorder may emerge from risk states not captured by UHR criteria. The paradigm has also illuminated risk factors and mechanisms involved in psychosis onset. However, findings from this and related paradigms indicate the need to develop new identification and diagnostic strategies. These findings include the high prevalence and impact of mental disorders in young people, the limitations of current diagnostic systems and risk identification approaches, the diffuse and unstable symptom patterns in early stages, and their pluripotent, transdiagnostic trajectories. The approach we have recently adopted has been guided by the clinical staging model and adapts the original "at risk mental state" approach to encompass a broader range of inputs and output target syndromes. This approach is supported by a number of novel modelling and prediction strategies that acknowledge and reflect the dynamic nature of psychopathology, such as dynamical systems theory, network theory, and joint modelling. Importantly, a broader transdiagnostic approach and enhancing specific prediction (profiling or increasing precision) can be achieved concurrently. A holistic strategy can be developed that applies these new prediction approaches, as well as machine learning and iterative probabilistic multimodal models, to a blend of subjective psychological data, physical disturbances (e.g., EEG measures) and biomarkers (e.g., neuroinflammation, neural network abnormalities) acquired through fine-grained sequential or longitudinal assessments. This strategy could ultimately enhance our understanding and ability to predict the onset, early course and evolution of mental ill health, further opening pathways for preventive interventions.

Key words: At risk mental state, psychosis, ultra high risk, transition, transdiagnostic psychiatry, clinical staging, CHARMS, prediction strategies, network theory, dynamical systems theory, joint modelling

(World Psychiatry 2018;17:00–00)

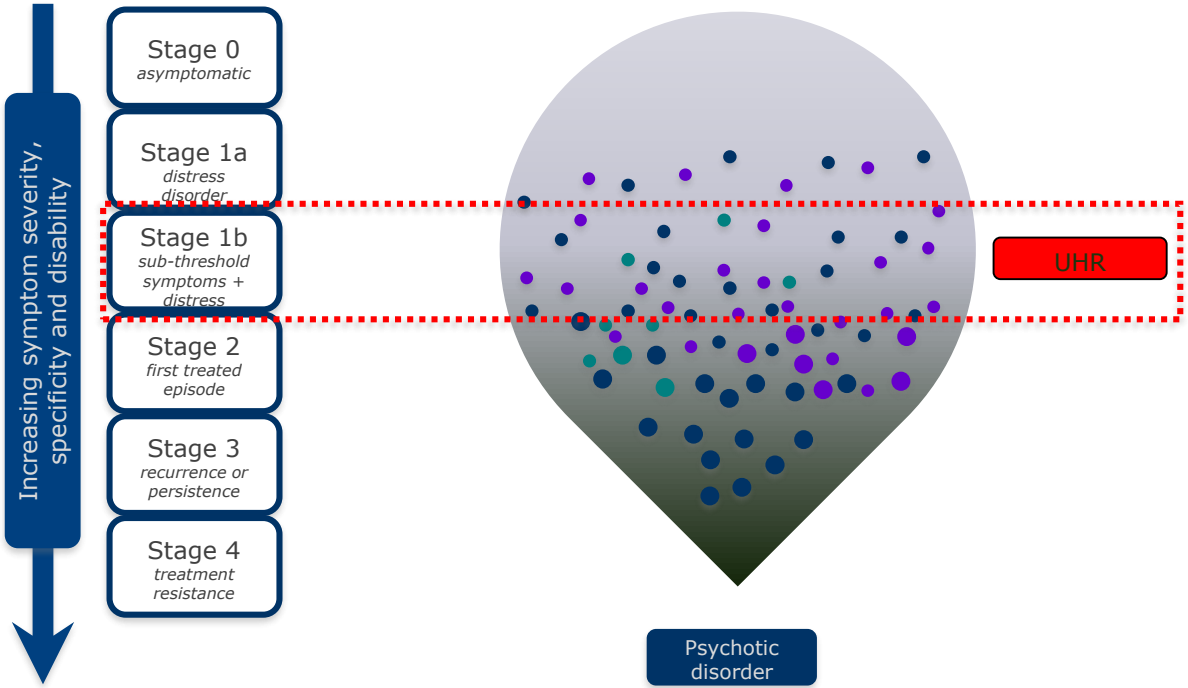


Figure 1A. Traditional UHR paradigm in the context of clinical staging

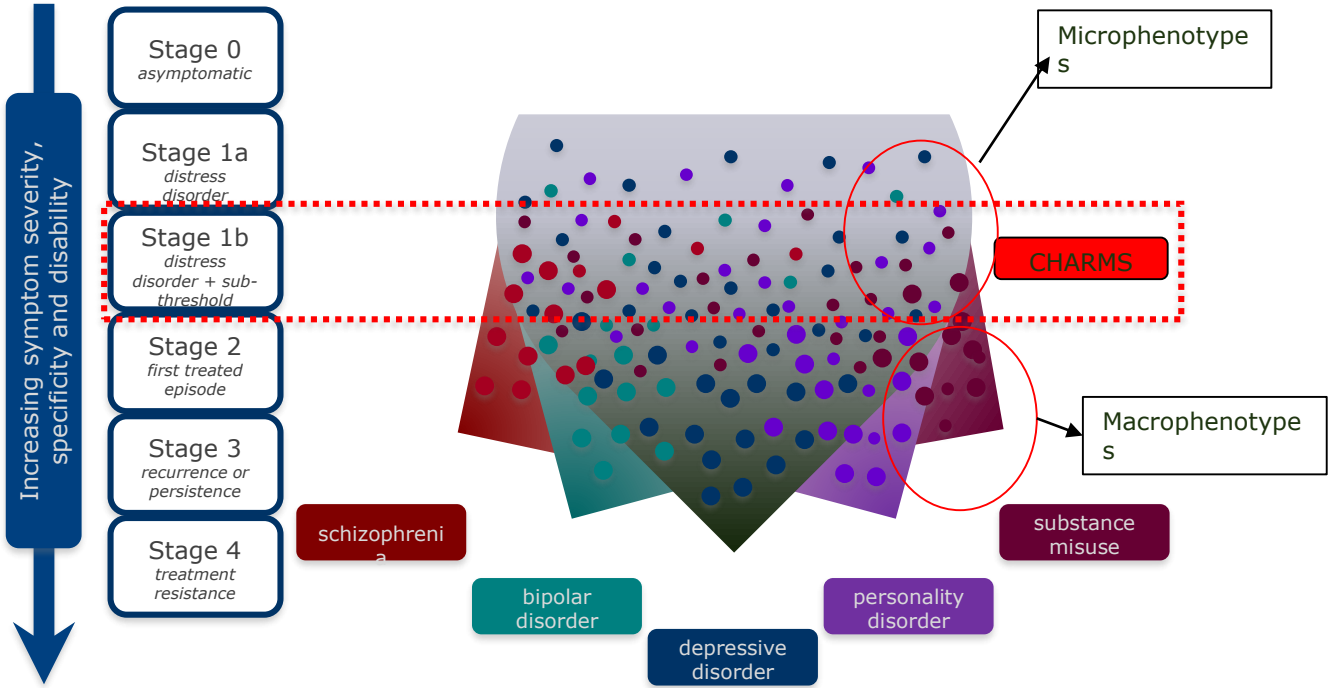
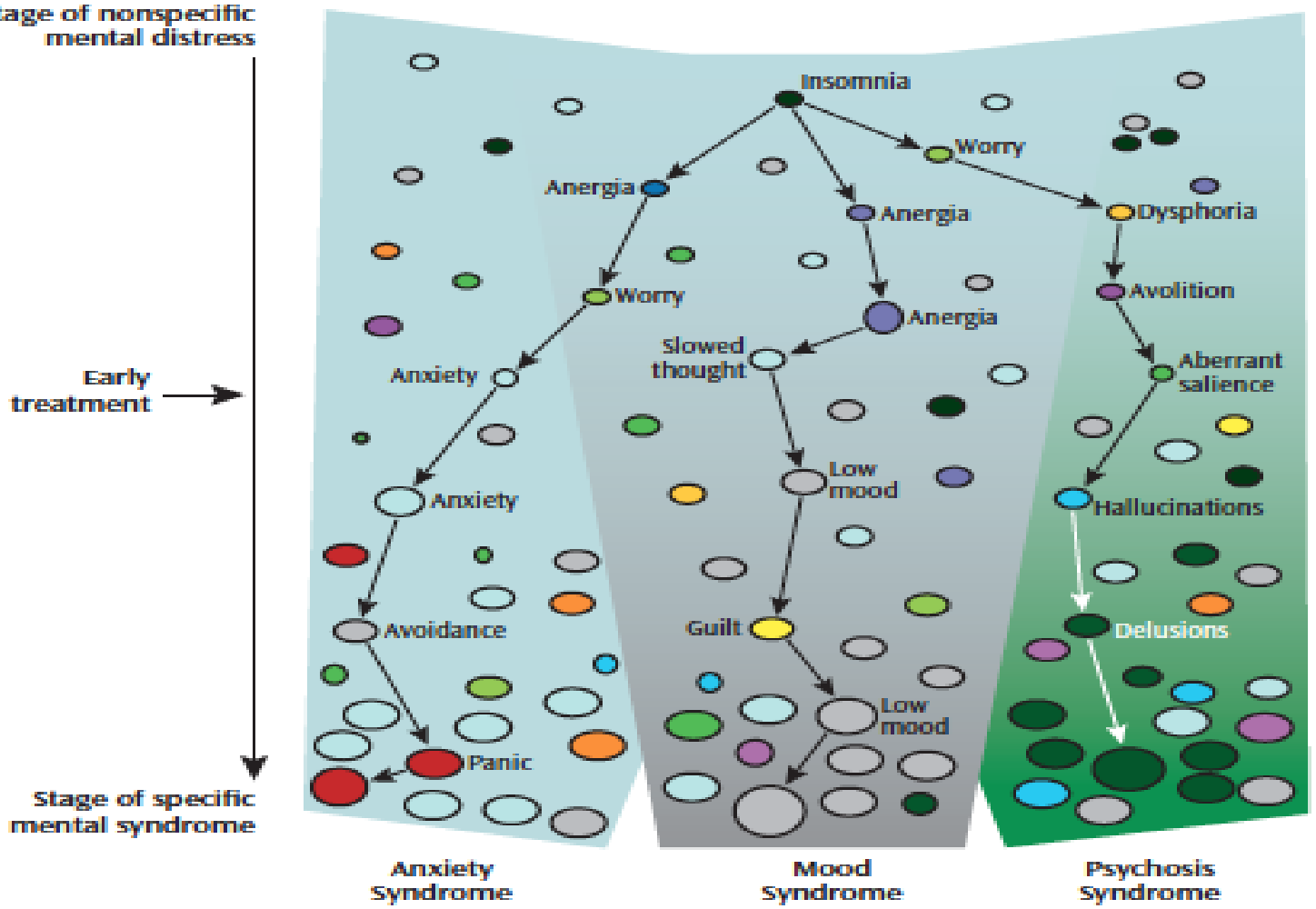


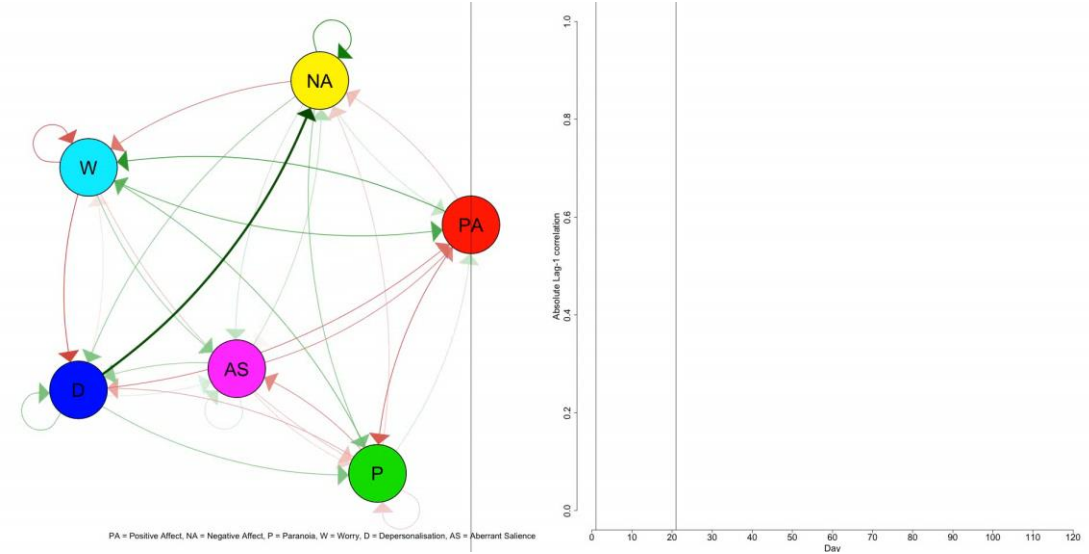
Figure 1B. New transdiagnostic CHARMS paradigm in the context of clinical staging

FIGURE 1. Staging Model of Causal Symptom Circuits[a]

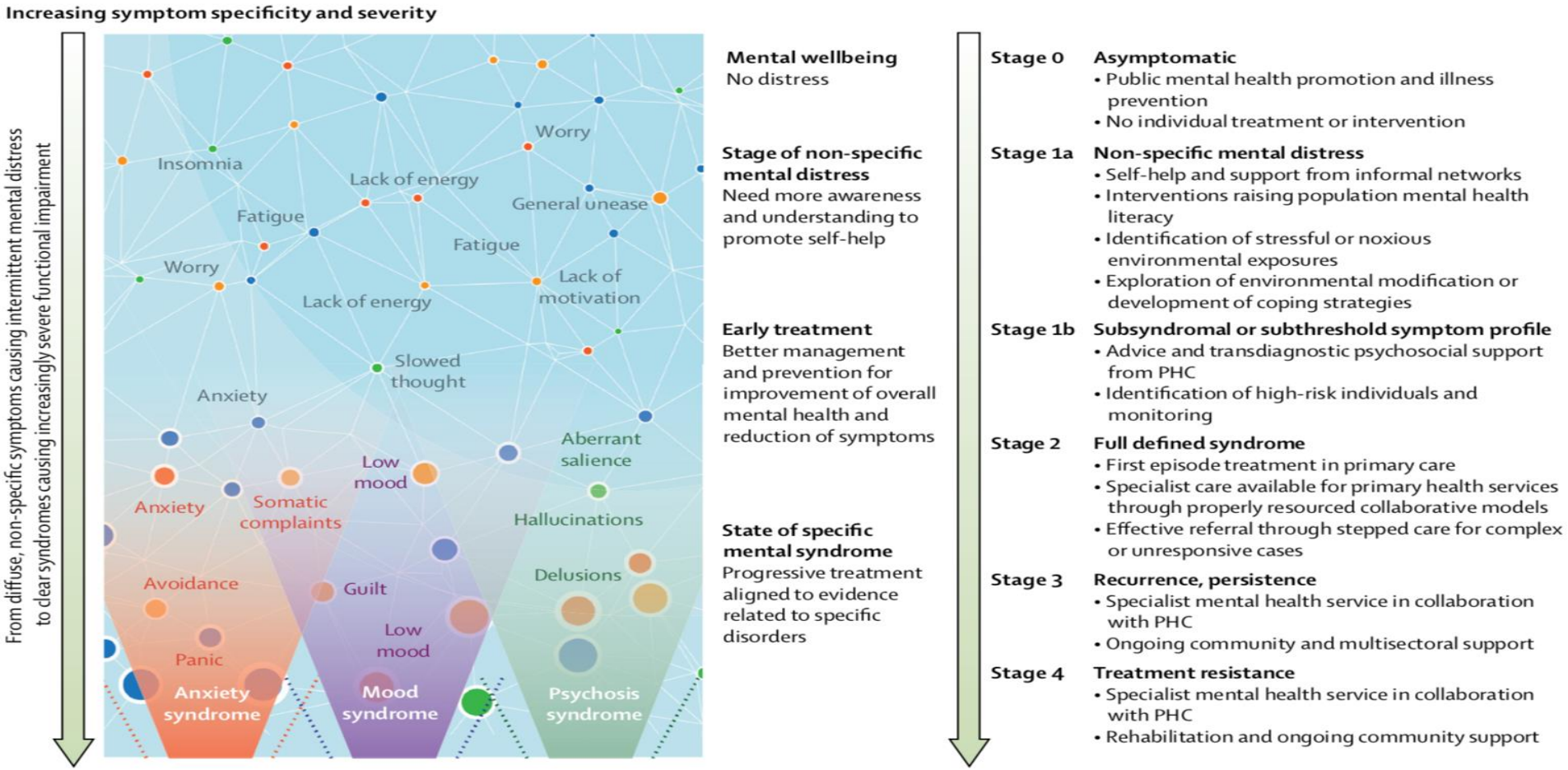


PSYCHOPATHOLOGY AS DYNAMIC SYSTEM

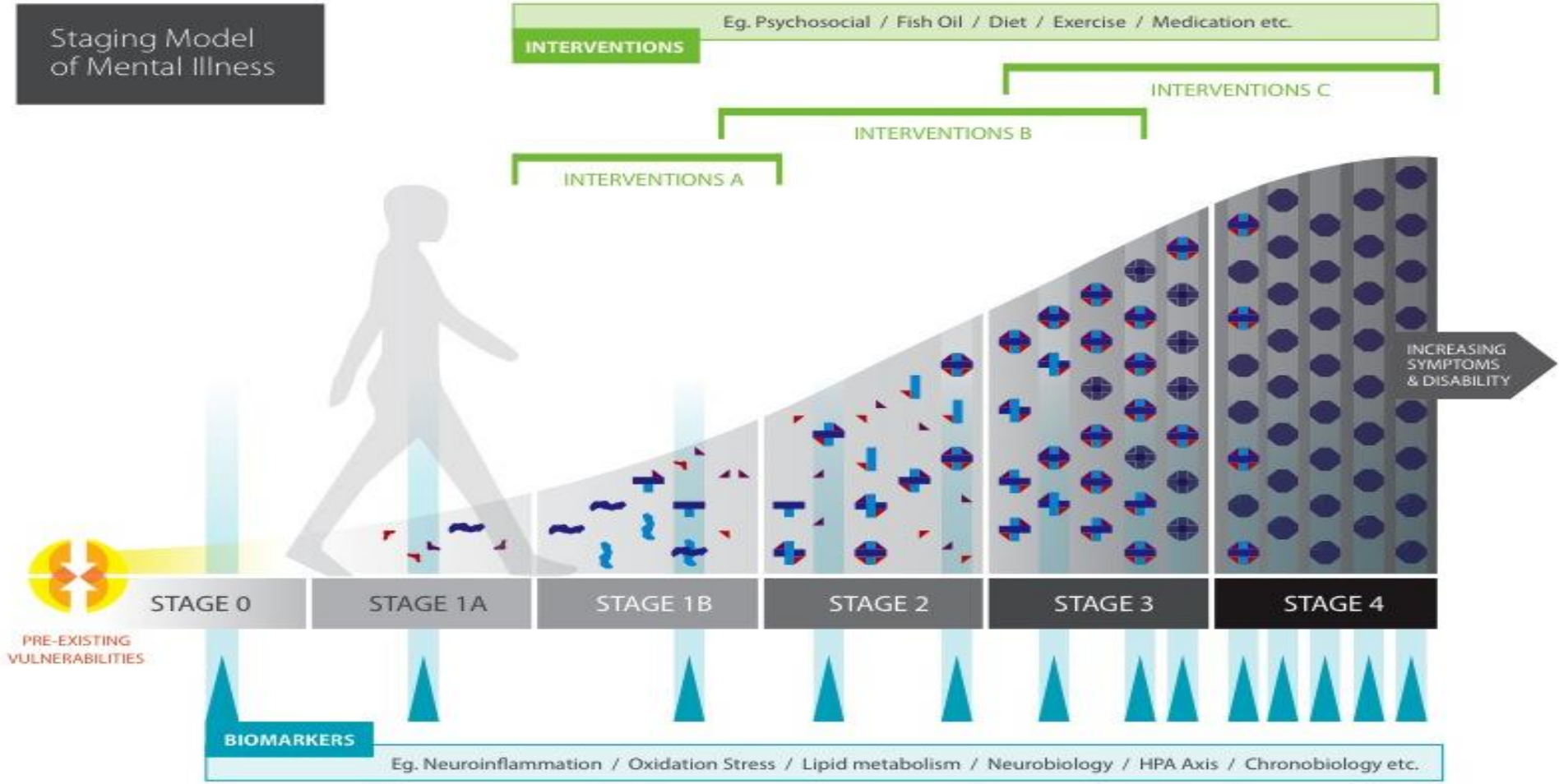
Network theory: Dynamic networks in CHARMS (pilot)

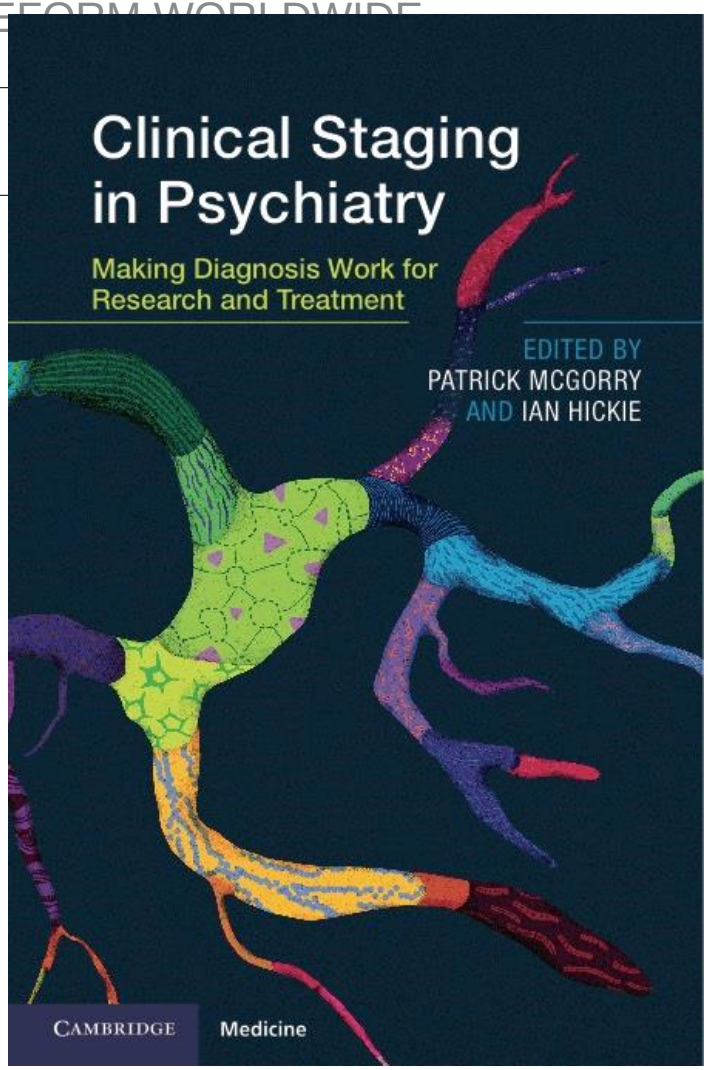


Hartmann, McGorry, Nelson. Predicting critical transitions in the mental health of young people at risk of serious mental illness: A pilot study. In preparation.



***gure 5*: A staging approach to the classification and treatment of mental disorders**
HC=primary health care. Adapted from McGorry et al[73] and McGorry and van Os.[74]


Staging Model of Mental Illness
INTERVENTIONS
Eg. Psychosocial / Fish Oil / Diet / Exercise / Medication etc.
INTERVENTIONS C
INTERVENTIONS B
INTERVENTIONS A
INCREASING SYMPTOMS & DISABILITY
STAGE 0
STAGE 1A
STAGE 1B
STAGE 2
STAGE 3
STAGE 4
PRE-EXISTING VULNERABILITIES
BIOMARKERS
Eg. Neuroinflammation / Oxidation Stress / Lipid metabolism / Neurobiology / HPA Axis / Chronobiology etc.


Clinical Staging in Psychiatry
Making Diagnosis Work for Research and Treatment
EDITED BY
PATRICK MCGORRY
AND IAN HICKIE
CAMBRIDGE
Medicine

STAGING: DIAGNOSIS SANS FRONTIERS

- Some authors have attempted to mould the staging idea to the procrustean silos of existing late macrophenotypes. However, the essential feature of the model is that it is transdiagnostic.
- This does not mean that late macrophenotypes such as mania, psychosis and anorexia cannot be accommodated as they differentiate out and stabilize.
- The specificity of treatment approaches or otherwise can be examined and the spurious precision of the licensing of medications and other therapies replaced by a more flexible and accurate evidence-based approach as in mainstream health care.

EDITORIAL

Why We Need a Transdiagnostic Staging Approach to Emerging Psychopathology, Early Diagnosis, and Treatment

Patrick McGorry, MD, PhD, FRCP, FRANZCP; Barnaby Nelson, PhD

One of the urgent challenges for psychiatry is to create a simpler, more useful approach to diagnosis.[1] Our traditional diagnostic systems are categorical and siloed, consisting of polythetic operational definitions of clinical phenotypes. The boundaries between syndromes and phenotypes are not clear and comorbidity is the rule rather than the exception. We know that dimensionality underlies most of these phenotypes and that distress, impairment, and need for care is not limited to the full threshold versions of these phenotypes. This means that a transdiagnostic approach is going to be necessary. The dynamics of early psychopathology are complex and emerging microphenotypes ebb, flow, and evolve in many patterns, which do not follow rigid train tracks to discrete macrophenotypes such as schizophrenia or bipolar disorder. The reification of these macrophenotypes has led to a spurious cer-

Related article page 211

There is a long tradition of conceptualization and study of brief or transient psychoses from the phenomenological tradition. In fact, much of this literature sought to distinguish these and similar phenotypes from the flawed but compelling concept of "process" schizophrenia. There are many interesting concepts from a range of cultures and traditions, and their common features included an abrupt onset, polymorphic and unstable features, a high level of disorganization, and very often an inference of psychogenic causation. For example, Brief Psychosis in the *DSM 3* was Brief Reactive Psychosis. These psychoses were, ironically in the present context, usually defined by the *lack* of a prodromal or dimensional precursor stage. In contrast, the concept of brief limited intermittent psychotic symptoms (BLIPS) as a warning sign for a first episode of sustained psychosis was part of an attempt to rise above the Kraepelinian framework and predict a first-episode psychosis (not merely nonaffective) of sufficient se-

IORFINO ET AL 2019 TRANSDIAGNOSTIC STAGING IN PRACTICE

Research

JAMA Psychiatry | Original Investigation

Clinical Stage Transitions in Persons Aged 12 to 25 Years Presenting to Early Intervention Mental Health Services With Anxiety, Mood, and Psychotic Disorders

Frank Iorfino, PhD; Elizabeth M. Scott, MD, FRANZCP; Joanne S. Carpenter, PhD; Shane P. Cross, PhD; Daniel F. Hermens, PhD; Madhura Killedar, PhD; Alissa Nichles, PGDipAppPsy; Natalia Zmicerevska, MCouns; Django White, BLaS (Stats); Adam J. Guastella, PhD; Jan Scott, PhD, FRCPsych; Patrick D. McGorry, MD, PhD, FRCP, FRANZCP; Ian B. Hickie, MD, FRANZCP, FASSA, FAHMS

Editorial

Supplemental content

IMPORTANCE The large contribution of psychiatric disorders to premature death and persistent disability among young people means that earlier identification and enhanced long-term care for those who are most at risk of developing life-threatening or chronic disorders is critical. Clinical staging as an adjunct to diagnosis to address emerging psychiatric disorders has been proposed for young people presenting for care; however, the longer-term utility of this system has not been established.

OBJECTIVES To determine the rates of transition from earlier to later stages of anxiety, mood, psychotic, or comorbid disorders and to identify the demographic and clinical characteristics that are associated with the time course of these transitions.

DESIGN, SETTING, AND PARTICIPANTS A longitudinal, observational study of 2254 persons aged 12 to 25 years who obtained mental health care at 2 early intervention mental health services in Sydney, Australia, and were recruited to a research register between June 18, 2008, and July 24, 2018 (the Brain and Mind Centre Optymise Cohort).

MAIN OUTCOMES AND MEASURES The primary outcome of this study was transition from earlier to later clinical stages. A multistate Markov model was used to examine demographic (ie, age, sex, engagement in education, employment, or both) and clinical (ie, social and occupational function, clinical presentation, personal history of mental illness, physical health comorbidities, treatment use, self-harm, suicidal thoughts and behaviors) factors associated with these transitions.

RESULTS Of the 2254 individuals included in the study, mean (SD) age at baseline was 18.18 (3.33) years and 1330 (59.0%) were female. Data on race/ethnicity were not available. Median (interquartile range) follow-up was 14 (5-33) months. Of 685 participants at stage 1a (nonspecific symptoms), 253 (36.9%) transitioned to stage 1b (attenuated syndromes). Transition was associated with lower social functioning (hazard ratio [HR], 0.77; 95% CI, 0.66-0.90), engagement with education, employment, or both (HR, 0.47; 95% CI, 0.25-0.91), manic-like experiences (HR, 2.12; 95% CI, 1.19-3.78), psychotic-like experiences (HR, 2.13; 95% CI, 1.38-3.28), self-harm (HR, 1.42; 95% CI, 1.01-1.99), and older age (HR, 1.27; 95% CI, 1.11-1.45). Of 1370 stage 1b participants, 176 (12.8%) transitioned to stage 2 (full-threshold) disorders. Transition was associated with psychotic-like experiences (HR, 2.31; 95% CI, 1.65-3.23), circadian disturbance (HR, 1.66; 95% CI, 1.17-2.35), psychiatric medication (HR, 1.43; 95% CI, 1.03-1.99), childhood psychiatric disorder (HR, 1.62; 95% CI, 1.03-2.54), and older age (HR, 1.24; 95% CI, 1.05-1.45).

CONCLUSIONS AND RELEVANCE Differential rates of progression from earlier to later stages of anxiety, mood, psychotic, or comorbid disorders were observed in young persons who presented for care at various stages. Understanding the rate and factors associated with transition assists planning of stage-specific clinical interventions and secondary prevention trials.

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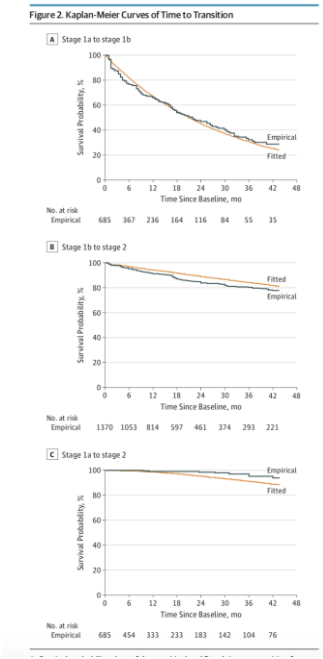


DUP

Care Pathways Before First Diagnosis of a Psychotic Disorder in Adolescents and Young Adults

Gregory E. Simon, M.D., M.P.H., Christine Stewart, Ph.D., Enid M. Hunkeler, M.A., Bobbi Jo Yarborough, Ph.D., Frances Lynch, Ph.D., Karen J. Coleman, Ph.D., Arne Beck, Ph.D., Belinda H. Operskalski, M.P.H., Robert B. Penfold, Ph.D., David S. Carrell, Ph.D.

Objective: The authors sought to describe patterns of health care use prior to first diagnosis of a psychotic disorder in a population-based sample.

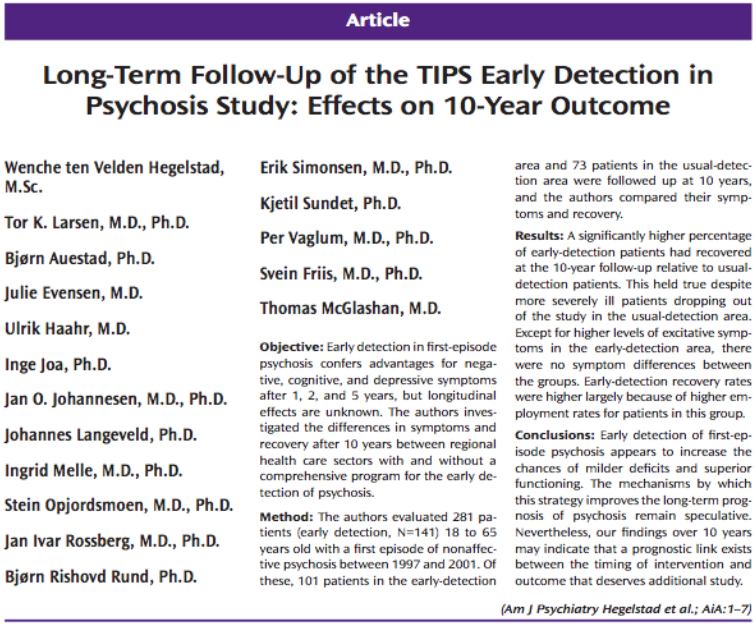
Method: Electronic health records and insurance claims from five large integrated health systems were used to identify 624 patients 15–29 years old who received a first diagnosis of a psychotic disorder in any care setting and to record health services received, diagnoses assigned, and medications dispensed during the previous 36 months. Patterns of utilization were compared between patients receiving a first diagnosis of a psychotic disorder and matched samples of general health system members and members receiving a first diagnosis of unipolar depression.

Results: During the year before a first psychotic disorder diagnosis, 29% of patients had mental health specialty outpatient care, 8% had mental health inpatient care, 24% had emergency department mental health care, 29% made a primary care visit with a mental health diagnosis, and 60% received at least one mental health diagnosis (including substance use disorders). Compared with patients receiving a first diagnosis of unipolar depression, those with a first diagnosis of a psychotic disorder were modestly more likely to use all types of health services and were specifically more likely to use mental health inpatient care (odds ratio=2.96, 95% CI=1.97–4.43) and mental health emergency department care (rate ratio=3.74, 95% CI=3.39–4.53).

Conclusions: Most patients receiving a first diagnosis of a psychotic disorder had some indication of mental health care need during the previous year. General use of primary care or mental health services, however, does not clearly distinguish people who later receive a diagnosis of a psychotic disorder from those who later receive a diagnosis of unipolar depression. Use of inpatient or emergency department mental health care is a more specific indicator of risk.

AJP in Advance (doi: 10.1176/appi.ajp.2017.17080844)

TREATMENT DELAY (DUP) MATTERS



Article

Long-Term Follow-Up of the TIPS Early Detection in Psychosis Study: Effects on 10-Year Outcome

Wenche ten Velden Hegelstad, M.Sc.

Tor K. Larsen, M.D., Ph.D.

Bjørn Auestad, Ph.D.

Julie Evensen, M.D.

Ulrik Haahr, M.D.

Inge Joa, Ph.D.

Jan O. Johannesen, M.D., Ph.D.

Johannes Langeveld, Ph.D.

Ingrid Melle, M.D., Ph.D.

Stein Opjordsmoen, M.D., Ph.D.

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Bjørn Rishovd Rund, Ph.D.

Erik Simonsen, M.D., Ph.D.

Kjetil Sundet, Ph.D.

Per Vaglum, M.D., Ph.D.

Svein Friis, M.D., Ph.D.

Thomas McGlashan, M.D.

Objective: Early detection in first-episode psychosis confers advantages for negative, cognitive, and depressive symptoms after 1, 2, and 5 years, but longitudinal effects are unknown. The authors investigated the differences in symptoms and recovery after 10 years between regional health care sectors with and without a comprehensive program for the early detection of psychosis.

Method: The authors evaluated 281 patients (early detection, N=141) 18 to 65 years old with a first episode of nonaffective psychosis between 1997 and 2001. Of these, 101 patients in the early-detection area and 73 patients in the usual-detection area were followed up at 10 years, and the authors compared their symptoms and recovery.

Results: A significantly higher percentage of early-detection patients had recovered at the 10-year follow-up relative to usual-detection patients. This held true despite more severely ill patients dropping out of the study in the usual-detection area. Except for higher levels of excitative symptoms in the early-detection area, there were no symptom differences between the groups. Early-detection recovery rates were higher largely because of higher employment rates for patients in this group.

Conclusions: Early detection of first-episode psychosis appears to increase the chances of milder deficits and superior functioning. The mechanisms by which this strategy improves the long-term prognosis of psychosis remain speculative. Nevertheless, our findings over 10 years may indicate that a prognostic link exists between the timing of intervention and outcome that deserves additional study.

(Am J Psychiatry Hegelstad et al.; AiA:1–7)

Effect of delaying treatment of first-episode psychosis on symptoms and social outcomes: a longitudinal analysis and modelling study

Richard J Drake, Nusrat Husain, Max Marshall, Shôn W Lewis, Barbara Tomenson, Imran B Chaudhry, Linda Everard, Swaran Singh, Nick Freemantle, David Fowler, Peter B Jones, Tim Amos, Vimal Sharma, Chloe D Green, Helen Fisher, Robin M Murray, Til Wykes, Iain Buchan, Max Birchwood

Lancet Psychiatry 2020; 7: 602–10

See Comment page 563

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Summary

Background Delayed treatment for first episodes of psychosis predicts worse outcomes. We hypothesised that delaying treatment makes all symptoms more refractory, with harm worsening first quickly, then more slowly. We also hypothesised that although delay impairs treatment response, worse symptoms hasten treatment, which at presentation mitigates the detrimental effect of treatment delay on symptoms.

Methods In this longitudinal analysis and modelling study, we included two longitudinal cohorts of patients with first-episode psychosis presenting to English early intervention services from defined catchments: NEDEN (recruiting 1003 patients aged 14–35 years from 14 services between Aug 1, 2005, and April 1, 2009) and Outlook (recruiting 399 patients aged 16–35 years from 11 services between April 1, 2006, and Feb 28, 2009). Patients were assessed at baseline, 6 months, and 12 months with the Positive and Negative Symptom Scale (PANSS), Calgary Depression Scale for Schizophrenia, Mania Rating Scale, Insight Scale, and Social and Occupational Functioning Assessment Scale. Regression was used to compare different models of the relationship between duration of untreated psychosis (DUP) and total symptoms at 6 months. Growth curve models of symptom subscales tested predictions arising from our hypotheses.

Findings We included 948 patients from the NEDEN study and 332 patients from the Outlook study who completed baseline assessments and were prescribed dopamine antagonist antipsychotics. For both cohorts, the best-fitting models were logarithmic, describing a curvilinear relationship of DUP to symptom severity: longer DUP predicted reduced treatment response, but response worsened more slowly as DUP lengthened. Increasing DUP by ten times predicted reduced improvement in total symptoms (ie, PANSS total) by 7·339 (95% CI 5·762 to 8·916; p<0·0001) in NEDEN data and 3·846 (1·689 to 6·003; p=0·0005) in Outlook data. This was true of treatment response for all symptom types. Nevertheless, longer DUP was not associated with worse presentation for any symptoms except depression in NEDEN (coefficients 0·099 [95% CI 0·033 to 0·164]; p=0·0028 in NEDEN and 0·007 [−0·081 to 0·095]; p=0·88 in Outlook).

Interpretation Long DUP was associated with reduced treatment response across subscales, consistent with a harmful process upstream of individual symptoms' mechanisms; response appeared to worsen quickly at first, then more slowly. These associations underscore the importance of rapid access to a comprehensive range of treatments, especially in the first weeks after psychosis onset.

Funding UK Department of Health, National Institute of Health Research, and Medical Research Council.

UK WAITING TIME TARGETS – PARITY OF ESTEEM WITH PHYSICAL HEALTH AND S

NICE National Institute for Health and Care Excellence

NHS England

RESEARCH ARTICLE

WILEY Health Economics

The impact of waiting time on patient outcomes: Evidence from early intervention in psychosis services in England

Anika Reichert | Rowena Jacobs

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Abstract

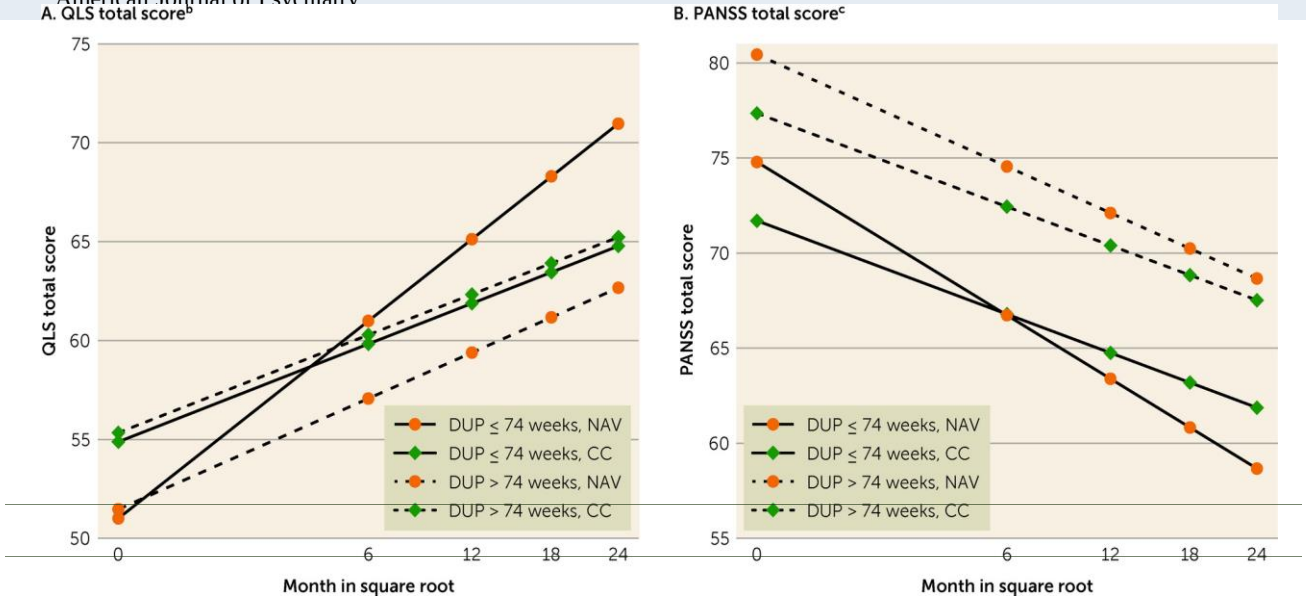
Recently, new emphasis was put on reducing waiting times in mental health services as there is an ongoing concern that longer waiting time for treatment leads to poorer health outcomes. However, little is known about delays within the mental health service system and its impact on patients. We explore the impact of waiting times on patient outcomes in the context of early intervention in psychosis (EIP) services in England from April 2012 to March 2015. We use the Mental Health Services Data Set and the routine outcome measure the Health of the Nation Outcome Scale. In a generalised linear regression model, we control for baseline outcomes, previous service use, and treatment intensity to account for possible endogeneity in waiting time. We find that longer waiting time is significantly associated with a deterioration in patient outcomes 12 months after acceptance for treatment for patients that are still in EIP care. Effects are strongest for waiting times longer than 3 months, and effect sizes are small to moderate. Patients with shorter treatment periods are not affected. The results suggest that policies should aim to reduce excessively long waits in order to improve outcomes for patients waiting for treatment for psychosis.

KEYWORDS
mental health, psychosis, routine outcome measures, treatment intensity, waiting times

THE AMERICAN JOURNAL OF PSYCHIATRY

From: Comprehensive Versus Usual Community Care for First-Episode Psychosis: 2-Year Outcomes From the NIMH RAISE Early Treatment Program

American Journal of Psychiatry



c DUP by treatment by square root of time interaction, p=0.043.

npj | Schizophrenia

www.nature.com/npjschz

ARTICLE OPEN

The effect of duration of untreated psychosis and treatment delay on the outcomes of prolonged early intervention in psychotic disorders

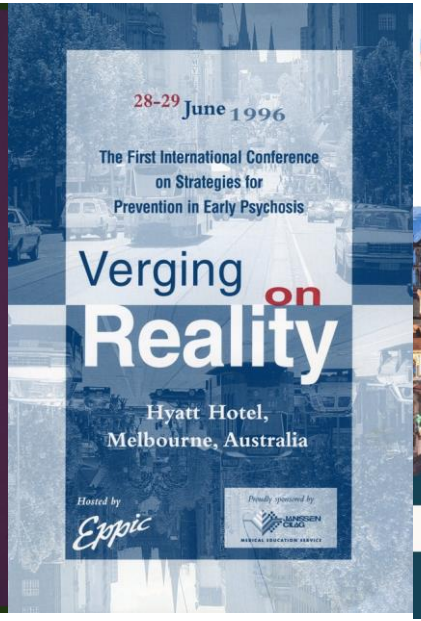
Nikolai Albert[1,2], Marianne Melau[1], Heidi Jensen[1], Lene Halling Hastrup[1,3], Carsten Hjorthøj[1] and Merete Nordentoft[1,2]

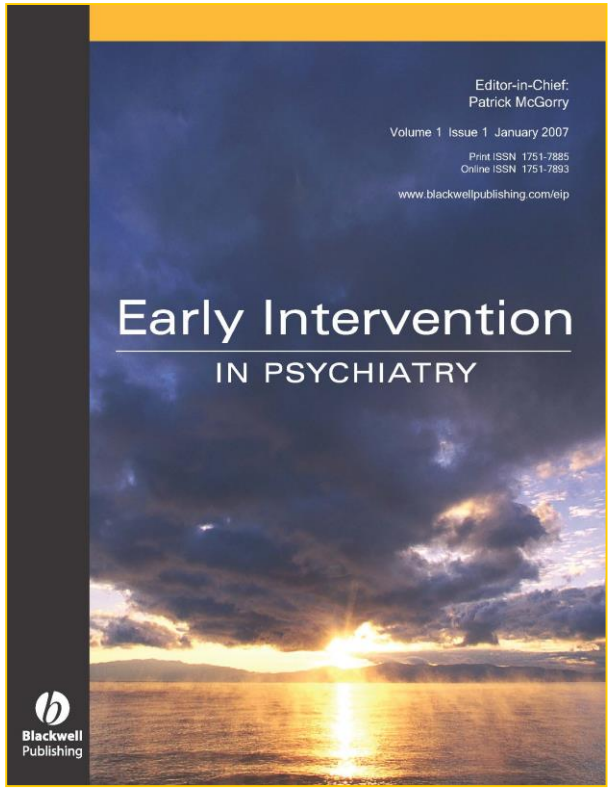
The duration of untreated psychosis (DUP) has been shown to have an effect on outcome after first-episode psychosis. The premise of specialized early intervention (SEI) services is that intervention in the early years of illness can affect long-term outcomes. In this study, we investigate whether DUP affects treatment response after 5 years of SEI treatment compared to 2 years of SEI treatment. As part of a randomized controlled trial testing the effect of prolonged SEI treatment 400 participants diagnosed within the schizophrenia spectrum were recruited. For this specific study participants were dichotomized based on DUP, treatment delay, and time from first symptom until start of SEI treatment. The groups were analyzed with regard to treatment response on psychopathology, level of functioning, and cognitive functioning. The participants with a short DUP had a tendency to respond better to the prolonged treatment with regards to disorganized and negative dimension. For participants with short duration from first symptom until start of SEI treatment there was a significant difference on the negative dimension favoring the prolonged OPUS treatment. The finding of an effect of prolonged treatment for participants with a short total treatment delay could mean that prolonged SEI treatment is more beneficial than treatment as usual (TAU) so long as it is provided in the early years of illness and not just in the early years after diagnosis.

npj Schizophrenia (2017)3:34 ; doi:10.1038/s41537-017-0034-4

WE CAN SCALE UP EIP REFORM IN MANY JURISDICTIONS IN EUROPE, NORTH AMERICA, AUSTRALIA AND ASIA

IEPA 1996-2022 FROM EARLY PSYCHOSIS TO FULL SPECTRUM





Early Intervention: A general principle in modern healthcare

JAMA Psychiatry | Original Investigation

Comparison of Early Intervention Services vs Treatment as Usual for Early-Phase Psychosis

A Systematic Review, Meta-analysis, and Meta-regression

Christoph U. Correll, MD; Britta Galling, MD; Aditya Pawar, MD; Anastasia Krivko, MD; Chiara Bonetto, MD; Mirella Ruggeri, MD; Thomas J. Craig, PhD; Merete Nordentoft, MD; Vinod H. Srihari, MD; Sinan Guloksuz, MD; Christy L. M. Hui, PhD; Eric Y. H. Chen, MD; Marcelo Valencia, PhD; Francisco Juarez, PhD; Delbert G. Robinson, MD; Nina R. Schooler, PhD; Mary F. Brunette, MD; Kim T. Mueser, PhD; Robert A. Rosenheck, MD; Patricia Marcy, BSN; Jean Addington, PhD; Sue E. Estroff, PhD; James Robinson, MEd; David Penn, PhD; Joanne B. Severe, MS; John M. Kane, MD

IMPORTANCE The value of early intervention in psychosis and allocation of public resources has long been debated because outcomes in people with schizophrenia spectrum disorders have remained suboptimal.

OBJECTIVE To compare early intervention services (EIS) with treatment as usual (TAU) for early-phase psychosis.

DATA SOURCES Systematic literature search of PubMed, PsycINFO, EMBASE, and ClinicalTrials.gov without language restrictions through June 6, 2017.

STUDY SELECTION Randomized trials comparing EIS vs TAU in first-episode psychosis or early-phase schizophrenia spectrum disorders.

DATA EXTRACTION AND SYNTHESIS This systematic review was conducted according to PRISMA guidelines. Three independent investigators extracted data for a random-effects meta-analysis and prespecified subgroup and meta-regression analyses.

MAIN OUTCOMES AND MEASURES The coprimary outcomes were all-cause treatment discontinuation and at least 1 psychiatric hospitalization during the treatment period.

RESULTS Across 10 randomized clinical trials (mean [SD] trial duration, 16.2 [7.4] months; range, 9-24 months) among 2176 patients (mean [SD] age, 27.5 [4.6] years; 1355 [62.3%] male), EIS was associated with better outcomes than TAU at the end of treatment for all 13 meta-analyzable outcomes. These outcomes included the following: all-cause treatment discontinuation (risk ratio [RR], 0.70; 95% CI, 0.61-0.80; $P < .001$), at least 1 psychiatric hospitalization (RR, 0.74; 95% CI, 0.61-0.90; $P = .003$), involvement in school or work (RR, 1.13; 95% CI, 1.03-1.24; $P = .01$), total symptom severity (standardized mean difference [SMD], −0.32; 95% CI, −0.47 to −0.17; $P < .001$), positive symptom severity (SMD, −0.22; 95% CI, −0.32 to −0.11; $P < .001$), and negative symptom severity (SMD, −0.28; 95% CI, −0.42 to −0.14; $P < .001$). Superiority of EIS regarding all outcomes was evident at 6, 9 to 12, and 18 to 24 months of treatment (except for general symptom severity and depressive symptom severity at 18-24 months).

CONCLUSIONS AND RELEVANCE In early-phase psychosis, EIS are superior to TAU across all meta-analyzable outcomes. These results support the need for funding and use of EIS in patients with early-phase psychosis.

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Editorial
Supplemental content

Author Affiliations: Author affiliations are listed at the end of this article.

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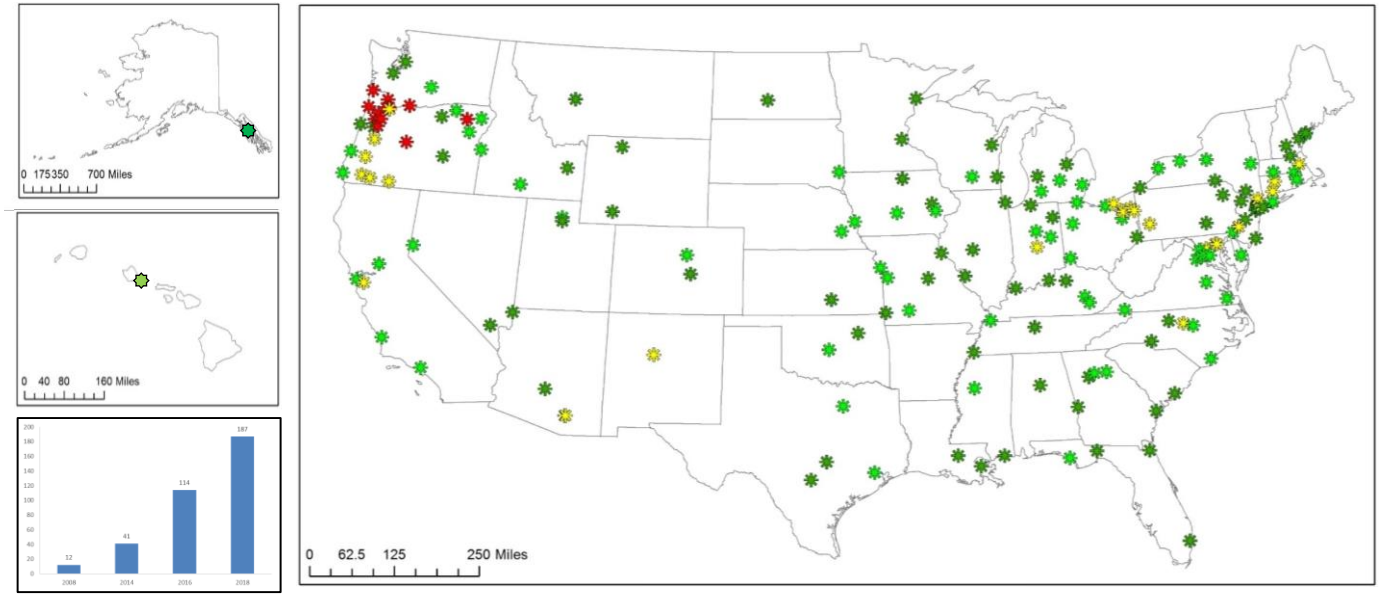
$100M in FY16 – FY17: 187 community clinics



2008 2014 2016 2018

EIP SAVES A LOT OF MONEY

EIP CREATES “MENTAL WEALTH”

EIP SAVES LIVES

	Economic payoffs at scale
Primary prevention of mental disorder	
School-based social and emotional learning programmes for 10-year-olds to prevent conduct disorder,[8] which result in £83·73 net savings for each £1 spent	Net savings of £6532 million after 10 years from provision to all 651 000 10-year-olds in England[9] (£5729 million in crime-related savings, £748 million in health-care service savings, and £121 million in education savings); timeframes of savings: net cost of £5 million after 1 year, net saving of £4147 million after 5 years, net saving of £6532 million after 10 years
School-based interventions to reduce bullying,[8] which result in £14·35 saved for each £1 spent	Net savings of £9726 million from provision to all 9 005 000 individuals aged 5–18 years in England,[9] which are long-term in nature and accrue to individuals mainly as increased wages
Secondary prevention of mental disorder	
Parenting interventions for conduct disorder,[8] which result in £7·89 net savings for each £1 spent	Net savings of £386 million from provision to parents of all 41 500 individuals with conduct disorder aged 5 years in England[5,9] (£311 million in crime-related savings, £53 million in health service savings, and £18 million in education savings); timeframe of net savings: £14 million by age 6 years, £300 million between ages 7 and 16 years, £72 million over 17 years of age

Early intervention for first-episode psychosis,[11] which results in £17·97 net savings for each £1 spent

	timeframe of net savings: £457 million after 1 year, £1067 million during years 2–5, £169 million during years 6–7
Tertiary prevention of mental disorder	
CBT for each person with schizophrenia,[11] which results in overall savings of £989 per person to health and social care	Net savings of £310 million after 3 years to the NHS if all people aged over 15 years in England with schizophrenia in previous year[4,9] received CBT
Primary promotion of mental wellbeing	
Work-based mental wellbeing promotion,[8] which results in £9·69 net savings for each £1 spent	Net savings of £18 864 million within one year to employers from provision of a simple set of interventions to promote the wellbeing of all 27 125 000 employees in England[10] (£15 038 million savings from reduced presenteeism, £5996 million savings from reduced absenteeism, £2170 million intervention costs)

GP=general practitioner. CBT=cognitive behavioural therapy. NHS=National Health Service.

Table: **Conservative estimates of economic savings in England from complete coverage of nine cost-effective public mental health interventions identified as part of the England mental health strategy**

Campion et al Lancet Psychiatry 2017

Effectiveness of Early Psychosis Intervention: Comparison of Service Users and Nonusers in Population-Based Health Administrative Data

Kelly K. Anderson, Ph.D., Ross Norman, Ph.D., Arlene MacDougall, M.D., M.Sc., Jordan Edwards, M.Sc., Lena Palaniyappan, M.D., Ph.D., Cindy Lau, M.Sc., Paul Kurdyak, M.D., Ph.D.

Objective: Early psychosis intervention (EPI) programs improve clinical and functional outcomes for people with first-episode psychosis. Less is known about the impact of these programs on the larger health care system. The authors sought to compare indicators of health service use, self-harm, suicide, and mortality between people with first-episode psychosis who were using EPI services and a propensity-matched group of concurrent control subjects who were not accessing EPI services.

Method: A retrospective cohort of incident cases of nonaffective psychosis in the catchment area of the Prevention and Early Intervention Program for Psychoses in London, Ontario, between 1997 and 2013 was constructed using health administrative data. This cohort was linked to primary data from the same program to identify people who used EPI services. Outcomes for people who used EPI services and those who did not were compared using Cox proportional hazards models.

Results: People who used EPI services had substantially lower rates of all-cause mortality in the 2-year period after EPI program admission (hazard ratio=0.24, 95% CI=0.11–0.53), although a significant difference in self-harm (hazard ratio=0.86, 95% CI=0.18–4.24) and suicide (hazard ratio=0.73, 95% CI=0.29–1.80) between the two groups was not observed. Those who used EPI services also had lower rates of emergency department presentation (hazard ratio=0.71, 95% CI=0.60–0.83) but higher rates of hospitalization (hazard ratio=1.42, 95% CI=1.18–1.71). These benefits were not observed after 2 years, when EPI care is typically stepped down to medical management.

Conclusions: People with first-episode psychosis who used EPI services had mortality rates that were four times lower than those with first-episode psychosis who did not use these services, as well as better outcomes across several health care system indicators. These findings support the effectiveness of EPI services for the treatment of first-episode psychosis in the larger context of the overall health care system.

AJP in Advance (doi: 10.1176/appi.ajp.2017.17050480)

Improving outcomes of first-episode psychosis: an overview

Paolo Fusar-Poli[1,2], Patrick D. McGorry[3], John M. Kane[4]

[1]Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK; [2]OASIS Service, South London and Maudsley NHS Foundation Trust, London, UK; [3]Orygen, the National Centre of Excellence in Youth Mental Health, Parkville, Australia; Centre for Youth Mental Health, University of Melbourne, Melbourne, Australia; [4]Zucker Hillside Hospital, Glen Oaks, NY, USA; Departments of Psychiatry and Molecular Medicine, Hofstra Northwell School of Medicine, Hempstead, NY, USA

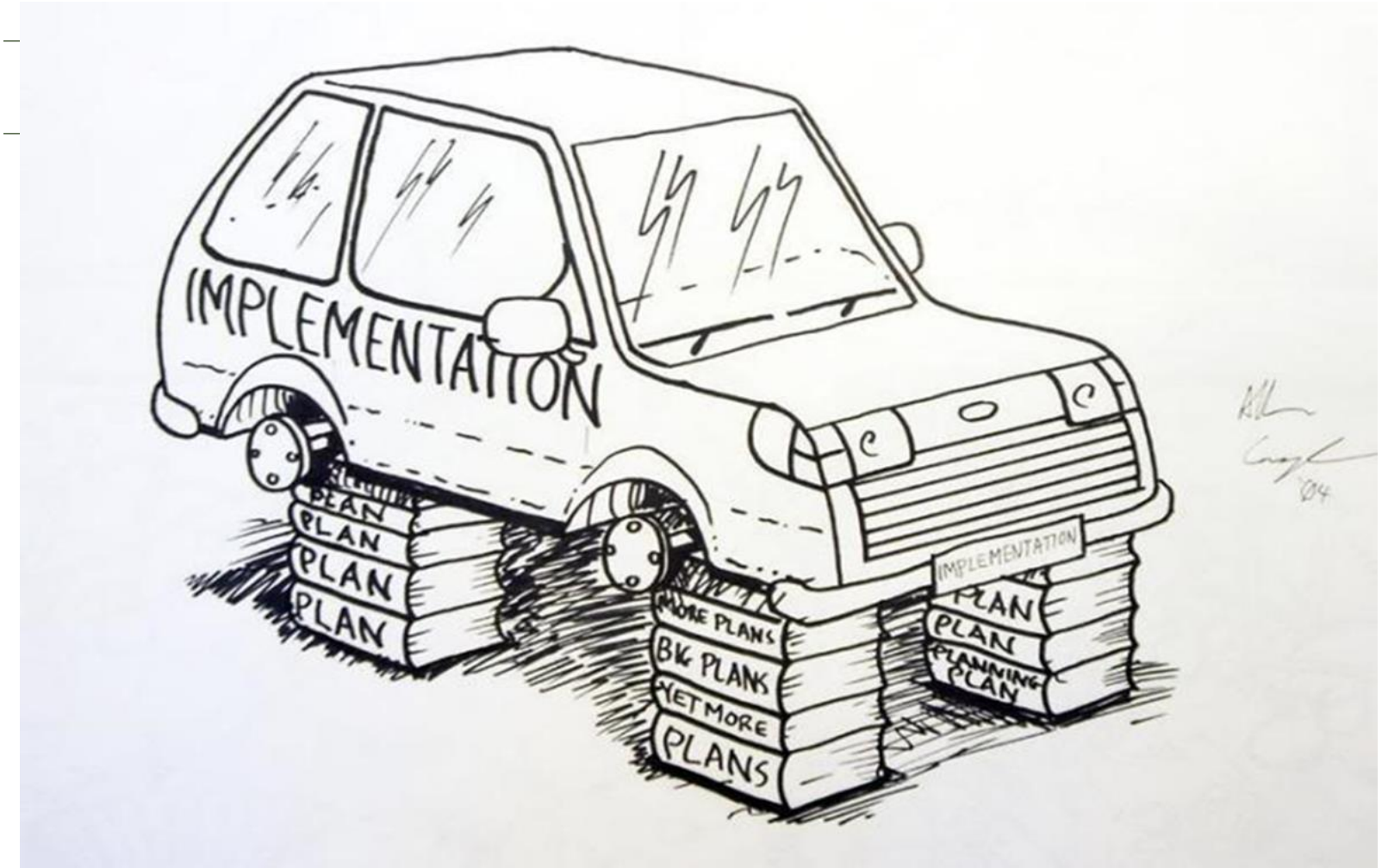
Outcomes of psychotic disorders are associated with high personal, familiar, societal and clinical burden. There is thus an urgent clinical and societal need for improving those outcomes. Recent advances in research knowledge have opened new opportunities for ameliorating outcomes of psychosis during its early clinical stages. This paper critically reviews these opportunities, summarizing the state-of-the-art knowledge and focusing on recent discoveries and future avenues for first episode research and clinical interventions. Candidate targets for primary universal prevention of psychosis at the population level are discussed. Potentials offered by primary selective prevention in asymptomatic subgroups (stage 0) are presented. Achievements of primary selected prevention in individuals at clinical high risk for psychosis (stage 1) are summarized, along with challenges and limitations of its implementation in clinical practice. Early intervention and secondary prevention strategies at the time of a first episode of psychosis (stage 2) are critically discussed, with a particular focus on minimizing the duration of untreated psychosis, improving treatment response, increasing patients' satisfaction with treatment, reducing illicit substance abuse and preventing relapses. Early intervention and tertiary prevention strategies at the time of an incomplete recovery (stage 3) are further discussed, in particular with respect to addressing treatment resistance, improving well-being and social skills with reduction of burden on the family, treatment of comorbid substance use, and prevention of multiple relapses and disease progression. In conclusion, to improve outcomes of a complex, heterogeneous syndrome such as psychosis, it is necessary to globally adopt complex models integrating a clinical staging framework and coordinated specialty care programmes that offer pre-emptive interventions to high-risk groups identified across the early stages of the disorder. Only a systematic implementation of these models of care in the national health care systems will render these strategies accessible to the 23 million people worldwide suffering from the most severe psychiatric disorders.

Key words: Psychosis, schizophrenia, psychosis risk, clinical high risk, first episode psychosis, universal prevention, selective prevention, indicated prevention, outcomes, clinical staging

(World Psychiatry 2017;16:00–00)

EVIDENCE:

NECESSARY BUT NOT SUFFICIENT


IMPLEMENTATION
PLAN
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MORE PLANS
BIG PLANS
YET MORE
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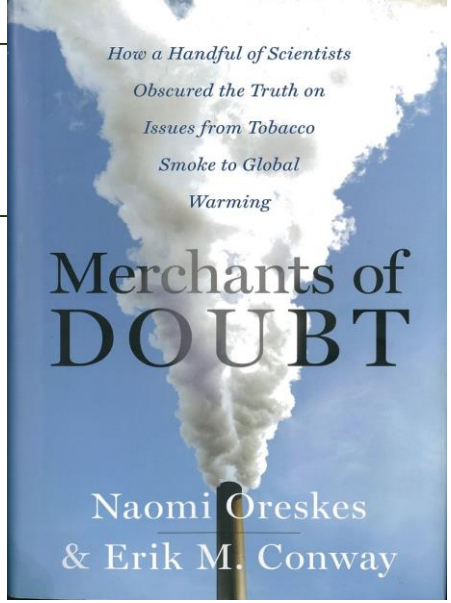
PLANNING
PLAN

IMPLEMENTATION FATIGUE SLUDGE FACTORS



The “Treatment Gap”

Merchants of Doubt

Devolved commissioning

Poor model fidelity

Weak and patchy financial models

Pressure to diffuse model across lifespan and diagnostic spectrum

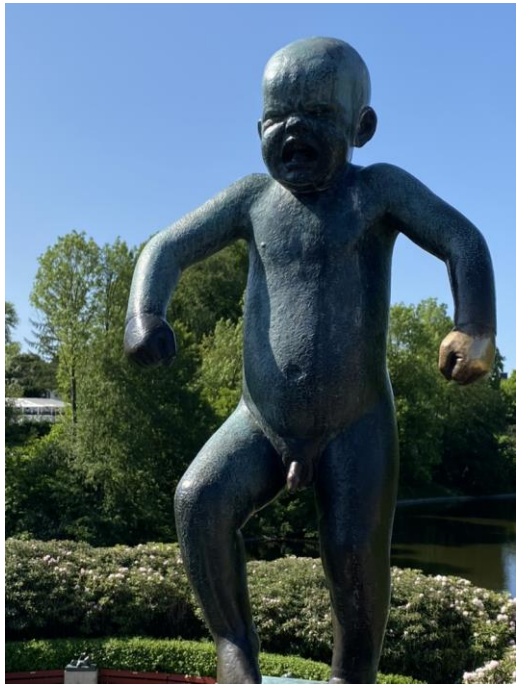
Professional resistance to key evidence based elements, especially community education, mobile detection and round the clock home based care

Challenges in designing and locating streamed and optimistic cultures of care

Challenge in mobilising political will

“One-fifth of the people are against everything all the time.”

Robert Kennedy



Psychiatric Services

AUSTRALASIAN PSYCHIATRY

Why do psychiatrists doubt the value of early intervention? The power of illusion

Australasian Psychiatry
2020, Vol 28(3) 331–334

DOI: 10.1177/1039856220924323
journals.sagepub.com/home/apy
SAGE

Patrick D McGorry Orygen, Australia; and Center for Youth Mental Health, The University of Melbourne, Australia
Cristina Mei Orygen, Australia; and Center for Youth Mental Health, The University of Melbourne, Australia

Abstract

Objective: Face validity and the best available evidence strongly support the value of early intervention (EI) for psychotic disorders, and increasingly for other mental illnesses. Yet its value continues to be intensely criticised by some academics and doubted by many psychiatrists. This disconnect is examined through the lens of the 'clinician's illusion'.
Conclusions: A number of sources fuel resistance to EI; however, the cumulative exposure to persistent and disabling illness that dominates the day-to-day experience of psychiatrists may be a key influence. This experience forms the basis of the clinician's illusion, a hidden bias health professionals develop as a natural consequence of their clinical experiences, which shapes belief and perception of prognosis, and breeds therapeutic nihilism. This bias has been reinforced by grossly under-resourced systems of mental health care, undermining morale and adding a sense of learned helplessness to our mindset.

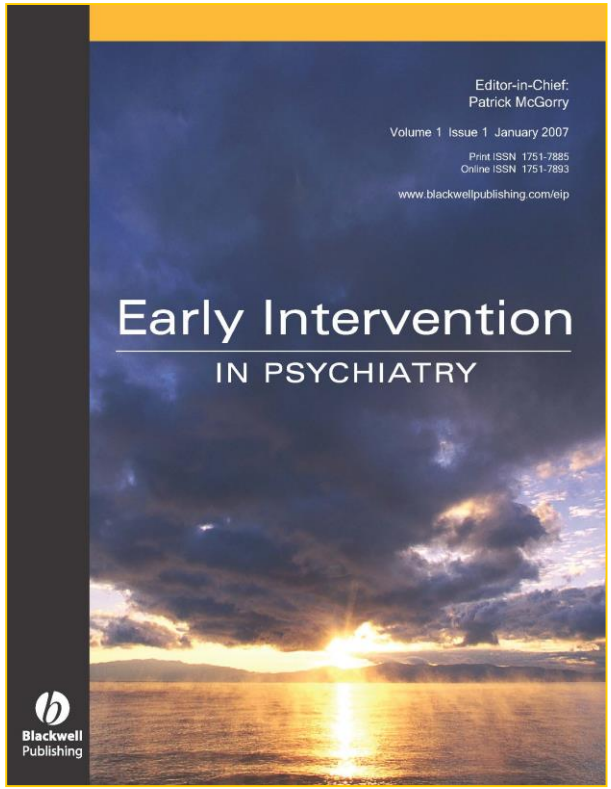
Keywords: Early intervention, youth mental health, psychosis, clinician's illusion, clinical staging

GOOD TO GREAT

REALIZING THE FULL POTENTIAL OF EARLY INTERVENTION

GOOD TO GREAT

- Widen the UHR/ARMS channel: delay onset & ameliorate impact
- Reduce DUP to a matter of weeks: CE and DTs
- Identify Early TR CLOZAPINE
- Stage specific care not just increased dose
- Holistic care – physical health, sexual health, substance use, family, vocational interventions
- Mobile home and assertive community treatment
- Extended tenure
- Online augmentation of care MOST
- Adherence vs dose reduction?



Early Intervention: A general principle in modern healthcare

From early intervention in psychosis to youth mental health reform: a review of the evolution and transformation of mental health services for young people.

Ashok Malla, Srividya Iyer, Patrick McGorry, Mary Cannon, Helen Coughlan, Swaran Singh, Peter Jones & Ridha Joober

Social Psychiatry and Psychiatric Epidemiology

The International Journal for Research in Social and Genetic Epidemiology and Mental Health Services

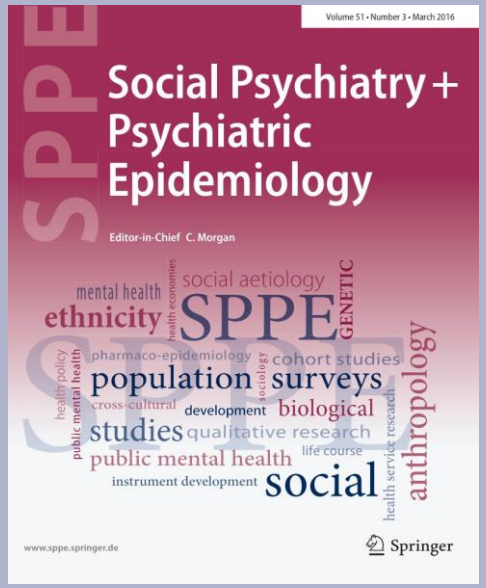
ISSN 0933-7954

Volume 51

Number 3

Soc Psychiatry Psychiatr Epidemiol (2016) 51:319-326

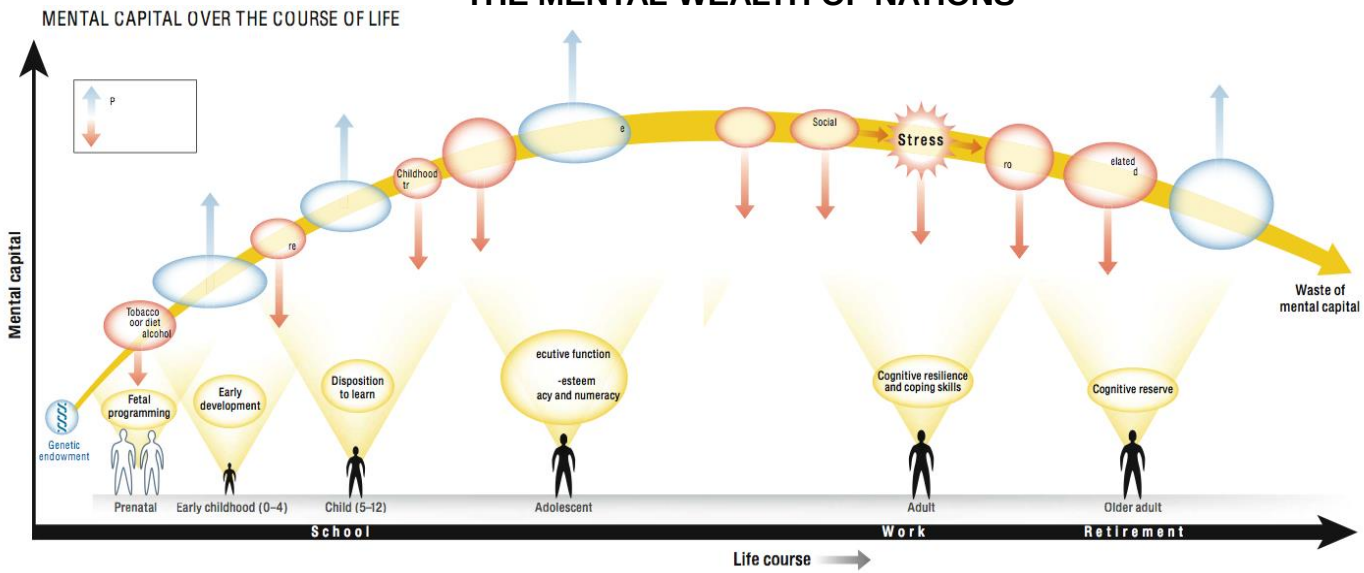
DOI 10.1007/s00127-015-1165-4




Mental
illness
#1 threat
to young lives
and futures

DEVELOPMENTAL PERSPECTIVE:

THE MENTAL WEALTH OF NATIONS



Beddington et al 2008 Nature

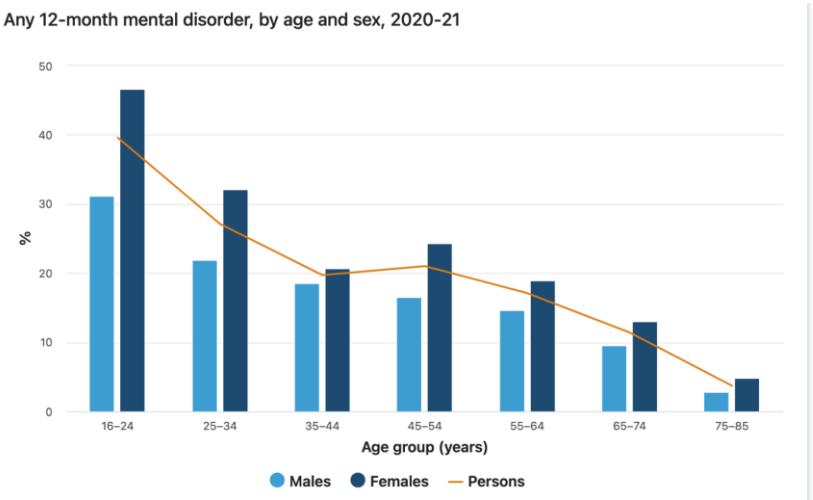
50% INCREASE IN PREVALENCE OF MENTAL DISORDERS IN YP SINCE 2007

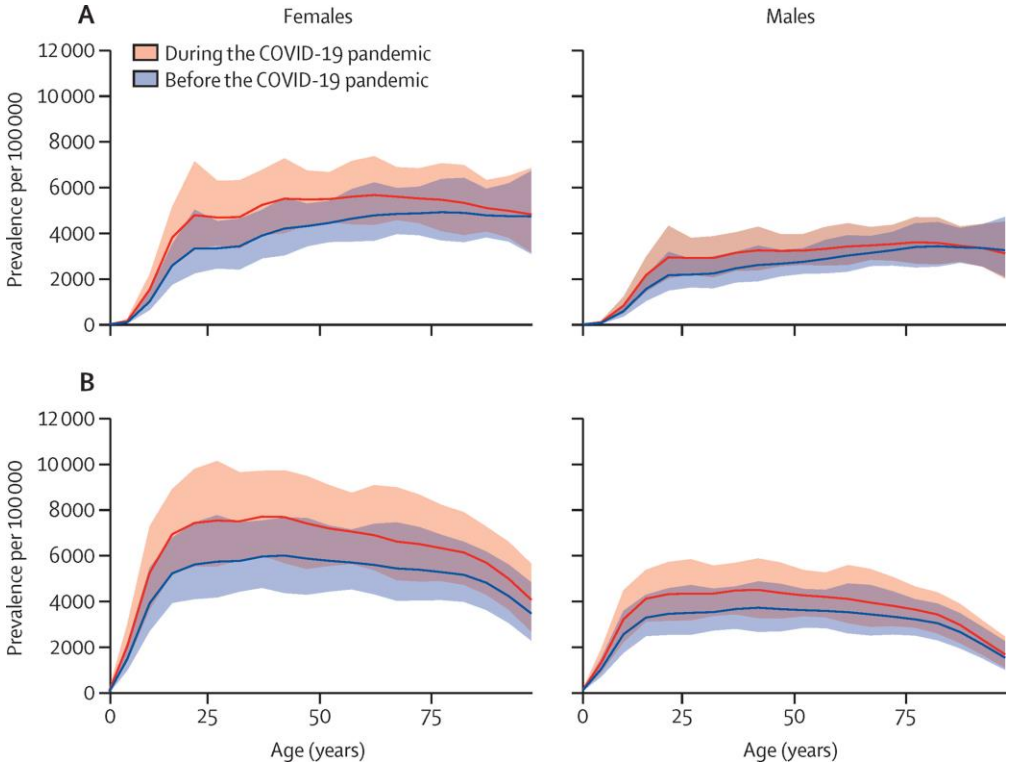
ABC NEWS

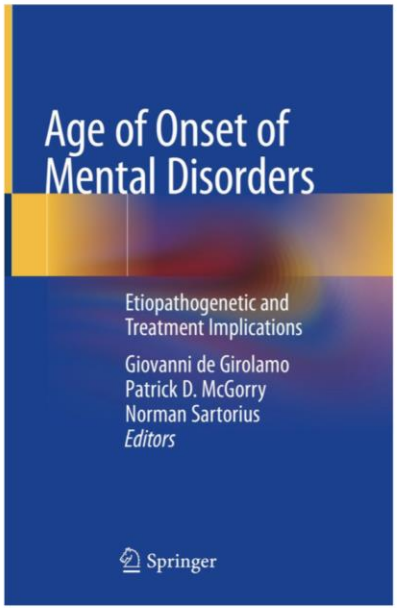
ANALYSIS

About 40 per cent of young Australians have experienced mental illness — and it's high time we do something about it

By Patrick McGorry
Posted Thu 4 Aug 2022 at 8:00pm




A
Females
Males
During the COVID-19 pandemic
Before the COVID-19 pandemic
Prevalence per 100 000
12 000
10 000
8000
6000
4000
2000
0
B
0
25
50
75
Age (years)



1st ed. 2019, XVI, 261 p. 30 illus., 24 illus. in color.

Printed book

Giovanni de Girolamo, Patrick D. McGorry, Norman Sartorius (Eds.)

Age of Onset of Mental Disorders

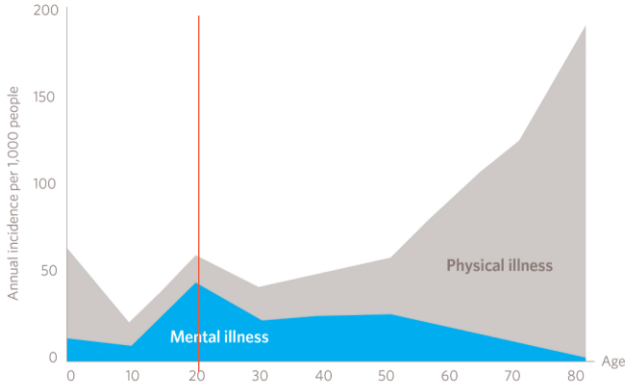
Etiopathogenetic and Treatment Implications

- Brings together the available evidence regarding the age of onset of mental disorders and its significance
- Covers all the most important mental disorders
- Written by outstanding, well-known contributors and edited by leading experts

This book presents a thorough and critical review of current knowledge about the age of onset of mental disorders. The opening chapters offer information about the impact of the age of onset on the clinical picture, course, and outcome of physical illnesses, and about the neurobiological implications and correlates of different ages of onset. The impact and correlates of the ages of onset of all the most important mental disorders are then discussed in detail by internationally renowned scientists. The background to the book is the recognition that a better understanding of age of onset makes it possible to estimate the lifetime risk of disorders, helps to elucidate pathogenesis, and facilitates efficient, targeted clinical management. The book will be of value for clinicians, mental health professionals, mental health researchers, epidemiologists, and different stakeholders in the mental health field.

TIMING IS EVERYTHING

- 75% of mental health problems have their onset in young people aged 12 to 25
- The developmental trajectory for young people has changed
- Current service system not equipped to deal with economic and social challenges associated with mental health
- Peak need for care, worst access
- Loss of lives, futures and ”mental wealth”



World Economic Forum ®

AGE OF ONSET OF DISORDERS

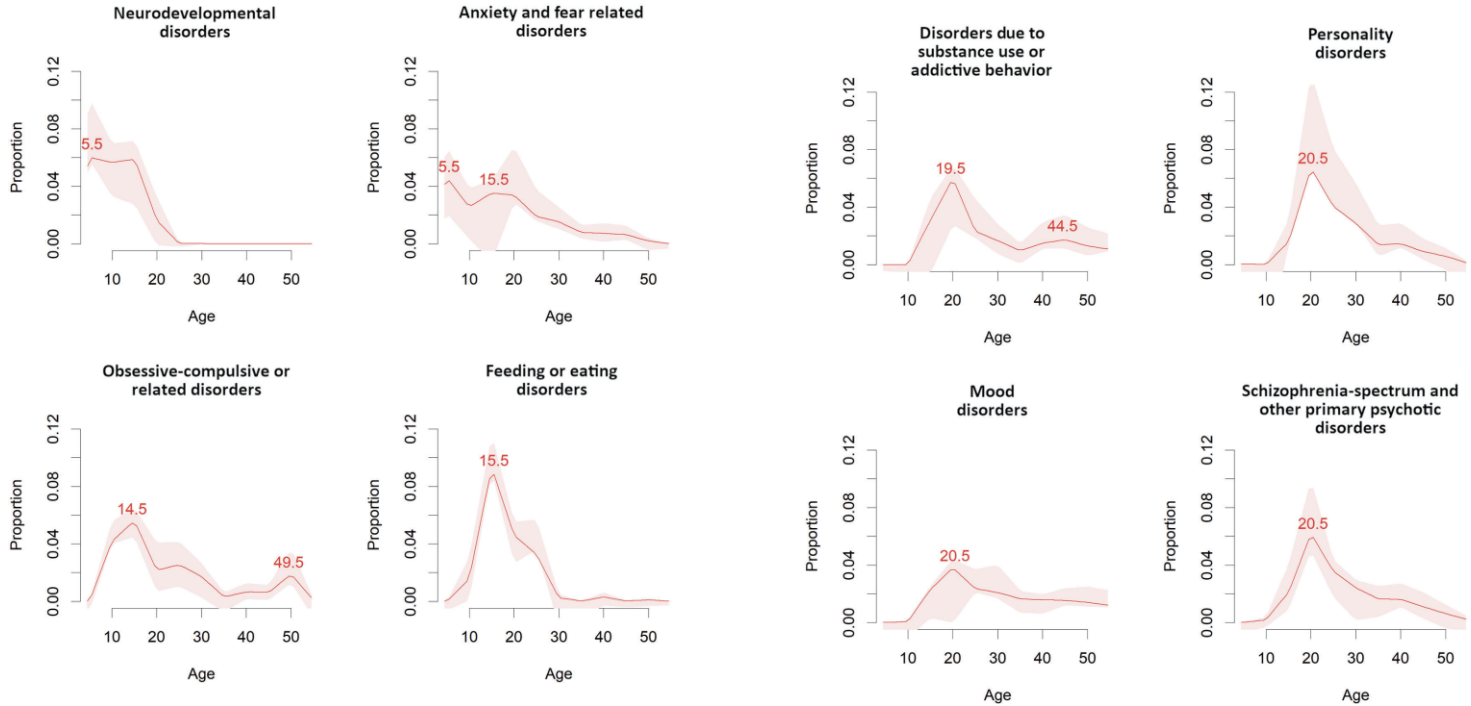
Molecular Psychiatry (2022) 27:281–295
https://doi.org/10.1038/s41380-021-01161-7

REVIEW ARTICLE

Age at onset of mental disorders worldwide: large-scale meta-analysis of 192 epidemiological studies

Marco Solmi[1,2,3] · Joaquim Radua[3,4,5] · Miriam Olivola[3] · Enrico Croce[6] · Livia Soardo[7] · Gonzalo Salazar de Pablo[8,8,9] · Jae Il Shin[10] · James B. Kirkbride[11] · Peter Jones[12,13] · Jae Han Kim[14] · Jong Yeob Kim[14] · Andrè F. Carvalho[15] · Mary V. Seeman[16] · Christoph U. Correll[17,18,19,20] · Paolo Fusar-Poli[3,7,21,22]

Received: 6 March 2021 / Revised: 28 April 2021 / Accepted: 5 May 2021 / Published online: 2 June 2021



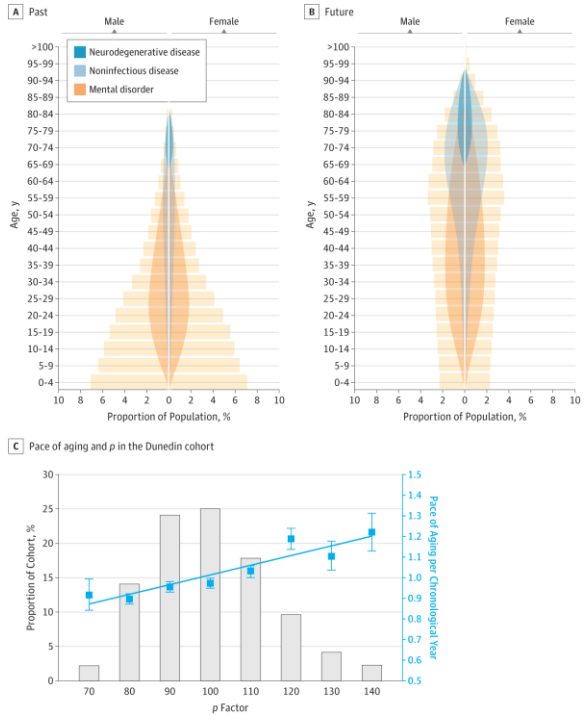
March 27, 2019

Psychiatry's Opportunity to Prevent the Rising Burden of Age-Related Disease

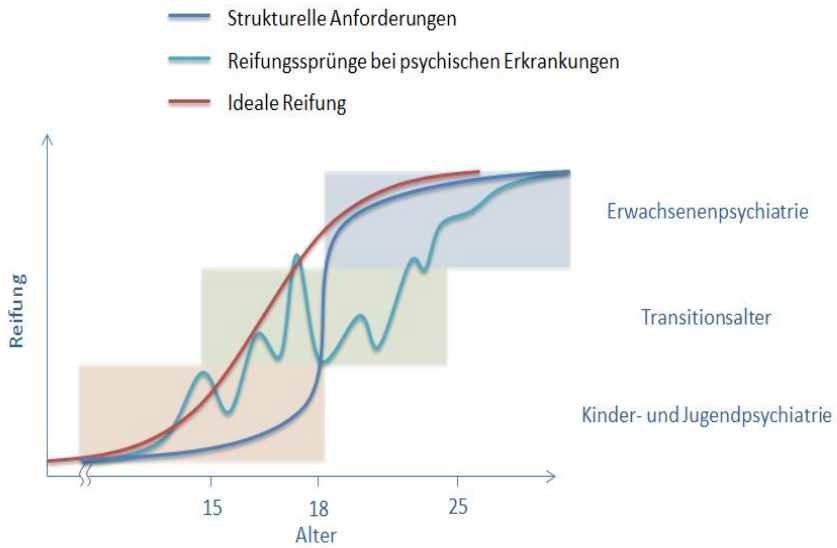
Terrie E. Moffitt, PhD[1,2]; Avshalom Caspi, PhD[1,2]

» Author Affiliations

JAMA Psychiatry. Published online March 27, 2019. doi:10.1001/jamapsychiatry.2019.0037



REAL MATURATION



Actual development in the context of mental ill-health in young people

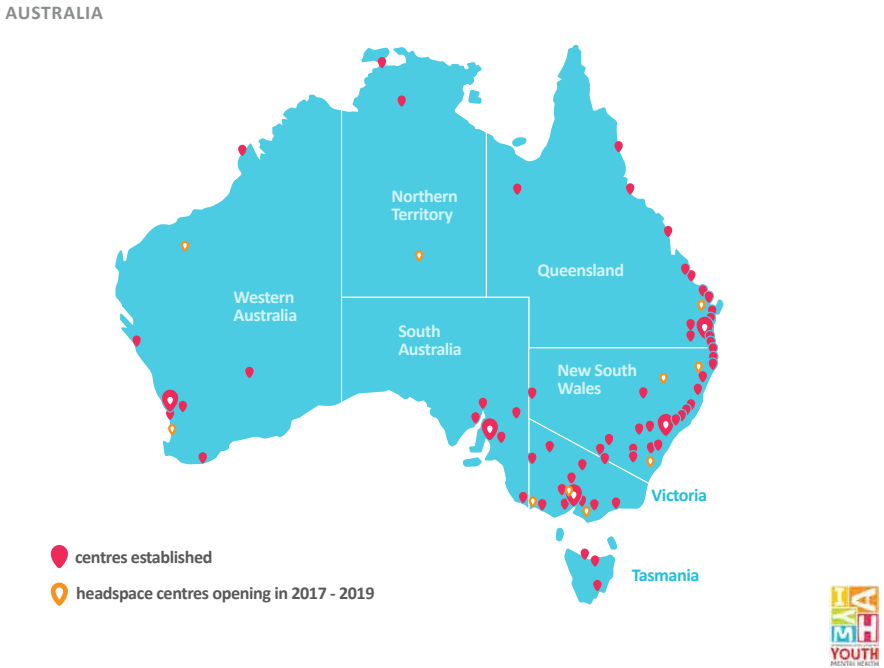
Vital to acknowledge the impact of illness on developmental trajectories


MJA
SUPPLEMENT
Orygen,
The National Centre of Excellence
in Youth Mental Health
20 NOVEMBER 2017 VOLUME 207 NO 10
Established 1914
THE MEDICAL JOURNAL OF AUSTRALIA
www.mja.com.au
Beyond brand
Inside youth
mental health
AMA
Journal of the Australian Medical Association
AMPCo
Australasian Medical Publishing Company

Youth Mental Health Programs

headspace - Australia

FROM 2006 - 10 CENTRES → 164 CENTRES BY 2023



From Australian communities to Prime Ministers: Sustained universal support for headspace

GLOBAL PROGRESS

WEF AND MENTAL HEALTH

Davos 2019

Davos 2020

DENMARK WELCOMES

iaymh2022

The 6th International Conference on Youth Mental Health

REIMAGINING | Youth Mental Health

COPENHAGEN

29 September - 1 October, 2022

WELCOME FROM THE IAYMH EXECUTIVE

REGISTER HERE

WORLD ECONOMIC FORUM

COMMITTED TO IMPROVING THE STATE OF THE WORLD

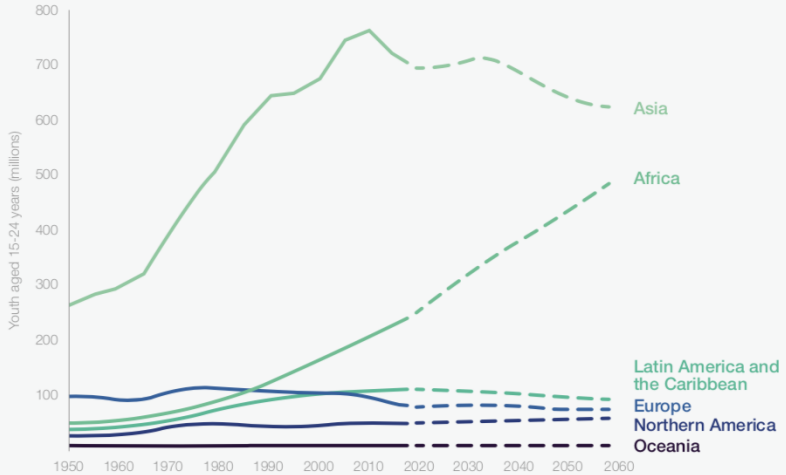
A Global Framework for Youth Mental Health:

Investing in Future Mental Capital for Individuals, Communities and Economies

May 2020

FIGURE 6

Global youth population by region from 1950, with projection to 2050



Source: United Nations, World Population Prospects: The 2012 Revision. 2013

FIGURE 8

Countries that participated in consultations or surveys with the project

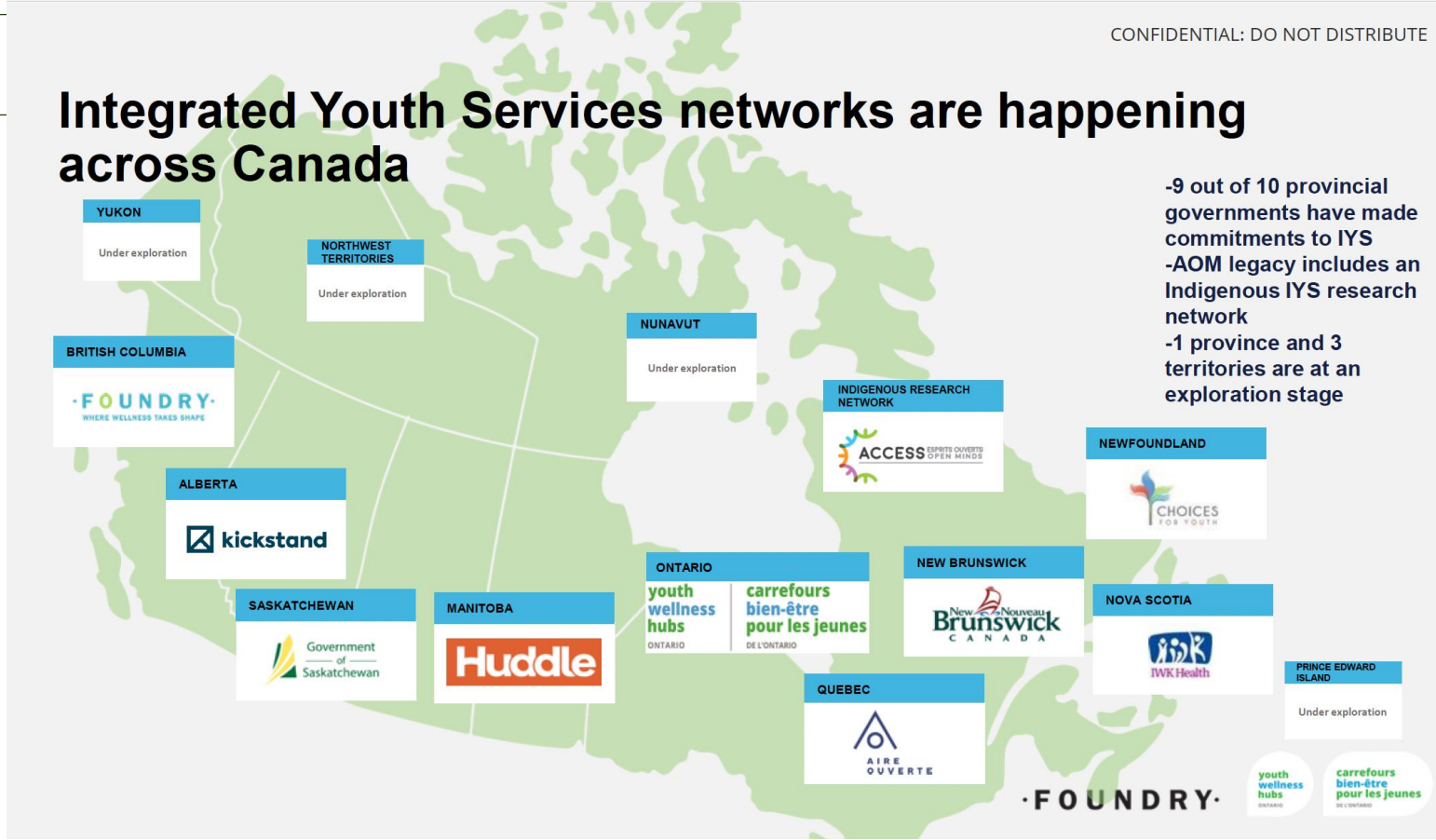
Youth Mental Health Programs

Jigsaw - Ireland

Youth Mental Health Programs

Foundry – BC Canada

Integrated Youth Services networks are happening across Canada



-9 out of 10 provincial governments have made commitments to IYS
-AOM legacy includes an Indigenous IYS research network
-1 province and 3 territories are at an exploration stage

Youth Mental Health Programs

@ ease - Netherlands

Youth Mental Health Programs

headspace - Denmark

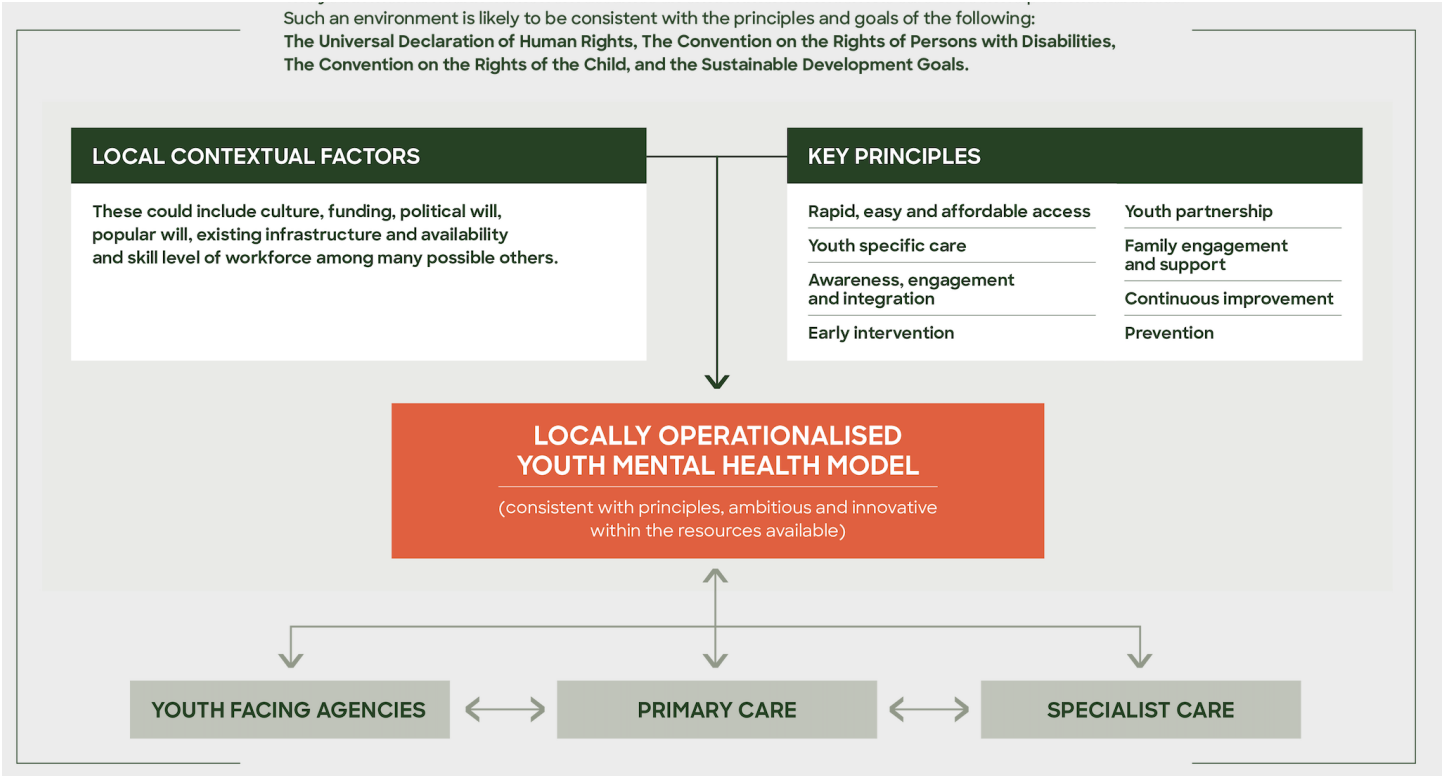
YOUTH MENTAL HEALTH PROGRAMS

HEADSPACE ISRAEL

Youth Mental Health Programs

Maison des Adolescents - France

Such an environment is likely to be consistent with the principles and goals of the following:
The Universal Declaration of Human Rights, The Convention on the Rights of Persons with Disabilities, The Convention on the Rights of the Child, and the Sustainable Development Goals.



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OFFICIAL JOURNAL OF THE WORLD PSYCHIATRIC ASSOCIATION (WPA)
Volume 21, Number 1 February 2022

WILEY IMPACT FACTOR: 49.548 ISSN 1723-8617

Designing and scaling up integrated youth mental health care

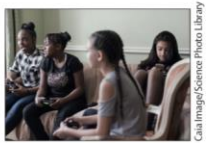
Patrick D. McGorry, Cristina Mei, Andrew Chanen, Craig Hodges, Mario Alvarez-Jimenez, Eóin Killackey
Orygen, National Centre of Excellence in Youth Mental Health; Centre for Youth Mental Health, University of Melbourne, Parkville, VIC, Australia

Mental ill-health represents the main threat to the health, survival and future potential of young people around the world. There are indications that this is a rising tide of vulnerability and need for care, a trend that has been augmented by the COVID-19 pandemic. It represents a global public health crisis, which not only demands a deep and sophisticated understanding of possible targets for prevention, but also urgent reform and investment in the provision of developmentally appropriate clinical care. Despite having the greatest level of need, and potential to benefit, adolescents and emerging adults have the worst access to timely and quality mental health care. How is this global crisis to be addressed? Since the start of the century, a range of co-designed youth mental health strategies and innovations have emerged. These range from digital platforms, through to new models of primary care to new services for potentially severe mental illness, which must be locally adapted according to the availability of resources, workforce, cultural factors and health financing patterns. The fulcrum of this progress is the advent of broad-spectrum, integrated primary youth mental health care services. They represent a blueprint and beach-head for an overdue global system reform. While resources will vary across settings, the mental health needs of young people are largely universal, and underpin a set of fundamental principles and design features. These include establishing an accessible, "soft entry" youth primary care platform with digital support, where young people are valued and essential partners in the design, operation, management and evaluation of the service. Global progress achieved to date in implementing integrated youth mental health care has highlighted that these services are being accessed by young people with genuine and substantial mental health needs, that they are benefiting from them, and that both these young people and their families are highly satisfied with the services they receive. However, we are still at base camp and these primary care platforms need to be scaled up across the globe, complemented by prevention, digital platforms and, crucially, more specialized care for complex and persistent conditions, aligned to this transitional age range (from approximately 12 to 25 years). The rising tide of mental ill-health in young people globally demands that this focus be elevated to a top priority in global health.

LANCET PSYCHIATRY COMMISSION ON YOUTH MENTAL HEALTH

Building the momentum and blueprint for reform in youth mental health

Mental disorders have been well characterised as "the chronic diseases of the young"[1] and continue to disproportionately affect young people worldwide.[2] They are a major contributor to the overall burden of disease between 10 and 24 years of age,[3] making them the leading cause of disability and premature death for this age group. Societies across the globe are heavily weakened by mental disorders. Projections suggest that by 2030, among the non-communicable diseases, mental illness will pose the greatest threat to worldwide economic growth.[4] This threat to economic growth is a direct result of the timing in the lifecycle of mental disorders; 75% emerge by 24 years of age,[5] with the major syndromes, which so often persist and disable across adulthood, emerging during the transition from puberty to the mid-20s. This critical developmental period is especially important for completing education, securing employment, and growing social relationships. Consequently, the long-term effects on fulfillment of human potential and productivity are enormous, through poor economic and vocational outcomes.[6] This erosion of so-called mental wealth[7] demands an urgent response to mental disorders in young people at an individual, societal, and global level.



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Published Online
April 16, 2019
http://dx.doi.org/10.1016/
S2215-0366(19)30050-1

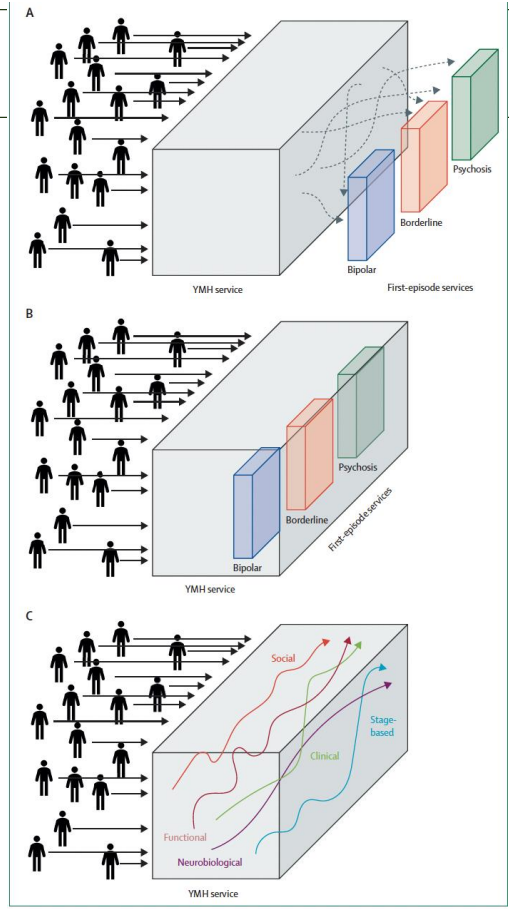
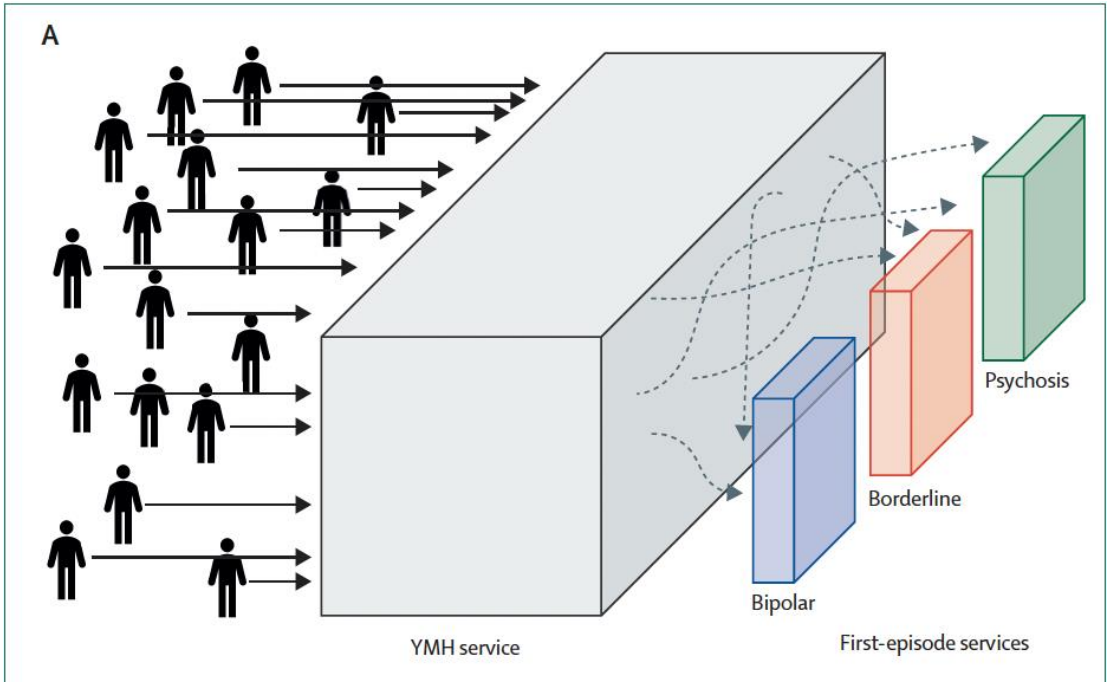
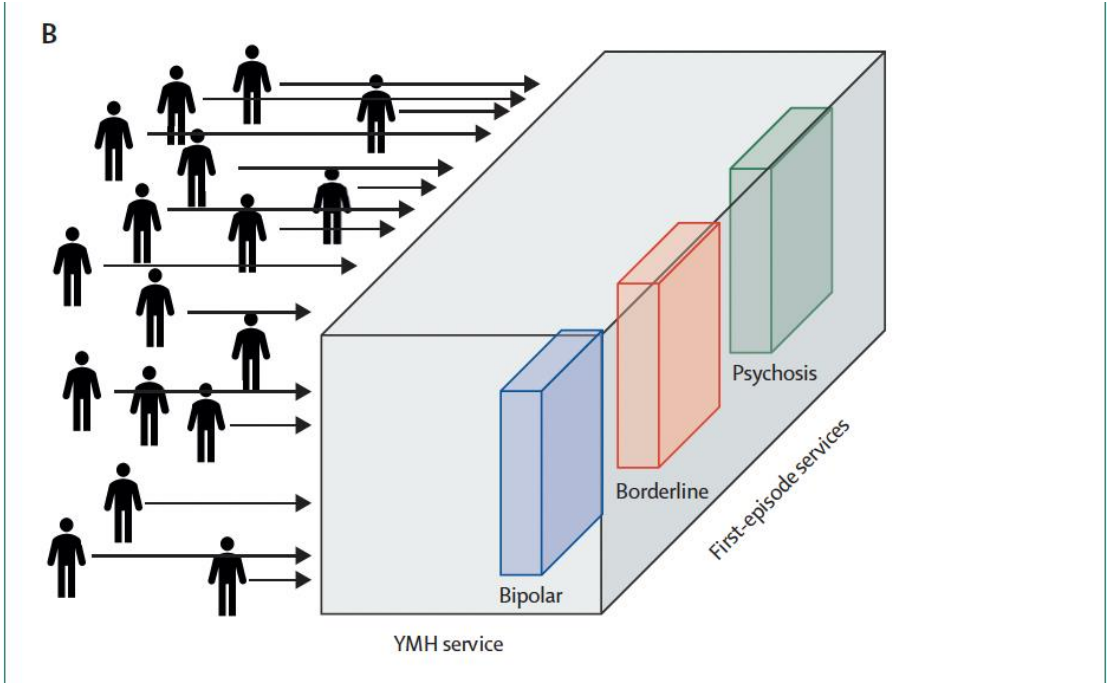
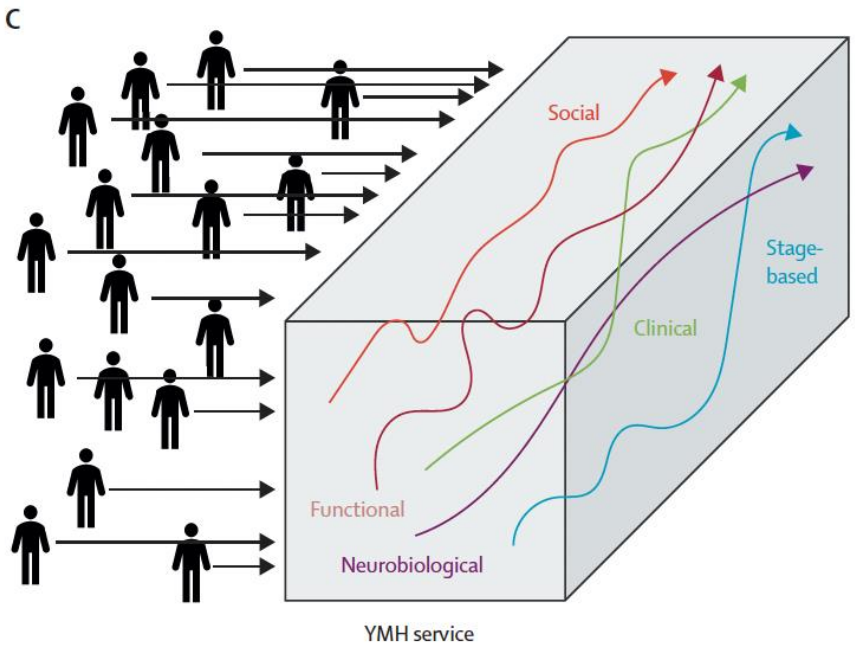


Figure 2: **Potential multi-stage service configurations, in increasing levels of integration**
(A) Separated, diagnostically organised services for early-stage mental health problems and illnesses. (B) Integrated but still diagnostically organised services for early-stage mental health problems and illnesses. (C) Integrated early-stage services for mental health problems and illnesses that are organised around individual needs and outcomes. YMH=youth mental health.

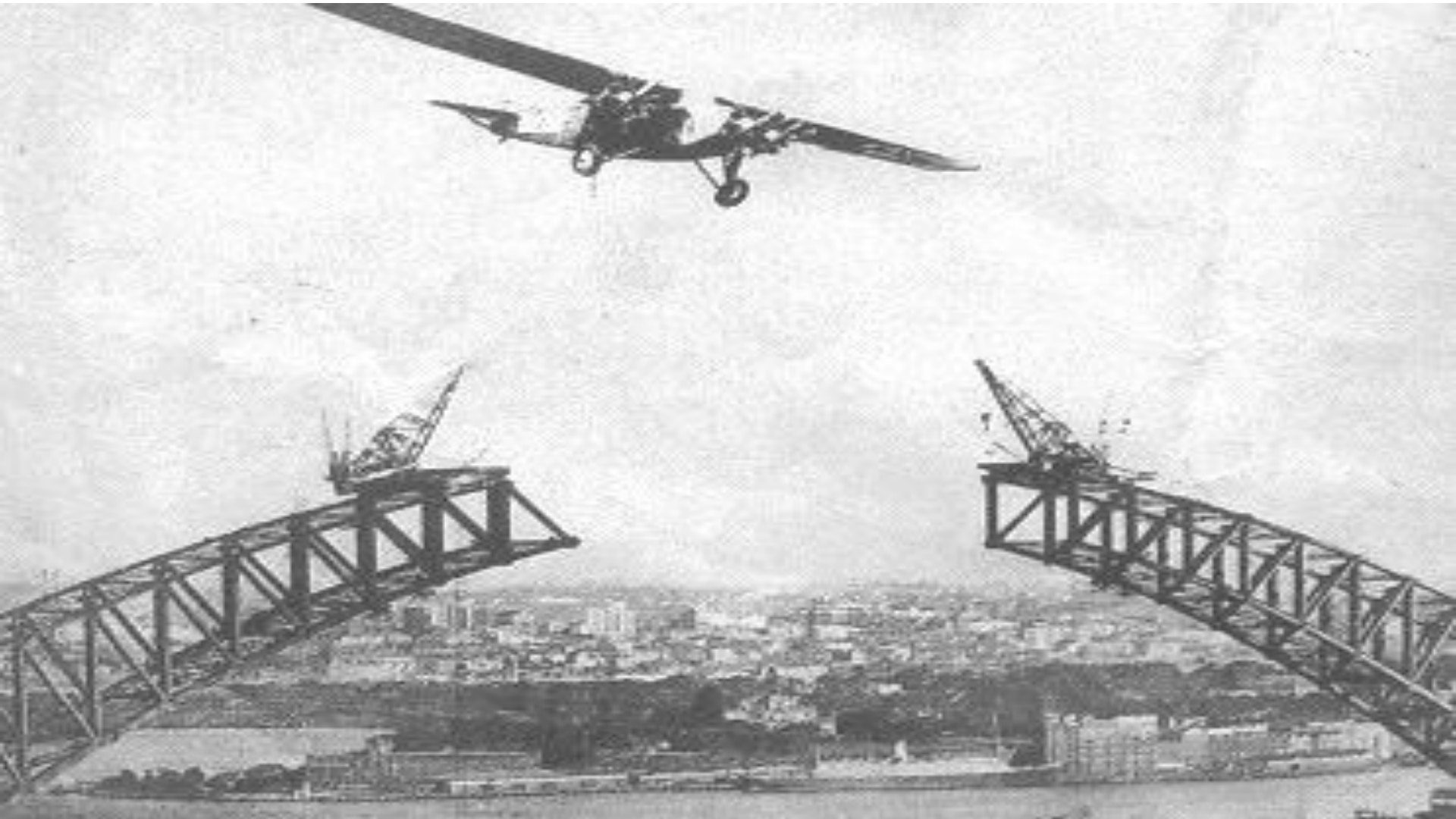

A
Psychosis
Borderline
Bipolar
YMH service
First-episode services


B
Psychosis
Borderline
Bipolar
First-episode services
YMH service

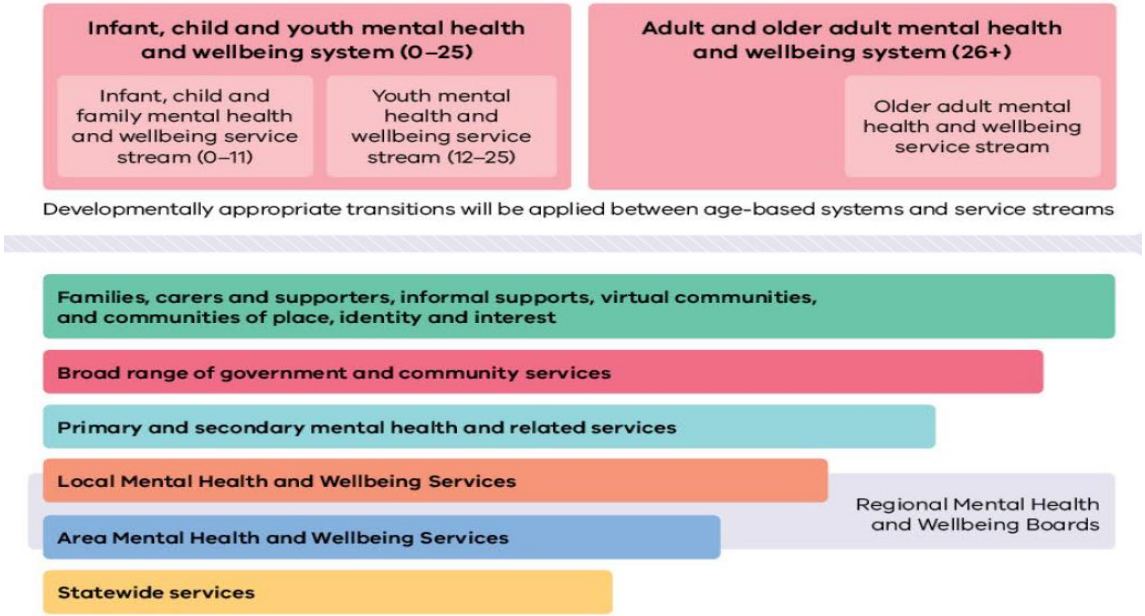

C
Social
Stage-based
Clinical
Functional
Neurobiological
YMH service

THE FINAL REPORT

- Delivered March 2021.
- 12,500 contributions.
- Over 3,000 pages.
- Five volumes.
- 65 recommendations in addition to the nine from the Interim report.



A NEW SIX LEVEL SERVICE SYSTEM



120

- Established by the end of 2022.
- Services for young people aged 12 to 25 (until a person's 26th birthday), age transitions applied flexibly by services in partnership with young people and their families, carers and supporters.
- Rigid geographic boundaries will be removed.
- Delivered through a partnership between a health service or hospital and a Non Government Organisation*

ORYGEN'S STRATEGIC PLAN AND ROLE IN REFORM

REACH AND REFORM

Partners with organisations in
28 COUNTRIES
across six continents.

Partnerships span research, clinical service delivery, and advocacy.

Developed the global framework for youth mental health with the World Economic Forum.

CLINICAL CARE

Provide in-person mental health services to
MORE THAN 4000 YOUNG AUSTRALIANS
annually, with hundreds more supported online.

ORYGEN SPECIALIST PROGRAM*

1036 New clients

327 Inpatient admissions

ORYGEN PRIMARY CARE SERVICES (HEADSPACE)*

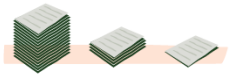
19743 Services provided to young people

3702 Young people accessed a headspace centre

1627 Young people came to headspace for the first time

RESEARCH IMPACT*

Research papers published	Research projects	Clinical trials
251	58	18



FUNDING*

INCOME OF $65.4 MILLION
in 2019-20.

Funding is received from Australian governments and charitable organisations as well as the US National Institute of Mental Health and the UK's Wellcome Trust.

STAFFING*

603 EMPLOYEES

302	165	136
clinical	research	operations

INCLUDING 11 PROFESSORS

* 2019–2020 FINANCIAL YEAR

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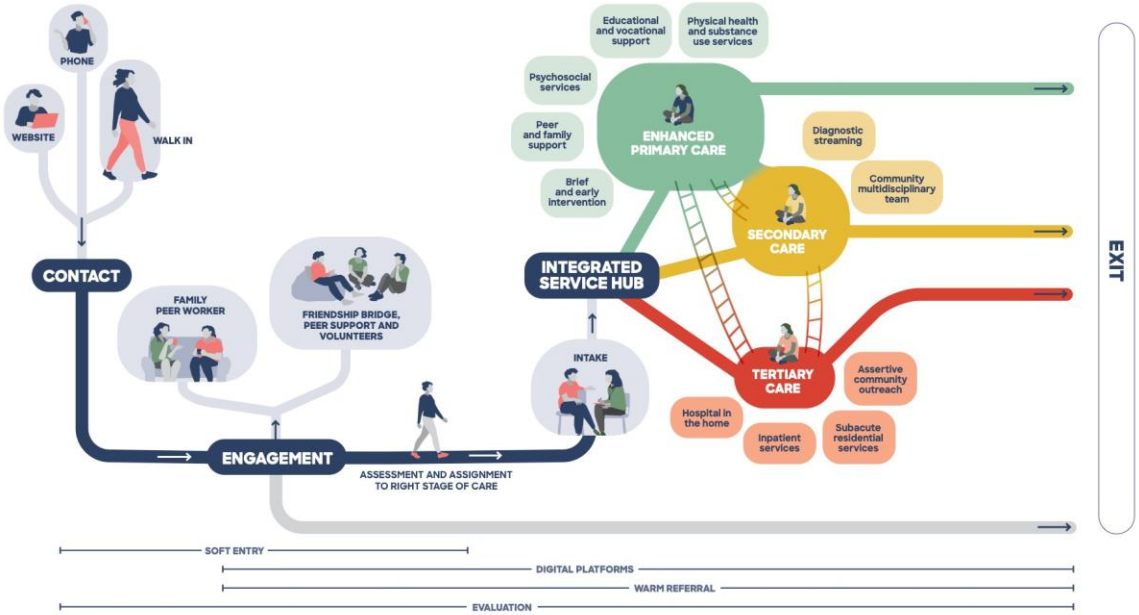
REVOLUTION IN MIND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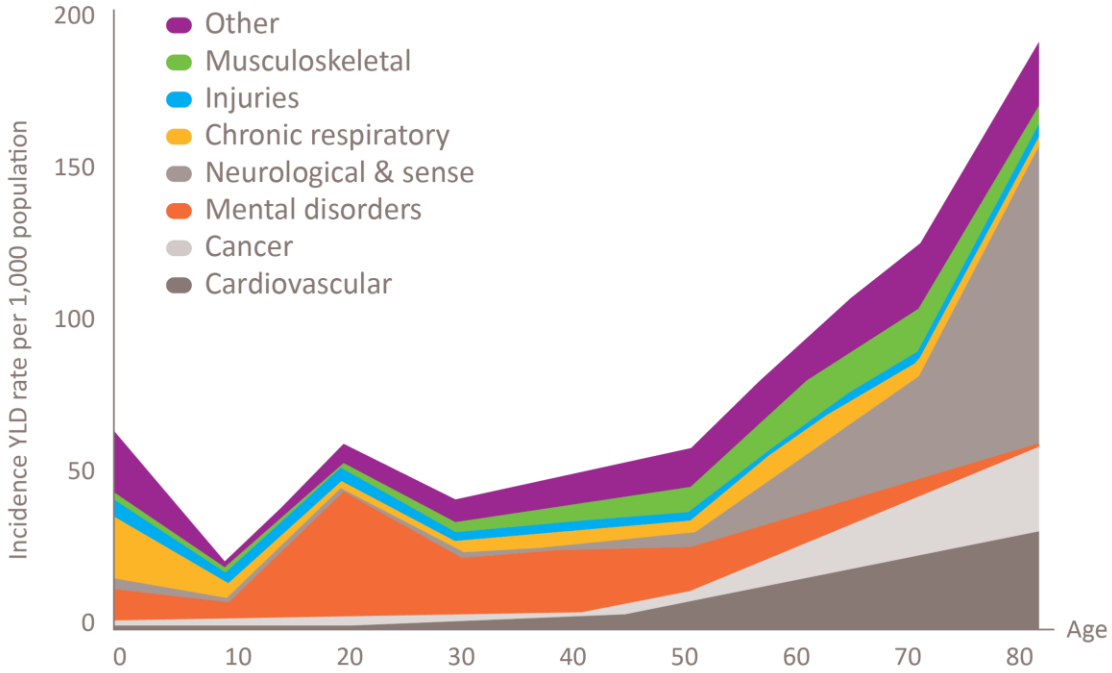
WEBSITE
WALK IN
CONTACT
FAMILY PEER WORKER
FRIENDSHIP BRIDGE, PEER SUPPORT AND VOLUNTEERS
ENGAGEMENT
ASSESSMENT AND ASSIGNMENT TO RIGHT STAGE OF CARE
INTAKE
INTEGRATED SERVICE HUB
Educational and vocational support
Physical health and substance use services
Psychosocial services
Peer and family support
Brief and early intervention
ENHANCED PRIMARY CARE
Diagnostic streaming
Community multidisciplinary team
SECONDARY CARE
TERTIARY CARE
Assertive community outreach
Hospital in the home
Inpatient services
Subacute residential services
EXIT
SOFT ENTRY
DIGITAL PLATFORMS
WARM REFERRAL
EVALUATION

PREVENTION

THE CHANGING LANDSCAPE OF YOUTH MENTAL HEALTH

THE GLOBAL BURDEN OF DISEASE



IS THERE A YOUTH MENTAL HEALTH CRISIS?

- High Prevalence of Distress and Disorders with Need for Care
- But is it getting worse? Where?
- If so, why?
- What is to be done?

  Prevention

  Early Intervention, Treatment & Care

YOUTH MH CRISIS

The New York Times

A CONVERSATION WITH

The Surgeon General's New Mission: Adolescent Mental Health

In an interview with The Times, Dr. Vivek Murthy ascribed the mental health challenges among young people in part to "hustle culture" values.

"Every child's path to adulthood—reaching developmental and emotional milestones, learning healthy social skills, and dealing with problems—is different and difficult. Many face added challenges along the way, often beyond their control. There's no map, and the road is never straight."

"But the challenges today's generation of young people face are **unprecedented and uniquely hard to navigate**. And the effect these challenges have had on their mental health is **devastating**."

Cross-cohort change in parent-reported emotional problem trajectories across childhood and adolescence in the UK

Jessica M Armitage, Alex S F Kwong, Foteini Tseliou, Ruth Sellers, Rachel Blakey, Rebecca Anthony, Frances Rice, Anita Thapar, Stephan Collishaw

Summary

Background Over the past three decades, the prevalence of adolescent emotional problems (ie, anxiety and depression) has risen. Although the onset and developmental course of emotional symptoms shows high variability, no study has directly tested secular differences across development. Our aim was to investigate whether and how developmental trajectories of emotional problems have changed across generations.

Methods We used data from two UK prospective cohorts assessed 10 years apart: the Avon Longitudinal Study of Parents and Children (ALSPAC) including individuals born in 1991–92, and the Millennium Cohort Study (MCS) with individuals born in 2000–02. Our outcome was emotional problems, assessed using the parent-rated emotional subscale of the Strengths and Difficulties Questionnaire (SDQ-E) at approximate ages 4, 7, 8, 10, 11, 13, and 17 years in ALSPAC and ages 3, 5, 7, 11, 14, and 17 years in MCS. Participants were included if the SDQ-E was completed at least once in childhood and at least once in adolescence. Trajectories were generated using multilevel growth curve models using the repeated assessments of the SDQ-E in children aged 3–17 years.

Findings Data were available for 19 418 participants (7012 from ALSPAC and 12 406 from the MCS), of whom 9678 (49·8%) were female and 9740 (50·2%) were male, and 17 572 (90·5%) had White mothers. Individuals born between 2000 and 2002 had higher emotional problem scores from around 9 years (intercept statistic β 1·75, 95% CI 1·71–1·79) than did individuals born in 1991–92 (1·55, 1·51–1·59). The later cohort had an earlier onset of problems than the earlier cohort, and sustained higher average trajectories from around 11 years, with female adolescents showing the steepest trajectories of emotional problems. Differences between cohorts peaked overall at age 14 years.

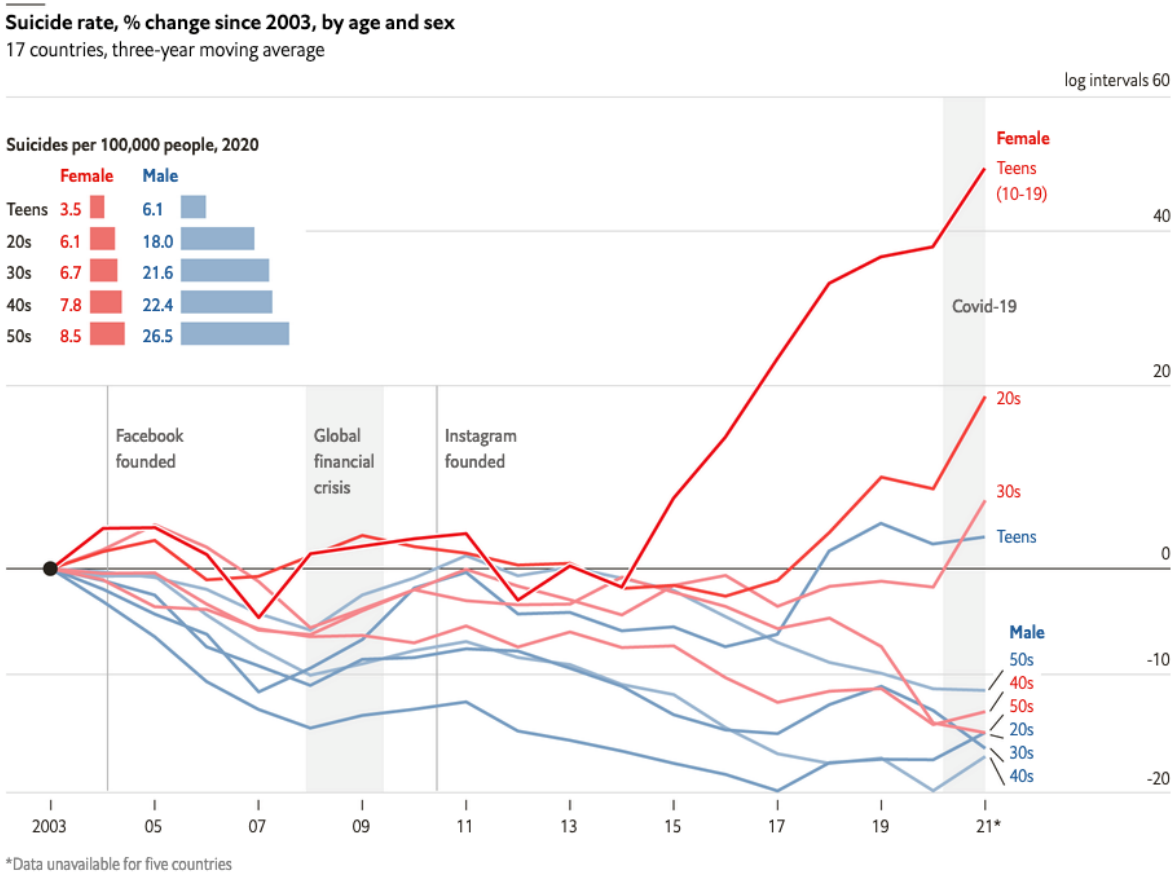
Interpretation Our comparison of two cohorts of young people provides evidence that compared with a cohort assessed 10 years prior, emotional problems emerge earlier in development in the more recent cohort, and these are especially pronounced for females during mid-adolescence. Such findings have implications for public health planning and service provision.

Funding Wolfson Centre for Young People's Mental Health, Wolfson Foundation.

Lancet Psychiatry 2023; 10: 509–17

Published Online May 24, 2023 https://doi.org/10.1016/S2215-0366(23)00175-X

Wolfson Centre for Young People's Mental Health (J M Armitage PhD, F Tseliou PhD, R Anthony PhD, Prof F Rice PhD, Prof Anita Thapar PhD, Prof Stephan Collishaw PhD), Centre for the Development, Evaluation, Complexity and Implementation in Public Health Improvement, School of Social Sciences (R Anthony), and Division of Psychological Medicine and Clinical Neurosciences, Centre for Neuropsychiatric Genetics and Genomics (J M Armitage, F Tseliou, R Sellers PhD, Prof F Rice, Prof A Thapar, Prof S Collishaw), Cardiff University, Cardiff, UK; Division of Psychiatry, University of Edinburgh, Edinburgh, UK (A S F Kwong PhD); Population Health Sciences and MRC Integrative Epidemiology Unit, University of Bristol, Bristol, UK (A S F Kwong, R Blakey PhD); Department of Primary Care and Public Health, Brighton and Sussex Medical School, Brighton, UK (R Sellers); Faculty



The Economist May 2023

A report of the Mental Health Million project

sapienlabs.org/mental-health-million-project

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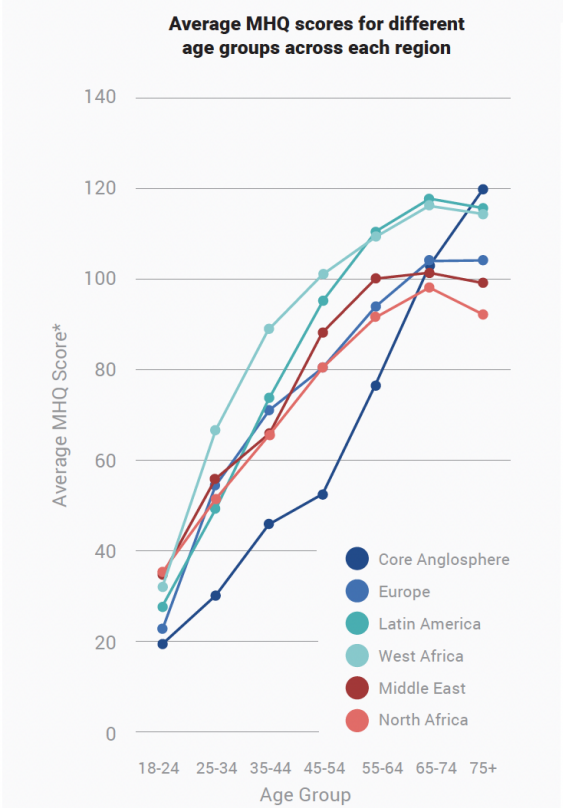
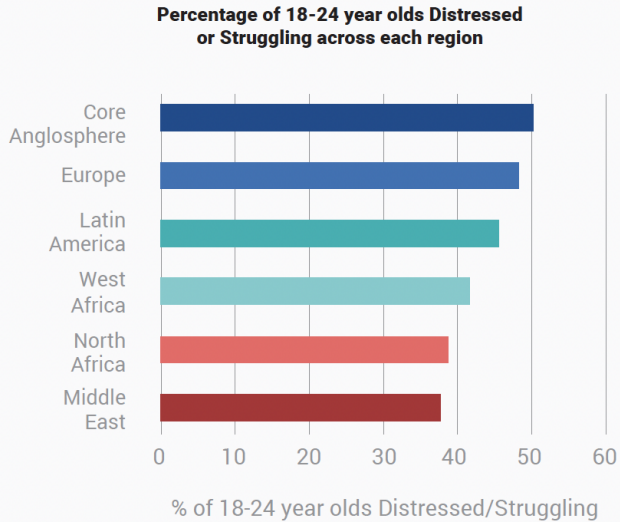
Take part at sapienlabs.org/mhq

sapienlabs.org

Figure 3.1: **MHQ score across age groups**





50% INCREASE IN PREVALENCE OF MENTAL DISORDERS IN YP SINCE 2007

ABC NEWS

ANALYSIS

About 40 per cent of young Australians have experienced mental illness — and it's high time we do something about it

By Patrick McGorry
Posted Thu 4 Aug 2022 at 8:00pm

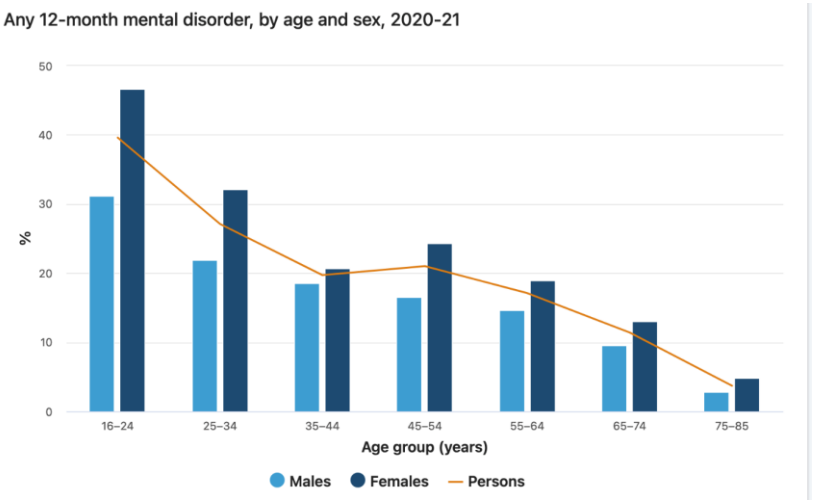
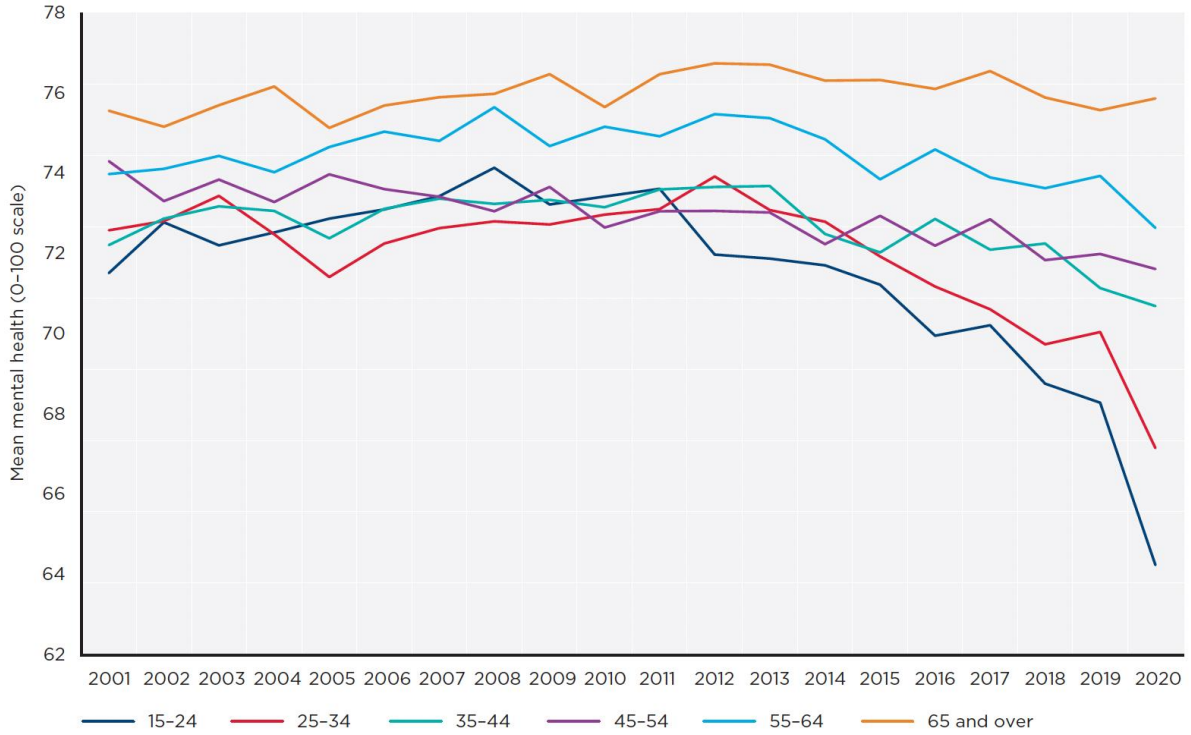
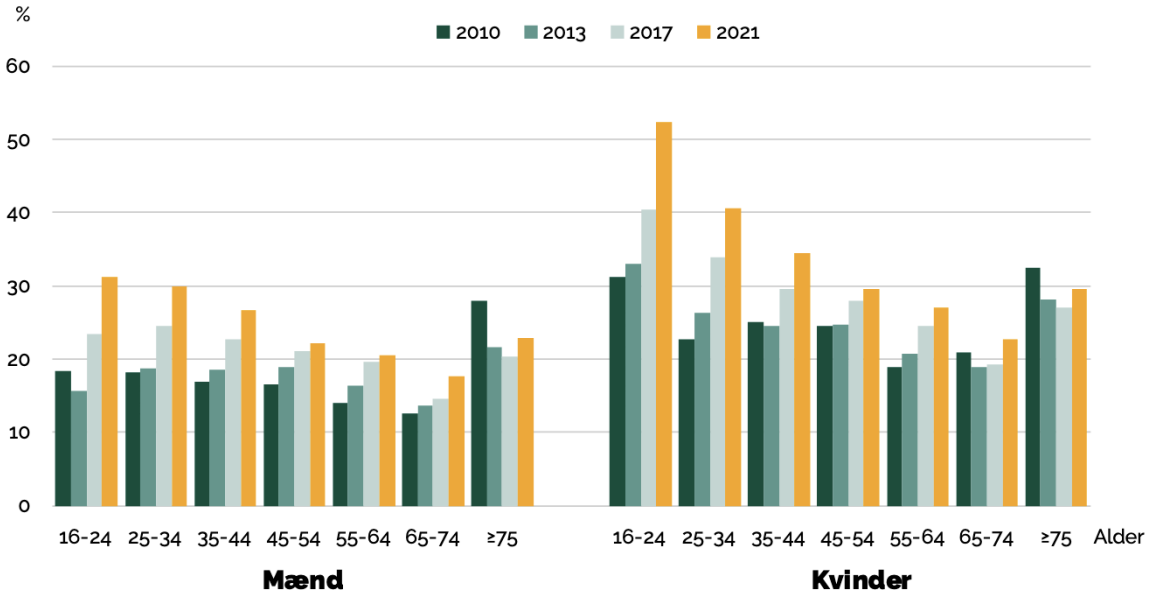


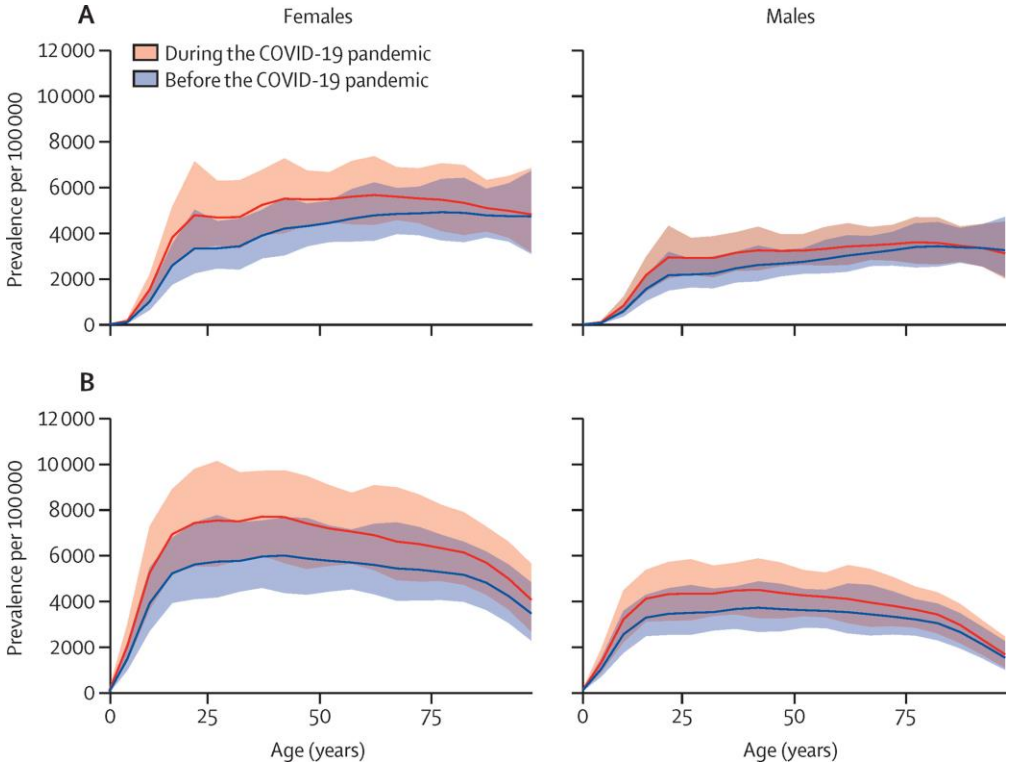
Figure 8.2: Average of the SF–36 mental health measure, by age group



DENMARK DATA

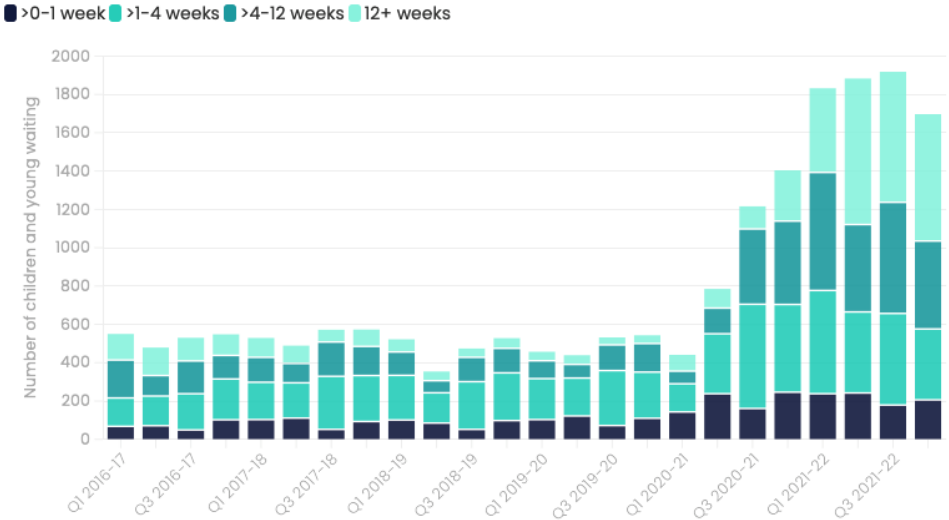
Figur 2.3.1 Andel, der har en høj score på stressskalaen, blandt mænd og kvinder i forskellige aldersgrupper. 2010, 2013, 2017 og 2021. Procent.




A
Females
Males
During the COVID-19 pandemic
Before the COVID-19 pandemic
Prevalence per 100 000
12 000
10 000
8000
6000
4000
2000
0
B
0
25
50
75
Age (years)

Children and young people waiting to start treatment by week since referral (routine cases)

Children and young people with eating disorders



MEGATRENDS

THE NEGLECT OF YOUNG PEOPLE

‘We get the raw deal out of almost everything’: a quarter of young Australians are pessimistic about having kids

February 21, 2022 12.07pm AEDT

A young woman in Melbourne in December 2021. Con Chronis/AAP

“…Gen Z are destined to be the worst-regarded generation ever. Both patterns are nothing but a reflection of ***our timeless denigration of young people***….”

Bobby Duffy, Professor of Public Policy and Director of the Policy Institute at KCL.

“It has always been a puzzle to me that the period of life of maximum disturbance, adolescence, is the one of ***least interest*** to both psychiatrists and governments….

…...the neglect of adolescent psychiatry is a special form of ***self-harm*** undertaken by adult society.”

Professor John Gunn 2004

“The future ain’t what it used to be”

Yogi Berra

VIEWPOINT

Addressing the Mental Health Crisis in Youth—Sick Individuals or Sick Societies?

Awais Aftab, MD
Department of Psychiatry, Case Western Reserve University, Cleveland, Ohio.

Benjamin G. Druss, MD, MPH
Department of Health Policy and Management, Rollins School of Public Health, Emory University, Atlanta, Georgia.

The prevalence of anxiety and depression has been increasing in the US as well as in many other parts of the world. This trend, beginning in the 2010s, has largely been concentrated among adolescents and youth.[1] At least 2 broad sets of characterizations have been proposed in the scientific literature and lay press, the first viewing this increase as an epidemic of psychiatric disorders[2] while the other seeing the increase in psychological distress in youth as reflective of sociopolitical adversity and disorganization.[3] At the risk of oversimplification, this contrast may be viewed as a sick individuals vs sick society polarity. Such explanatory dualities present clinicians with the challenge of how to navigate concerns about excessive medicalization and address complex social determinants of health in clinical settings. Moving past conceptual binary constructs fueling this polarization can be an important first step in addressing the mental health crisis in youth. Herein, we discuss the reasons for this polarization, strategies to overcome it, and how these insights should inform clinical practice.

how social factors may contribute to patients' clinical presentations.

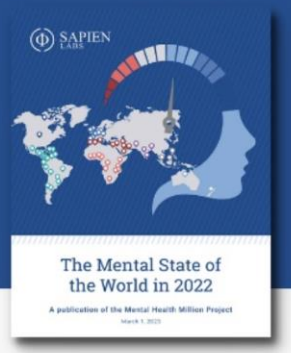
Ultimately, binary distinctions between disordered vs normal distress in the face of stressors, biological vs psychosocial etiologies, and individual treatment vs public health approaches boil down to a constricted and overly narrow view of the medical model. Concerns about medicalization of the psychological lives of youth are triggered by legitimate fears: critics are worried that by conceptualizing distressing responses in psychopathological terms, the relationship to context will be lost or minimized, self-understanding of individuals will be adversely changed, and sociopolitical activism will be replaced by individual medical treatment. Remedying these concerns requires actively emphasizing medical, public health, and policy approaches that take context, self-understanding, and political action seriously.

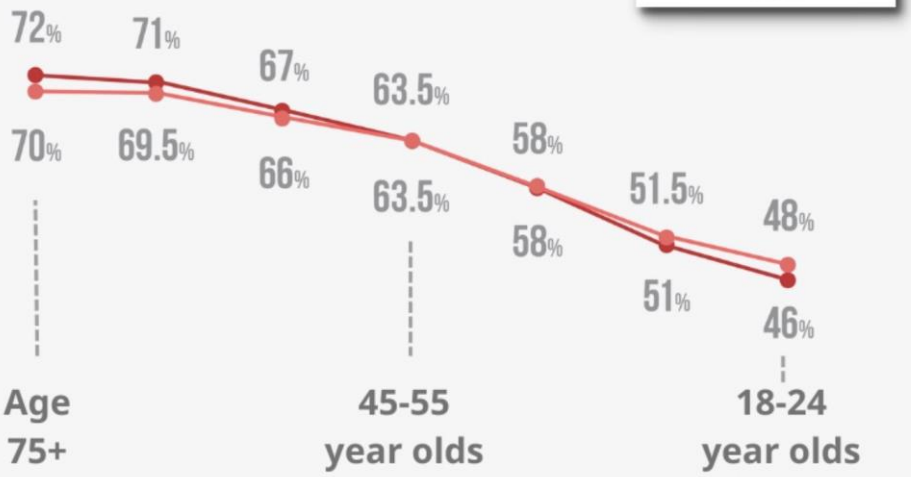
It has been argued that estimates of psychopathology based on symptom ratings and epidemiological questionnaires inflate the prevalence of mental

SICK INDIVIDUALS OR SICK SOCIETIES?

- Polarisation in part confuses cause and effect
- Michael Marmot: “what is the point of treating people and returning them to the circumstances that made them sick?”
- Social Determinants, Cohort Effects and Megatrends
- “The general awareness that the mental health crisis in youth is intertwined with sociopolitical turmoil has blurred the boundaries between social and medical perspectives.”
- “It has been argued estimates of psychopathology based on symptom ratings and epidemiological questionnaires inflate the prevalence of mental disorders.”
- Elevated symptomatology not sufficient evidence of psychopathology – different trajectories.
- However excluding subthreshold DSM states often clinically significant and warrant professional care (eg UHR psychosis)
- Soft entry key for EI but proportional response crucial: Clinical Staging Model

Stable and loving childhood homes are no longer the norm



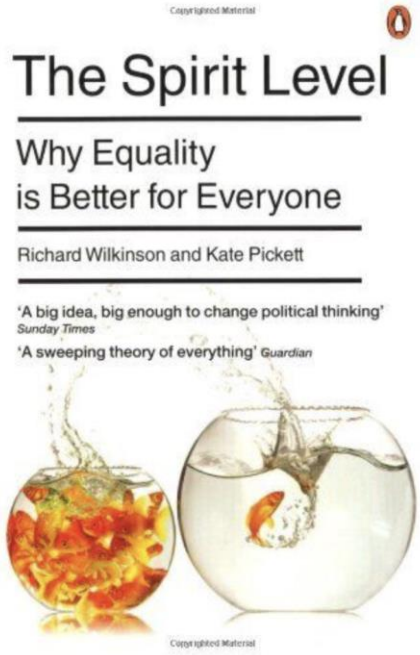


SAPIEN LABS

Explainer

Explained: How climate change affects mental health

Climate change is a global health crisis, and that includes mental health. Find out how it's impacting our mental health and what can be done to prevent and manage it.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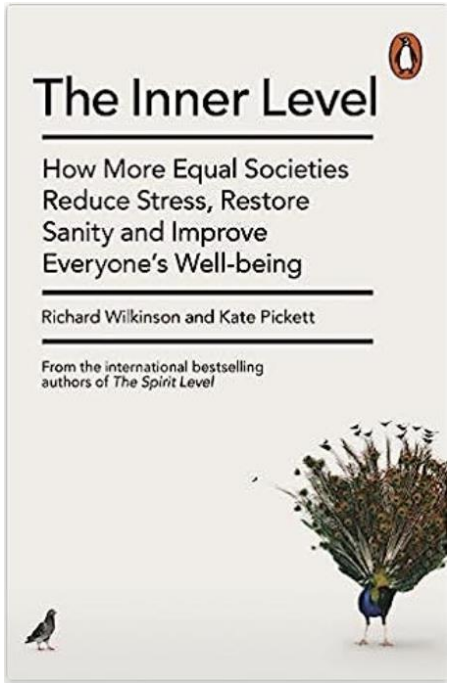

The Inner Level
How More Equal Societies
Reduce Stress, Restore
Sanity and Improve
Everyone's Well-being
Richard Wilkinson and Kate Pickett
From the international bestselling
authors of The Spirit Level

GEN F’D

PENNINGTON 2023

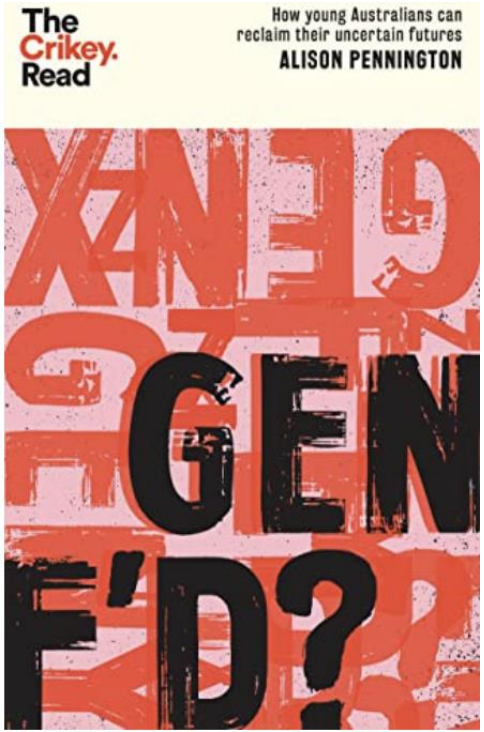
- **Precarity - The Precariat**
- THE END OF GOOD JOBS Insecure Work
- HOUSING CRISIS
- NEOLIBERALISM

  Tearing up the Social Contract

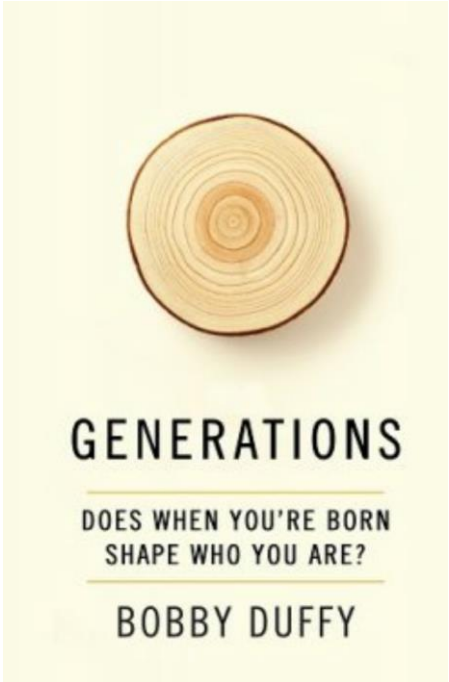
  Value Extraction and Rent Seeking
- INTERGENERATIONAL INEQUALITY
- SOCIAL MEDIA – limited forms of identity
- CLIMATE THREAT
- COHORT EFFECTS – GFC, PANDEMIC

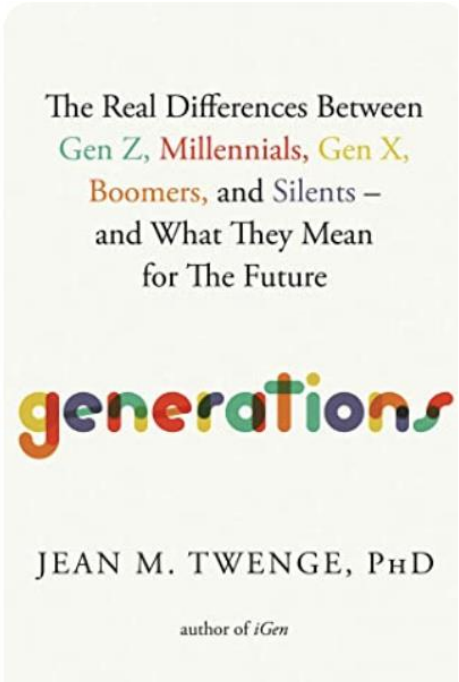
Loss of **Security**, Power, Connection & Solidarity.

The “Fair Go”: Organised Fairness



GENERATIONS





GEN Z

Gender Fluidity F to M and trans nonconforming (NB/Enby)

More LGB esp B

Delayed Adulthood

Sex Recession

Growing Up Slowly

Marriage and Childhood

Restricting Speech

Interest in Physical and Emotional Safety (The Coddling of the American Mind: Lukianoff and Haidt; Trigger Warnings)

Racial Consciousness

Worse Mental Health & Pessimism “Cards stacked against me” COVID

Worse Physical Health

Political Polarisation and Activism

THREE GRAND CHALLENGES

1. **INNOVATION IN DIAGNOSIS AND TREATMENT**

2. **FULL IMPLEMENTATION OF MODELS OF CARE**

3. **PREVENTION: THE YOUTH MENTAL HEALTH CRISIS**

“So you have the medicine, and you’re carrying the medicine, sometimes you have to carry it a long way.”

“Things change a little bit at a time and in my lifetime, things have not changed enough, but when I look back on the last 40 years, things have changed incredibly.”

Buffy Sainte Marie

“The lure of an imaginary land? Traveling somewhere that doesn’t exist? Of course I’m coming.”

Floki – Vikings Season 4, Episode 10: "The Last Ship"

REVOLUTION IN MIND

THANK YOU!

REVOLUTION IN MIND

THANK YOU