PSYCHOSIS: EARLY INTERVENTION AND BEYOND

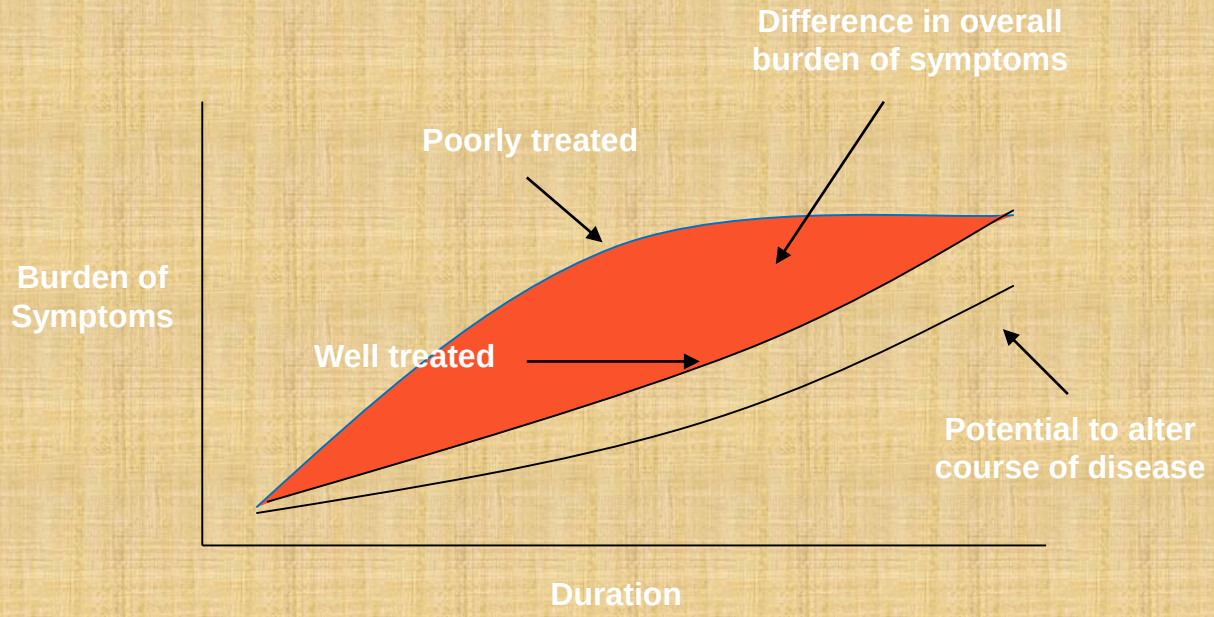
Patrick McGorry MD PhD

LAST EPISODE PSYCHOSIS

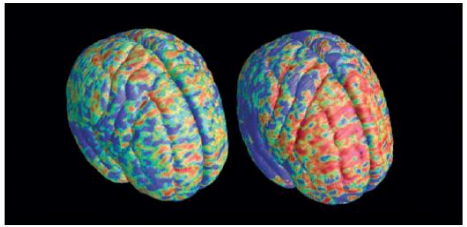
“An air of desolation more calculated to fix than to remove”

Emil Kraepelin

BURDEN OF DISEASE



OUTLOOK | SCHIZOPHRENIA



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

ELSEVIER SCIENCE PUBLISHING/TYRONE CANNON

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.

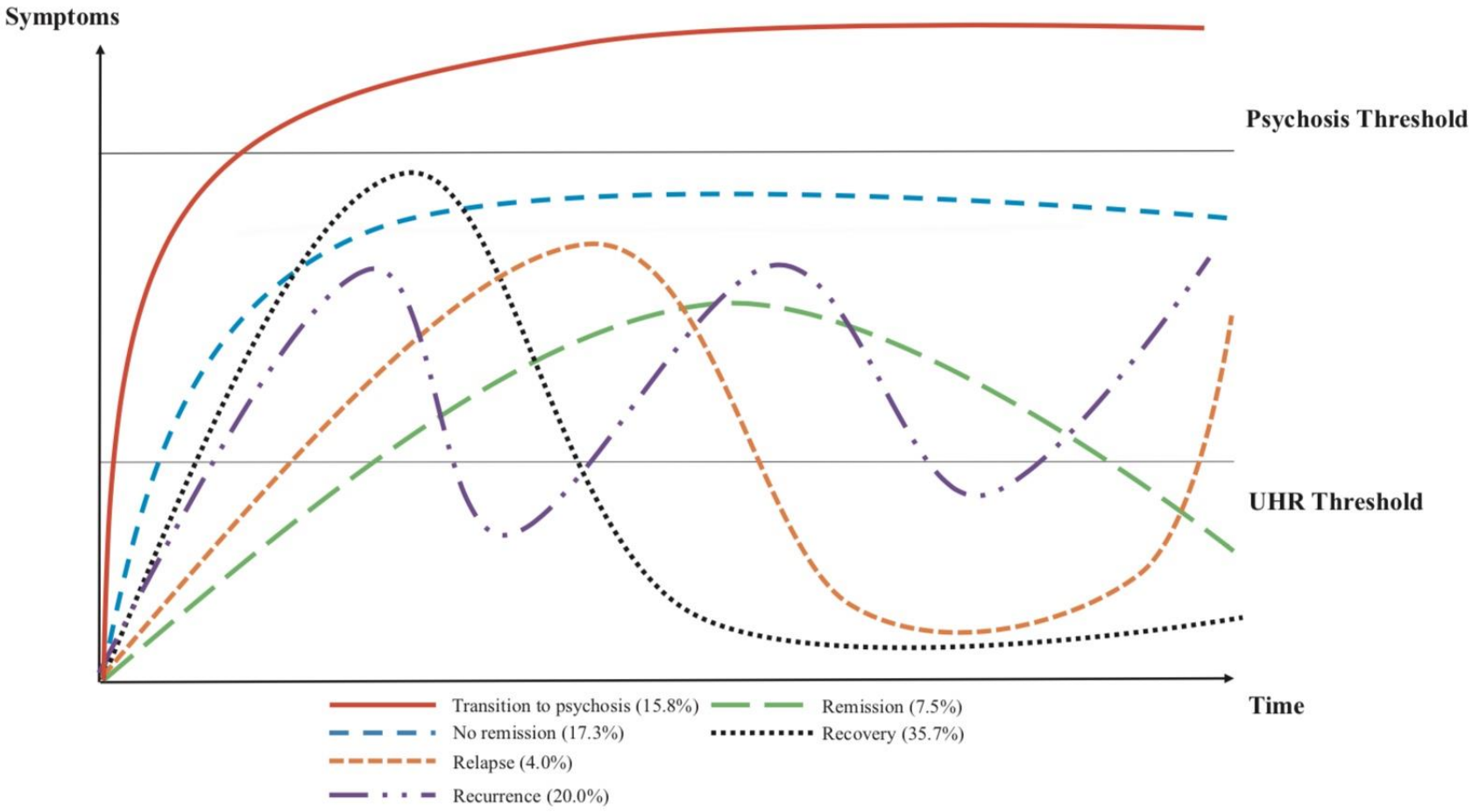
Study Selection: Twenty-seven studies met the inclusion criteria, comprising a total of 2502 patients.

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]dies 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

Received: 5 February 2018
Revised: 25 June 2018
Accepted: 26 November 2018

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

Author for correspondence:
Dr Olesya Ajnakina, E-mail: olesya.ajnakina@kcl.ac.uk

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

Olesya Ajnakina[1,2], Anthony S. David[3] and Robin M. Murray[1,4]

[1]Institute of Psychiatry, Psychology and Neuroscience, King's College London, De Crespigny Park, London, UK; [2]Department of Behavioural Science and Health, Institute of Epidemiology and Health Care, University College London, London, UK; [3]Institute of Mental Health, University College London, London, UK and [4]Department of Psychiatry, Experimental Biomedicine and Clinical Neuroscience (BIONEC), University of Palermo, Palermo, Italy

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.

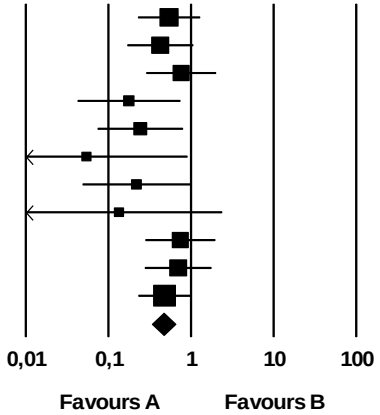
VAN DER GAAG ET AL (2013)

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

Contact address: Dina Bosnjak Kuharic, University Psychiatric Hospital Vrapče, Bolnicka cesta 32, Zagreb, Grad Zagreb, 10000, Croatia. dina.bosnjak@gmail.com.

Editorial group: Cochrane Schizophrenia Group
Publication status and date: New, published in Issue 11, 2019.

Citation: Bosnjak Kuharic D, Kekin I, Hew J, Rojnic Kuzman M, Puljak L. Interventions for prodromal stage of psychosis. *Cochrane Database of Systematic Reviews* 2019, Issue 11. Art. No.: CD012236. DOI: 10.1002/14651858.CD012236.pub2.

EVIDENCE IS LIKE BEAUTY - IN THE EYE OF THE BEHOLDER

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%

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

Schizophrenia Research 228 (2021) 344–356

Contents lists available at ScienceDirect

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

Patrick D. McGorry [a,b,*], Cristina Mei [a,b], Jessica Hartmann [a,b], Alison R. Yung [a,b,c], Barnaby Nelson [a,b]

[a] Orygen, Parkville, Victoria, Australia
[b] Centre for Youth Mental Health, The University of Melbourne, Parkville, Victoria, Australia
[c] School of Health Sciences, University of Manchester, Manchester, UK

ARTICLE INFO

Article history:
Received 1 May 2020
Received in revised form 2 October 2020
Accepted 31 December 2020
Available online xxxx

Keywords:
Ultra-high risk
Clinical high risk
At risk mental state
Psychosis
Randomized controlled trials

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

Clinical Psychology Review 86 (2021) 102005

Contents lists available at ScienceDirect

Clinical Psychology Review

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

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,*]

[a] Orygen, Parkville, VIC, Australia
[b] Centre for Youth Mental Health, The University of Melbourne, Parkville, VIC, Australia
[c] Department of Clinical, Neuro and Developmental Psychology, Amsterdam Public Health Research Institute, Vrije Universiteit Amsterdam, Amsterdam, the Netherlands
[d] Parnassia Psychiatric Institute, The Hague, the Netherlands
[e] Trimbos Institute, Netherlands Institute of Mental Health and Addiction, Centre of Mental Health and Prevention, Utrecht, the Netherlands
[f] Department of Epidemiology and Biostatistics, Amsterdam University Medical Centres, Amsterdam, the Netherlands
[g] School of Health Sciences, University of Manchester, Manchester, UK
[h] Department of Psychiatry, Psychotherapy and Psychosomatic Medicine, Vivantes Klinikum am Urban, Charite-Universitätsmedizin, Berlin, Germany
[i] Department of Psychiatry and Psychotherapy, University of Cologne, Cologne, Germany

ARTICLE INFO

Keywords:
Ultra-high risk
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

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

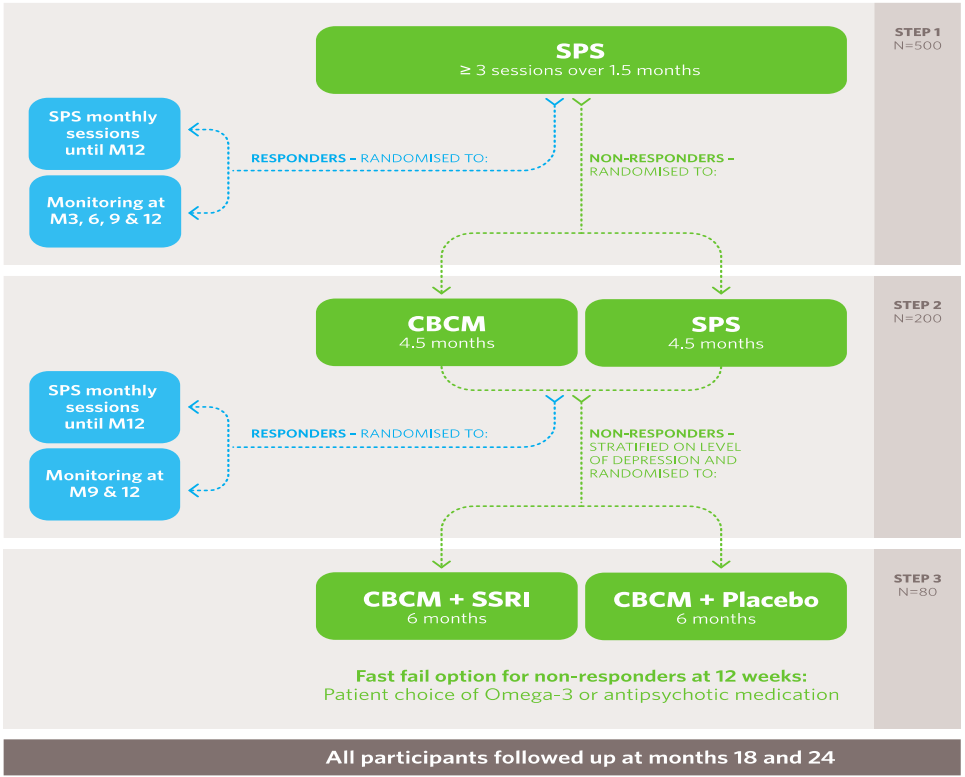
–We need to clarify the sequence of optimal treatment for UHR stage

–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

STEP Study Design



SPS = Support and Problem Solving

CBCM = Cognitive-Behavioural Case Management

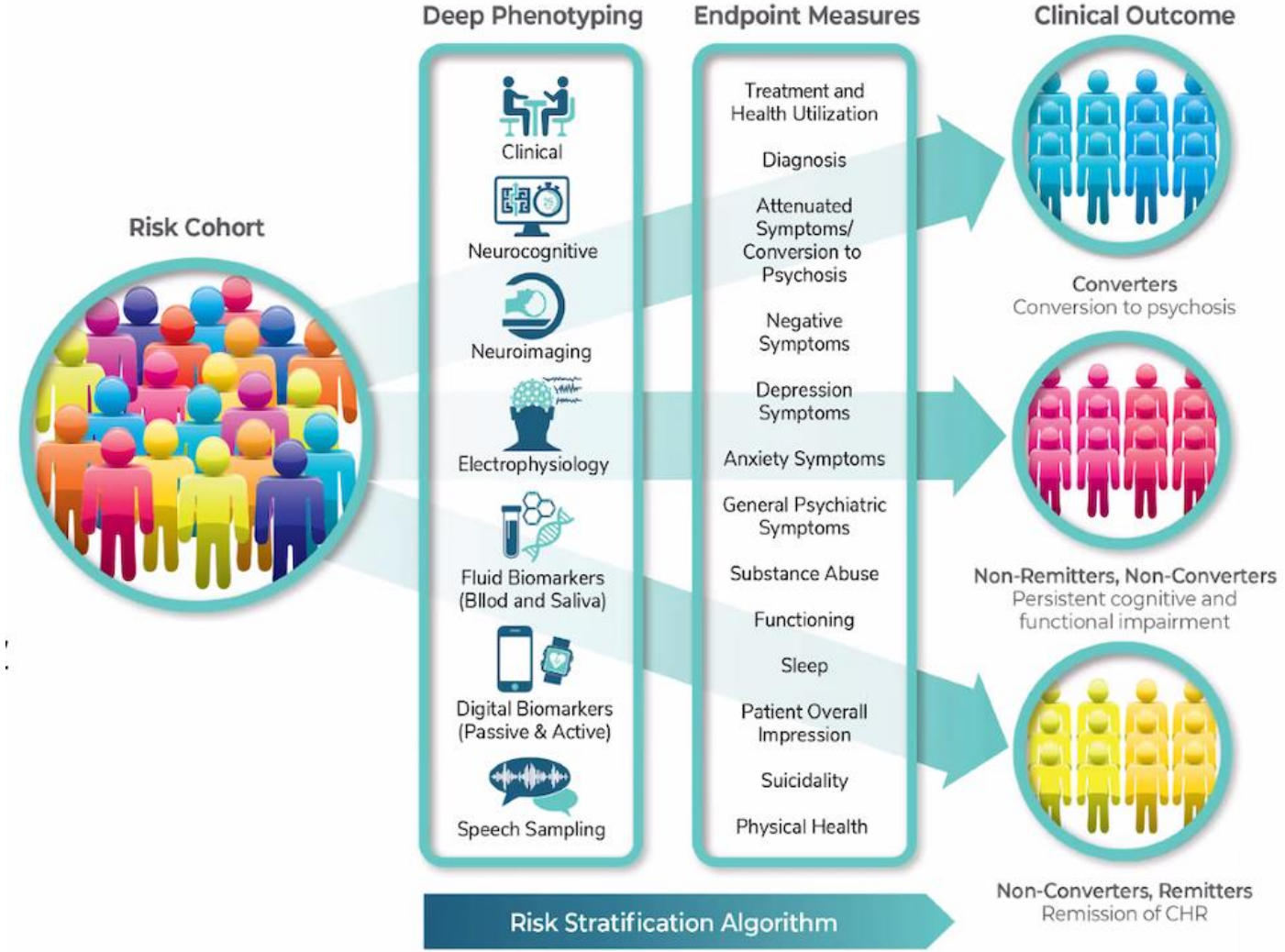
SSRI = Selective Serotonin Reuptake Inhibitor

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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Zimbabwe
Botswana
Madagascar
South Africa
South Atlantic Ocean
Indian Ocean
Gulf of Aden
Arabian Sea
Laccadive Sea
Bay of Bengal
Saudi Arabia
Yemen
Oman
Syria
Iraq
Iran
Afghanistan
Pakistan
India
Nepal
Kazakhstan
Uzbekistan
Kyrgyzstan
Turkmenistan
Mongolia
China
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Japan
Sea of Okhotsk
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SYDNEY
TELETHON KIDS INSTITUTE
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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

The AMP Schizophrenia public-private partnership is made possible through the generous support and participation of the following members

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

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)

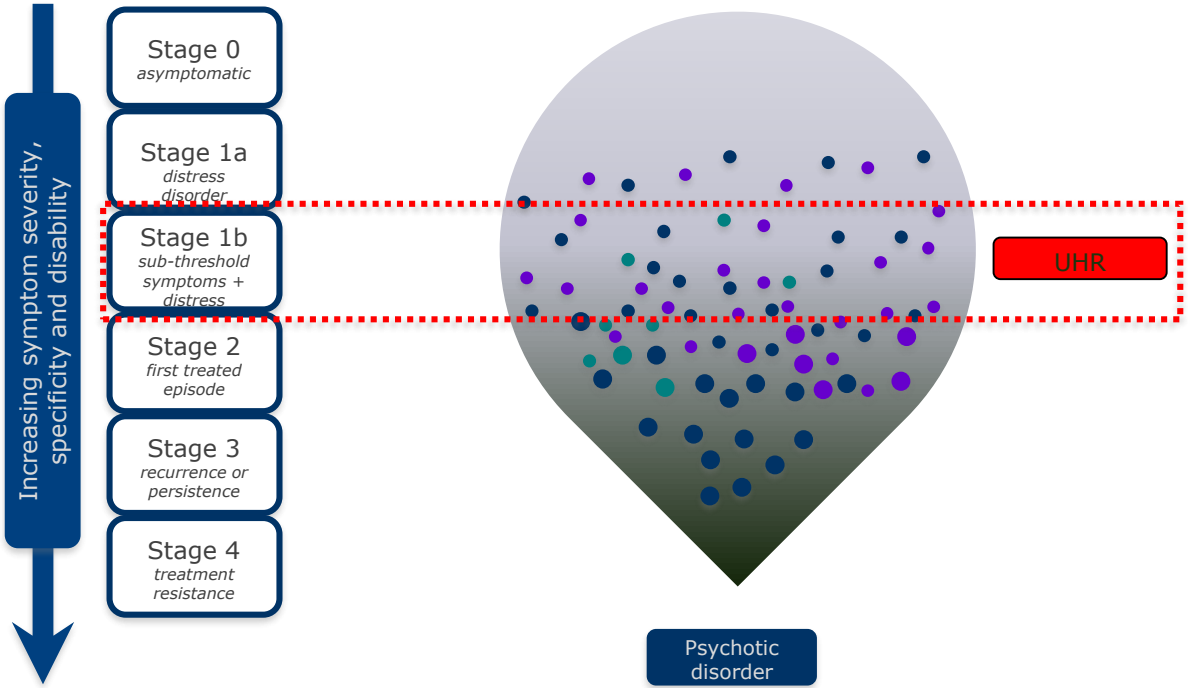


Figure 1A. Traditional UHR paradigm in the context of clinical staging

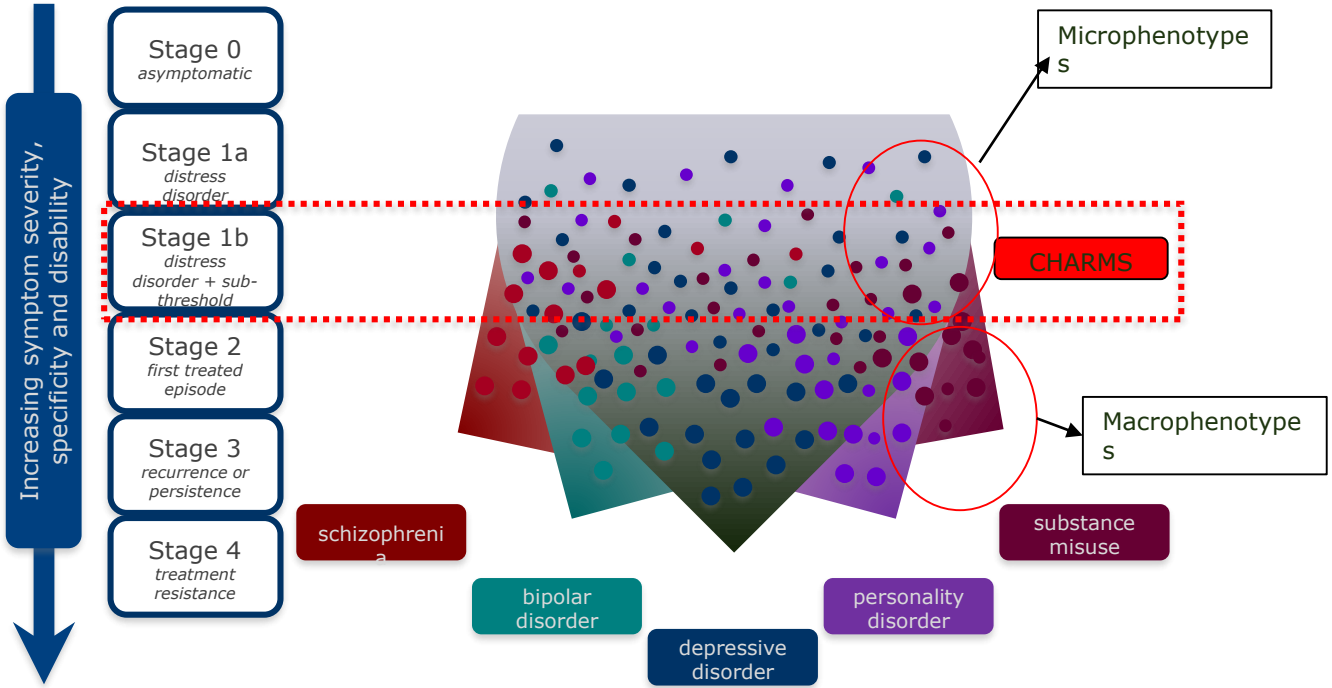
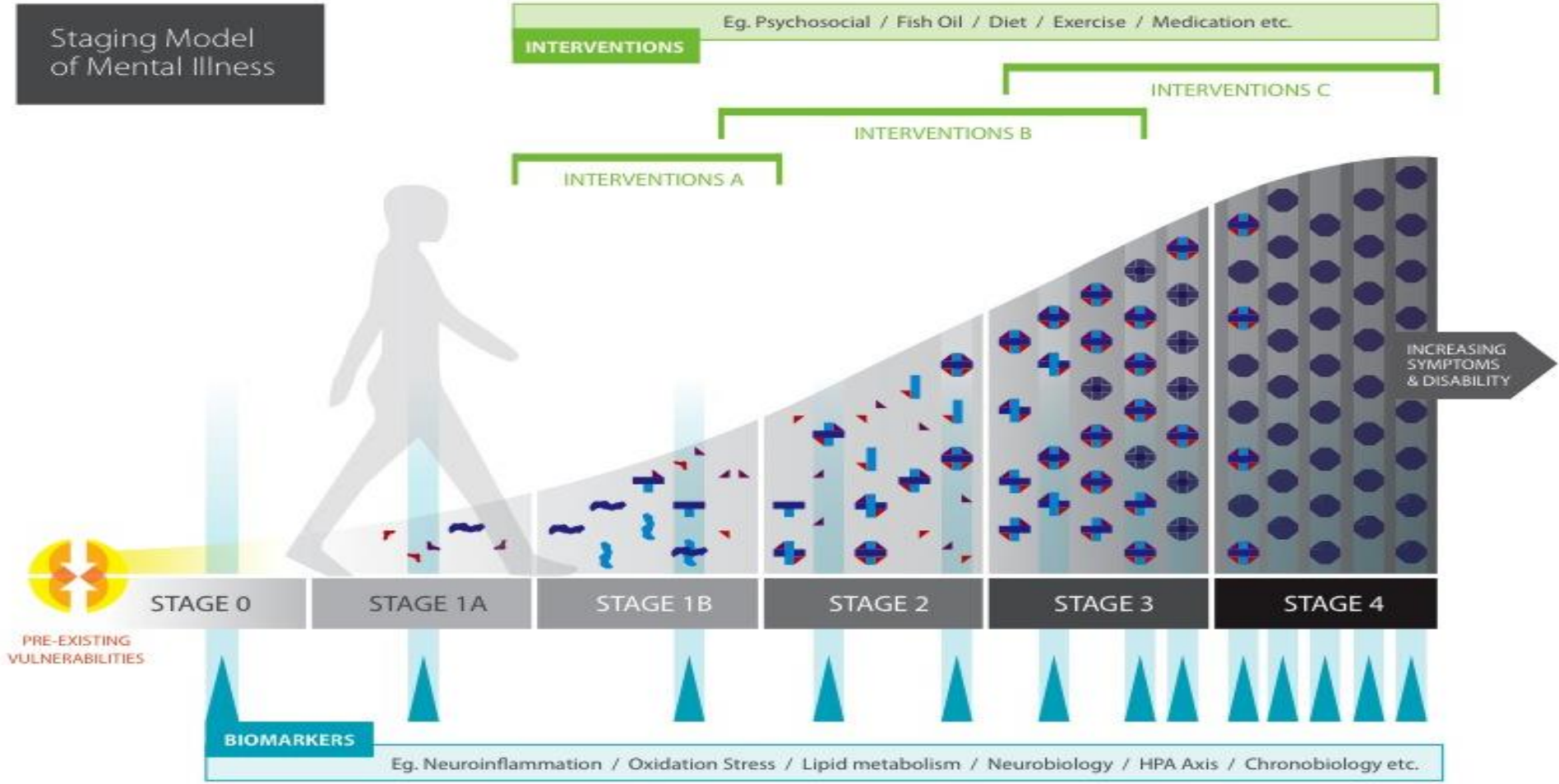


Figure 1B. New transdiagnostic CHARMS paradigm in the context of clinical staging


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.

EDITORIAL

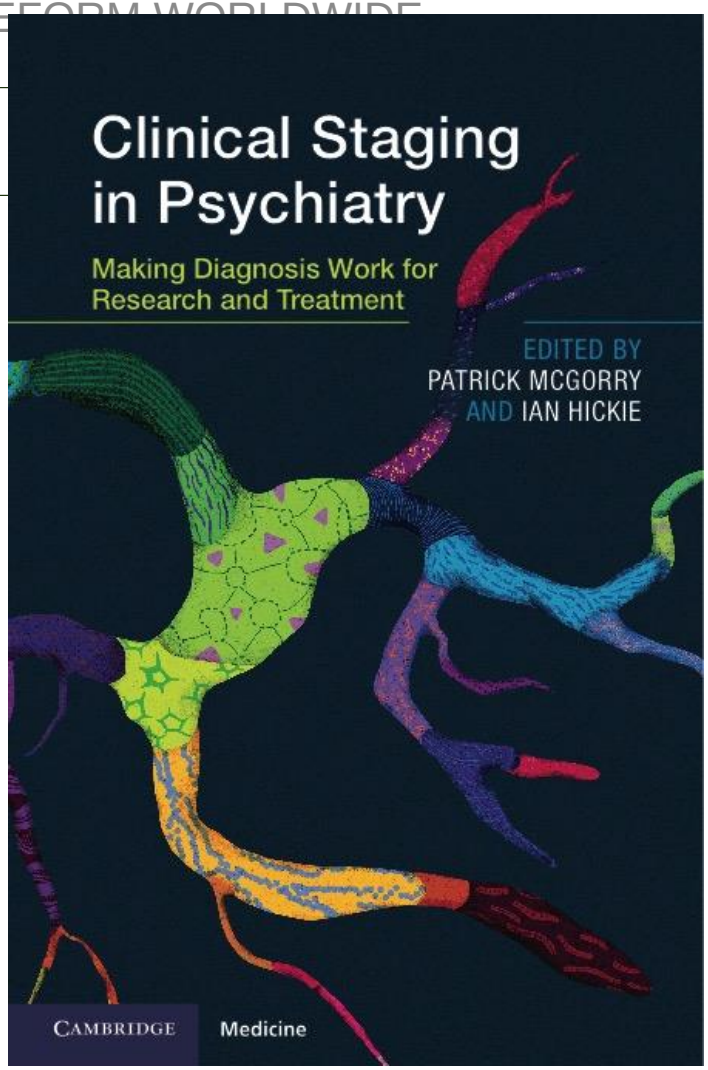
Why We Need a Transdiagnostic Staging Approach to Emerging Psychopathology, Early Diagnosis, and Treatment

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-


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

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.

Jan Ivar Rossberg, M.D., Ph.D.

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

Division of Psychology & Mental Health (R J Drake PhD, Prof N Husain MD, Prof S W Lewis FMedSci), **Division of Population Health, Health Services Research & Primary Care** (B Tomenson MSc), **Division of Neuroscience & Experimental Psychology** (Prof I B Chaudhry MD), **and Division of Informatics, Imaging & Data Sciences** (Prof I Buchan FFPH), **University of Manchester, Manchester, UK; Manchester Academic Health Science Centre, Manchester, UK** (R J Drake, Prof N Husain, Prof S W Lewis, B Tomenson, Prof I B Chaudhry, C D Green BSc, Prof I Buchan FFPH); **Greater Manchester Mental Health NHS Foundation Trust, Prestwich, Manchester, UK** (R J Drake, Prof S W Lewis, C D Green); **Lancashire Care & South Cumbria NHS Foundation Trust, Preston, Lancashire, UK** (Prof N Husain, Prof M Marshall MD); **Department of Psychiatry, Ziauddin University, Karachi, Pakistan** (Prof I B Chaudhry); **Birmingham and Solihull NHS, Mental Health Foundation, Trust, Birmingham, UK**

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

Centre for Health Economics, University of York, York, UK

Correspondence
Anika Reichert, Centre for Health Economics, University of York, Alcuin College Block A, York YO105DD, UK.
Email: ar1314@york.ac.uk

Abstract

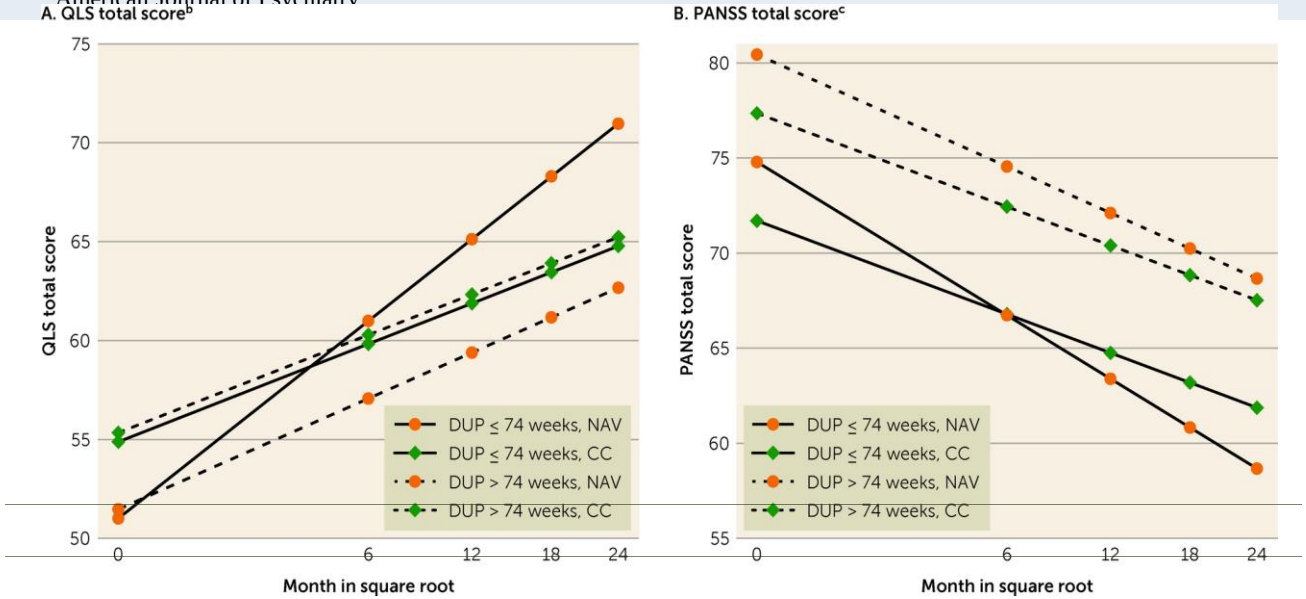
Recently, new emphasis was put on reducing waiting times in mental health services as there is an ongoing concern that longer waiting time for treatment leads to poorer health outcomes. However, little is known about delays within the mental health service system and its impact on patients. We explore 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

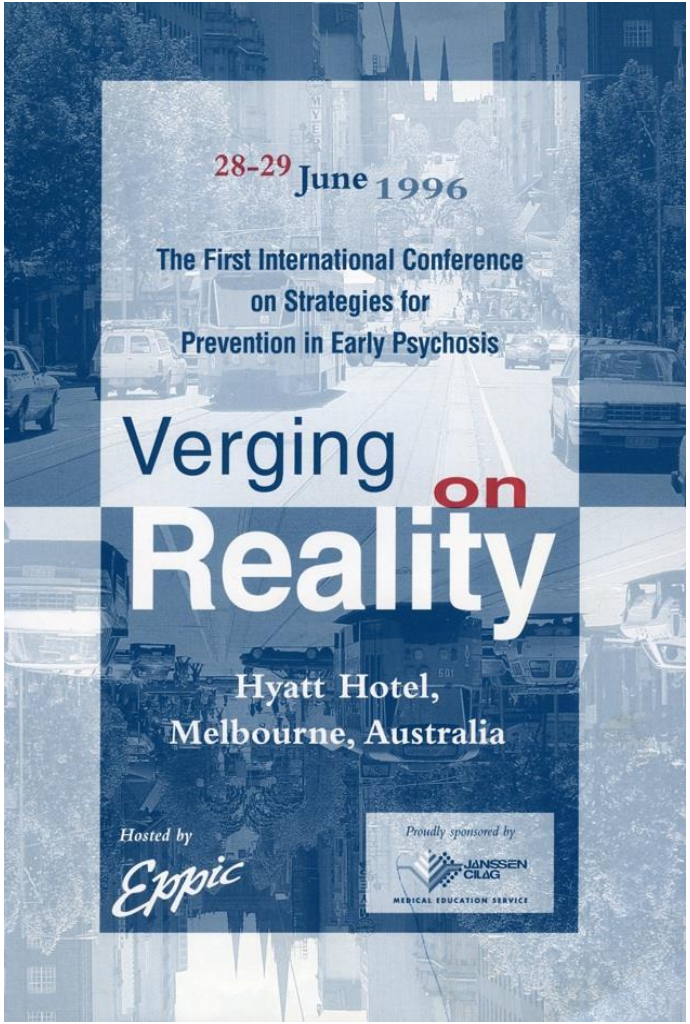
American Journal of Psychiatry



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

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


international early psychosis association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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.

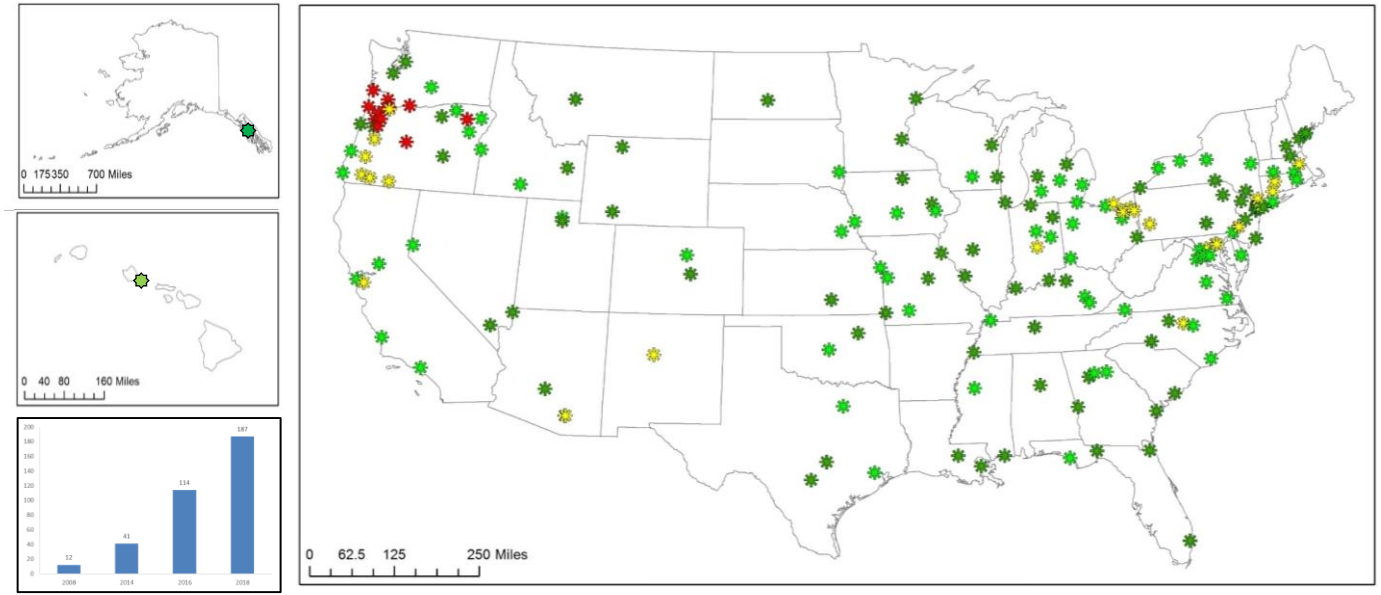
JAMA Psychiatry. doi:10.1001/jamapsychiatry.2018.0623
Published online May 2, 2018.

Editorial
Supplemental content

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

Corresponding Author: Christoph U. Correll, MD, Department of Psychiatry, The Zucker Hillside Hospital, 75-59 263rd St, Glen Oaks, NY 11004 (ccorrell@northwell.edu).

$100M in FY16 – FY17: 187 community clinics



2008 2014 2016 2018

	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.

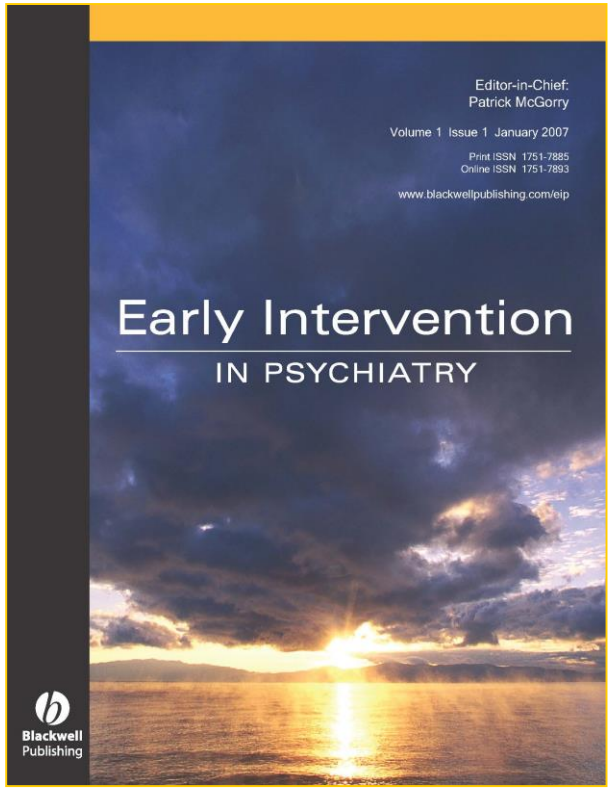
AJP in Advance (doi: 10.1176/appi.ajp.2017.17050480)

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

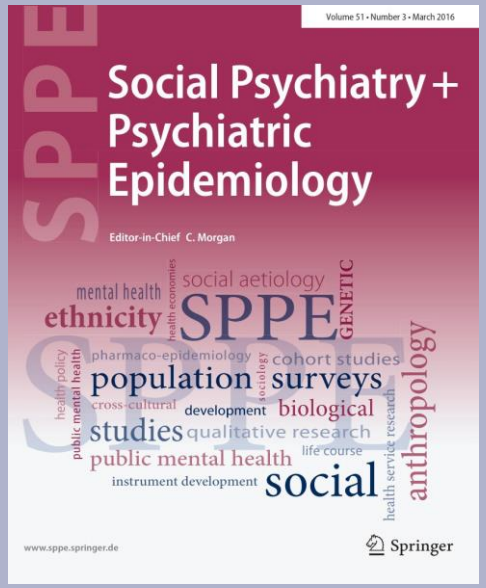
ISSN 0933-7954

Volume 51

Number 3

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

DOI 10.1007/s00127-015-1165-4



REVOLUTION IN MIND

THANK YOU