The story of reform of early psychosis services in England.

Scotland EIP Network Meeting, 1 December 2021

Max Birchwood.




Phase 1: Campaigning for service reform and the emerging science of the early intervention in psychosis

Phase 2: The trials

Phase 3: Implementation studies and challenges

Phase 4: National standards and performance monitoring.

Phase 5: EI non-responders: improving outcomes.

Phase 6: Phase-specific interventions.

Phase 1: Campaigning for service reform and the emerging science of the development of psychosis

Rethink Mental Illness.

Lost Generation

Why young people with psychosis are being left behind, and what needs to change.

British Journal of Psychiatry (1992), **161**, 783–790

The Influence of Ethnicity and Family Structure on Relapse in First-Episode Schizophrenia

A Comparison of Asian, Afro-Caribbean, and White Patients

MAX BIRCHWOOD, RAY COCHRANE, FIONA MACMILLAN, SONJA COPESTAKE, JO KUCHARSKA and MARGARET CARISS

There is overwhelming evidence that the outcome for people with schizophrenia in Western industrialised countries is inferior to that of those living in the Third World. Extended family structures, greater opportunities for social reintegration, and more positive constructions of mental illness have been offered as possible explanations for this effect. The Asian community in the UK retains many of these features as well as strong links with native cultures of origin. The issue arises as to whether similar differences in outcome may be observed in the UK. An exploratory study was undertaken, examining the early progress of schizophrenia in a first-episode sample ($n = 137$), and based on systematic examination of case-note data. A lower rate of relapse/readmission in the first 12 months after discharge was found in the Asian (16%) as compared with white (30%) and Afro-Caribbean (49%) patients. Available evidence suggested that speed of access to care, living with a family, and employment may account for this effect. Medication compliance may have contributed to differences in relapse between white and Afro-Caribbeans but was not a factor influencing the low rate among Asians. The limitations and strengths of case-note studies are discussed at length, and it is concluded that a prospective study is warranted and would be highly instructive.

There is now overwhelming evidence that the outcome for people with schizophrenia in Western industrialised countries is markedly inferior to that of those in the Third World (Lin & Kleinman, 1988).

Murphy & Rahman (1971) were among the first to make this observation in their study of African and Indian schizophrenic patients living in Mauritius. They found that after a 12-year follow-up involving 98% of their original sample, 64% reported no further episodes, as compared with 49% in a comparable UK sample followed up after 5 years (Brown *et al*, 1966). This apparent resistance to relapse has been documented in less industrialised countries by Verghese *et al* (1989) in India and Waxler (1979) and Mendis (1986) in Sri Lanka. A recent investigation using similar methods (Leff *et al*, 1987) compared first-episode samples in London and Chandigarh (a predominantly urban area of north India). They found a 9-month relapse rate of between 14% and 18% in Chandigarh, compared with 29% in London, a difference which did not appear to rest on the use of maintenance neuroleptic drugs (Leff *et al*, 1990).

The problem of achieving true comparability of sampling, measurement, outcome, and other criteria across cultures has been dealt with in the transcultural schizophrenia research programme of the World Health Organization (WHO, 1979; Sartorius *et al*, 1986). In the first of these studies, a cross-sectional sample covering eight countries was followed up over 2 years. On all measures, a greater proportion of patients in Agra (India), Cali (Colombia), and Ibadan (Nigeria) had more favourable, less disabling outcomes than did patients in Aarhus (Denmark), London, Prague, and Washington, DC. A further epidemiological study covering ten countries of first-episode patients (Sartorius *et al*, 1986) found a uniform annual incidence rate (1 per 10 000) but a variable 2-year outcome between countries, once again favouring less industrialised nations. In industrialised countries 40% of patients showed a 'severe' pattern (more than one episode and incomplete remission), as compared with 24% in developing ones.

Several hypotheses have been offered to account for this finding. The opportunity to engage in socially valued and productive roles may be enhanced in less industrial societies where there is a more flexible use of labour. The WHO fieldworkers in India, for example, had difficulty in interviewing ex-patients as the latter were so busy – the men in the fields and the women in domestic work. It is interesting to note that the pattern of recovery in Moscow paralleled that of less industrialised countries, perhaps a reflection of the emphasis on full employment and vocational rehabilitation in the former USSR (Warner, 1983).

According to another hypothesis, the extended family structure may help to diffuse burden and

Soc Psychiatry Psychiatr Epidemiol (1991) 26: 95–99

Second generation Afro-Caribbeans and young whites with a first admission diagnosis of schizophrenia

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Accepted: October 16, 1990

Summary. A study of young Afro-Caribbeans and whites diagnosed as suffering from schizophrenia on a first admission suggests that the over-representation of Afro-Caribbeans with this diagnosis is not explained by mis-diagnosis. The Afro-Caribbeans were more likely to live alone and to be in contact with the police or prison services before admission. They were also more likely to be admitted compulsorily, especially on forensic orders. They were less likely to make and maintain voluntary contact with the services. There was little difference in the physical treatment given to both groups but the Afro-Caribbeans were more likely to be re-admitted in subsequent years and one third of the Afro-Caribbean males were treated at some time in forensic units. Results are discussed with reference to previous literature and some recommendations made.

In a previous study of first psychiatric admissions we reported that second generation Afro-Caribbeans had greatly increased rates of first hospital admissions with a diagnosis of schizophrenia, compared to similarly aged whites (McGovern and Cope 1987 a). There had been no previous studies of second generation Afro-Caribbeans and the increased rates of schizophrenia were greater than any reported in other studies comparing first generation Afro-Caribbean migrants and whites (Cochrane 1977; Carpenter and Brockington 1980; Dean et al. 1981). Subsequently a small, carefully designed, prospective study in Nottingham, using clear diagnostic criteria revealed an even greater excess of schizophrenia in young Afro-Caribbeans (Harrison et al. 1988).

There is surprisingly little systematic research on the subsequent differential experiences of Afro-Caribbeans and white patients in terms of types of treatment given and co-operation with treatment. One study (Littlewood and Cross 1980) of a mixed diagnostic group of out-patients suggested that Afro-Caribbeans received more physical treatments than white patients. In the United States, black patients are more likely to receive physical than dynamic treatments regardless of the diagnosis (Cole and Pilisuk 1976; Thomas and Sillen 197 bimpe 1981).

This paper presents a detailed analysis of first sions of second generation Afro-Caribbeans anc with a diagnosis of schizophrenia, based on an an case notes. We describe the clinical picture in mo and whether the symptomatology correspondec search diagnostic criteria. Also we compare how A ribbeans and whites enter the psychiatric syst physical treatment received, co-operation with tr and, finally, some data on follow-up.

Method

In previous papers (McGovern and Cope 1987 a, b scribed the method for recording first psychiatric sions to a Birmingham Hospital over the 4 year 1980 to 1983. Afro-Caribbean patients aged bet and 29 years on admission, were classified as generation. They were compared with a similar white, British group. Our use of the term second ation is somewhat idiosyncratic, and includes both born Afro-Caribbeans and young Afro-Caribb grants aged under 30 years at the time of th (McGovern and Cope 1987 a). In this study the ca of both groups with a first admission diagnosis of phrenia were re-examined and the following info was recorded:

Demographic data

Age; whether or not employed; marital status married, cohabiting, separated, divorced); living stances (whether living alone or with family); age gration (if applicable); family history of mental (Family history was noted as positive if it was r that a first or second degree relative received tre from a psychiatrist).

British Journal of Psychiatry (1986), **148**, 115–120

The Northwick Park Study of First Episodes of Schizophrenia

I. Presentation of the Illness and Problems Relating to Admission

E. C. JOHNSTONE, T. J. CROW, A. L. JOHNSON and J. F. MacMILLAN

Collaborators: Drs B. Alapin, V. Baraniecka, U. Baruch, C. Benedek, M. Bowman, J. Bradley, J. Bruce, M. Carney, J. Candy, B. Chester, P. d'Orban, G. Edwards, K. Granville-Grossman, J. Hailstone, J. Hajioff, R. Henryk-Gutt, H. Hershon, Z. Huq, P. Jeffreys, M. Joyston-Bechal, W. Knapman, C. McEvedy, S. Mann, S. Montgomery, G. Nanayakkara, D. Owens, D. Pariente, R. Pinto, D. Pitcher, P. Pilkington, J. Price, R. Priest, M. Salasa, A. Shah, F. Sebastian-Pillai, H. Sergeant, G. Silverman, S. Spencer, J. Stead, C. Tonks.

Patients referred over 28 months from nine medical centres for a trial of prophylactic neuroleptic medication following first episodes of schizophrenic illness (462) were assessed with the Present State Examination, WHO scales for disability, past history, and socio-demographic factors, and a rating of disturbed behaviour; 253 fulfilled the study criteria; of the 209 who did not, 54 did not meet the diagnostic criteria, 65 had a history of a previous episode, and in 15 the psychotic illness was found to have an organic basis. The interval between onset of illness and admission varied widely, but was often more than one year and associated with severe behavioural disturbance and family difficulty e.g. in arranging appropriate care. Current arrangements for initiating management of first schizophrenic illnesses are frequently unsatisfactory.

Little systematic information has been collected on the mode of onset, presentation, and early course of schizophrenia. While data on age of onset (Norick & Odegard, 1966), rates of first admission (eg Dean *et al*, 1981), psychopathological aspects (Gillies, 1958: Chapman, 1966), and outcome (Cooper, 1961; Nyman & Jonsson, 1983) are available, there is no formal study of the duration and nature of the disturbance preceding first admission. Nor have the circumstances of admission been systematically examined. Similarly, while it is established that neuroleptic medication is effective in preventing relapse after discharge (Leff & Wing, 1971; Hirsch *et al*, 1973; Hogarty *et al*, 1973; Rifkin *et al*, 1977), a small proportion of patients remain well without active medication. If there is a group who experience only one or infrequent episodes of illness, such patients would be under-represented in studies of the generality of schizophrenic episodes, and thus the prophylactic value of neuroleptic medication may be exaggerated.

We examined the prophylactic effect of neuroleptic medication following first schizophrenic episodes in a large sample of patients, intending to assess the early course of the illness and the determinants of satisfactory outcome with and without active medication. We also studied the nature of the behavioural disturbance and social difficulties at presentation and the early outcome in clinical, social, and judicial terms, as well as the relationship of expressed emotion (EE) in the family to relapse following a first episode. This paper describes the nature and selection of the total referred sample of 462 cases and the difficulties occurring in the interval between onset and admission.

Method

To obtain an adequate sample, collaboration was sought from consultant psychiatrists in several medical centres within 35 miles of Harrow; collaborators were asked to make a referral to Northwick Park whenever a suitable patient was admitted, i.e. aged between 15 and 70 years, with a first psychotic illness, not unequivocally affective. For the purposes of referral, a "psychotic illness" was defined as one characterised by the presence of delusions or hallucinations occurring in clear consciousness. The clinicians were asked to refer any case that they thought might be suitable and to err on the side of over- rather than under-referral; referred patients remained under their care, and in the hospital to which they had been admitted. They were assessed there by the project psychiatrists (JFM; ECJ; TJC) using Present State Examination (PSE) (Wing *et al*, 1974), Past History and Sociodemographic Schedule (PHSD) (Jablensky *et al*, 1980), Disability Assessment Schedule (DAS) (Jablensky *et al*, 1980), Camberwell Family Interview (CFI) (Vaughn & Leff, 1976) and Disturbed Behaviour Rating (DBR).

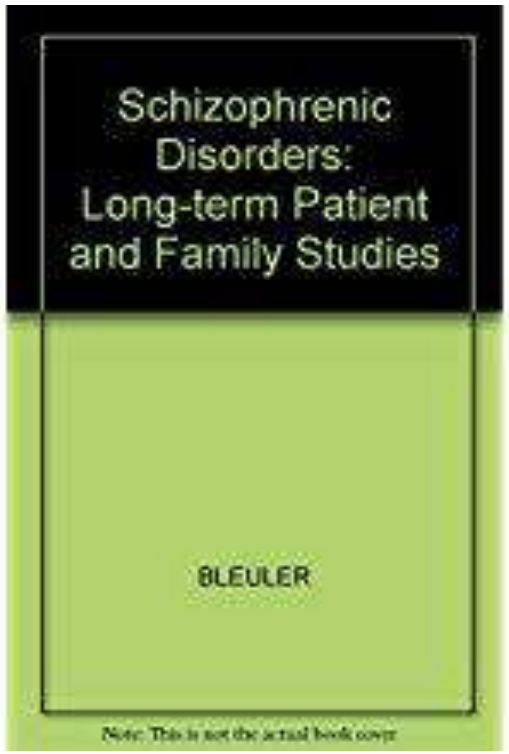
The PHSD concerns personal data, the presentation of the illness, and items of personal and family history; it is completed by the interviewer on the basis of an account from an informant as well as the patient. The DAS consists of two sections; one completed by interview of relatives or others who had been living with the patient before admission, and the other by interview with the nursing

The need for service reform:
if it's broke, fix it..

- Low engagement of YP in services & treatment (and poor early outcome)
- Long treatment delay (DUP 1-2 years)
- High use of coercion at entry to services
- "CAMHS don't do psychosis, AMHS don't do young people"
- Low acceptability of CMHT/hospital service model.

NICE Guidelines for schizophrenia(2014)

"Despite the fact that CMHTs remain the mainstay of community mental health care, there is surprisingly little evidence to show that they are an effective way of organizing services. As such, evidence for the effectiveness of CMHTs in the management of schizophrenia is insufficient to make any evidence-based recommendations" (P261)



Burghölzli, Zurich

- ‘Plateau effect’: ceiling of disability early in manifest course
- Open culture of community integration and meaningful activity
- Functional and symptomatic outcomes best in pre-neuroleptic era; comparable today??

Translating to EIP: the 'CRITICAL PERIOD'

BRITISH JOURNAL OF PSYCHIATRY (1998), 172 (suppl. 33), 53–59

Early intervention in psychosis

The critical period hypothesis

MAX BIRCHWOOD, PAULINE TODD and CHRIS JACKSON

Background We consider the evidence for the proposition that the early phase of psychosis (including the period of untreated psychosis) is a 'critical period' in which (a) long-term outcome is predictable, and (b) biological, psychological and psychosocial influences are developing and show maximum plasticity.

Method First-episode prospective studies, predictors of outcome and the genesis of patients' key appraisals of their psychosis are reviewed.

Results The data support the notion of the 'plateau effect', first coined by Tom McGlashan, which suggested that where deterioration occurs, it does so aggressively in the first 2–3 years; and that critical psychosocial influences, including family and psychological reactions to psychosis and psychiatric services, develop during this period.

Conclusions The early phase of psychosis presents important opportunities for secondary prevention. We outline a prototype of intervention appropriate to the critical period. The data challenge the widely held assumption that first-episode psychosis is a benign illness posing little risk.

Interventions in psychosis, whether biological or psychosocial, have been generally blind to the phase and age of illness. Such neglect reflects the dominance of the two main paradigms of care, in which treatment is provided in acute crisis care to achieve prophylaxis, and also in 'rehabilitation' involving amelioration of disabilities occasionally within a framework of relative asylum (Birchwood & Macmillan, 1993). Community outreach models frequently involve a blend of these two approaches. These paradigms are founded upon Kraepelinian nosology and while long-term follow-up studies demonstrate the heterogeneity of outcomes in psychosis, they do nevertheless appear to support the two paradigms: between a quarter and one-third of those affected have either single or multiple episodes with little or no residual symptoms, whereas the remainder have multiple episodes with varying and often increasing impairment (Shepherd et al, 1989). The early phase of psychosis may thus be viewed as a period during which it is possible to determine which path an individual is ultimately likely to follow. A radically different view argues that the early phase of psychosis is a major influence and that the early phase of psychosis is a 'critical period' with major implications for secondary prevention of the impairments and disabilities that accompany psychosis. In this paper, we will summarise evidence in support of this proposition and outline a prototype of intervention appropriate to the 'critical period'.

CRITICAL PERIODS

Prospective follow-up studies of people with first-episode psychosis

The bulk of follow-up studies of psychosis have taken samples of convenience which are inevitably drawn from those maintaining contact with services. Thus, a distorted picture, in particular biased in favour of chronicity, will be presented, although first-episode studies are not without their own problems. For example, determining their epidemiological representativeness is one issue that has been demonstrated only in the Determinants of Outcome of Severe Mental Disorder study (DOSMD; Jablensky *et al*, 1992). However, the follow-back and the prospective studies do permit certain conclusions and key hypotheses may be tested. Since we are concerned with a supposed critical period of early psychosis, in this section we will focus only on first-episode prospective studies.

Clinical and social outcomes

Strauss and Carpenter (1977) demonstrated that clinical recovery was not a pre-requisite for social recovery; in fact they reported substantial desynchrony between, for example, residual symptoms and social functioning, the correlations being no greater than 0.5. Normal processes as well as abnormal ones contribute to social readjustment (Birchwood *et al*, 1988) and the first-episode studies follow the same general rule. The correlation between symptoms and functioning are of the same order (Shepherd *et al*, 1989) and social outcome in the early phase is better than might be expected in the light of clinical outcome alone. Shepherd *et al* (1989) showed that 30% of people suffered moderate to severe social impairment whereas 70% have multiple episodes and/or residual symptoms over the first five years. Mason *et al* (1995) echo this point, "the status of symptoms may have little relevance to every-day social functioning". Schubart *et al* (1986) and the linked study of Biehl *et al* (1986) examine the course of social disability over the first five years using the World Health Organization Disability Assessment Schedule (WHODAS; WHO, 1992). Neither baseline clinical symptoms nor age or gender predicted social outcome at five years; only WHODAS scores at six months predicted outcome at one, two, three and five years. Like Strauss & Carpenter (1977) they find that the best predictor of social outcome is an earlier measure of social functioning. The corollary of this is that improving clinical functioning by itself will not guarantee improved social functioning, other interventions, both 'technical' and

"Early phase of psychosis is a stormy one, plateauing thereafter"

- Early trajectories predict long term trajectories
- The *plateau effect*: ceiling of disability/symptoms early in manifest course (Bleuler)
- Adolescent social functioning best predictor of early phase social functioning

From :Birchwood,M and Macmillan,JF (1993) Early intervention in schizophrenia *Australia & New Zealand Journal of Psychiatry 27 374-8*

BRITISH JOURNAL OF PSYCHIATRY (2001), 178, 506–517

Recovery from psychotic illness: a 15- and 25-year international follow-up study

G. HARRISON, K. HOPPER, T. CRAIG, E. LASKA, C. SIEGEL, J. WANDERLING, K. C. DUBE, K. GANEV, R. GIEL, W. AN DER HEIDEN, S. K. HOLMBERG, A. JANCA, P. W. H. LEE, C. A. LEÓN, S. MALHOTRA, A. J. MARSELLA, Y. NAKANE, N. SARTORIUS, Y. SHEN, C. SKODA, R. THARA, S. J. TSIRKIN, V. K. VARMA, D. WALSH and D. WIERSMA

'The predictive strength of early pattern of course and socio-cultural setting support the case for early intervention strategies with social and drug interventions' (p516)

BJPsych The British Journal of Psychiatry (2009) 194, 18–24. doi: 10.1192/bjp.bp.107.048942

Beyond the critical period: longitudinal study of 8-year outcome in first-episode non-affective psychosis

Niall Crumlish, Peter Whitty, Mary Clarke, Stephen Browne, Moayyad Kamali, Maurice Gervin, Orfhlaith McTigue, Anthony Kinsella, John L. Waddington, Conall Larkin and Eadbhard O'Callaghan

Background
The critical period hypothesis proposes that deterioration occurs aggressively during the early years of psychosis, with relative stability subsequently. Thus, interventions that shorten the duration of untreated psychosis (DUP) and arrest early deterioration may have long-term benefits.

Aims
To test the critical period hypothesis by determining whether outcome in non-affective psychosis stabilises beyond the critical period and whether DUP correlates with 8-year outcome; to determine whether duration of untreated illness (DUI) has any independent effect on outcome.

Method
We recruited 118 people consecutively referred with first-episode psychosis to a prospective, naturalistic cohort study.

Results
Negative and disorganised symptoms improved between 4 and 8 years. Duration of untreated psychosis predicted remission, positive symptoms and social functioning at 8 years. Continuing functional recovery between 4 and 8 years was predicted by DUI.

Conclusions
These results provide qualified support for the critical period hypothesis. The critical period could be extended to include the prodrome as well as early psychosis.

Declaration of interest
None. Funded by the Stanley Medical Research Institute.

BJPsych The British Journal of Psychiatry (2017) 211, 350–358. doi: 10.1192/bjp.bp.117.201475

Review article

Remission and recovery from first-episode psychosis in adults: systematic review and meta-analysis of long-term outcome studies†

John Lally,* Olesya Ajnakina,* Brendon Stubbs, Michael Cullinane, Kieran C. Murphy, Fiona Gaughran and Robin M. Murray

Background
Remission and recovery rates for people with first-episode psychosis (FEP) remain uncertain.

Aims
To assess pooled prevalence rates of remission and recovery in FEP and to investigate potential moderators.

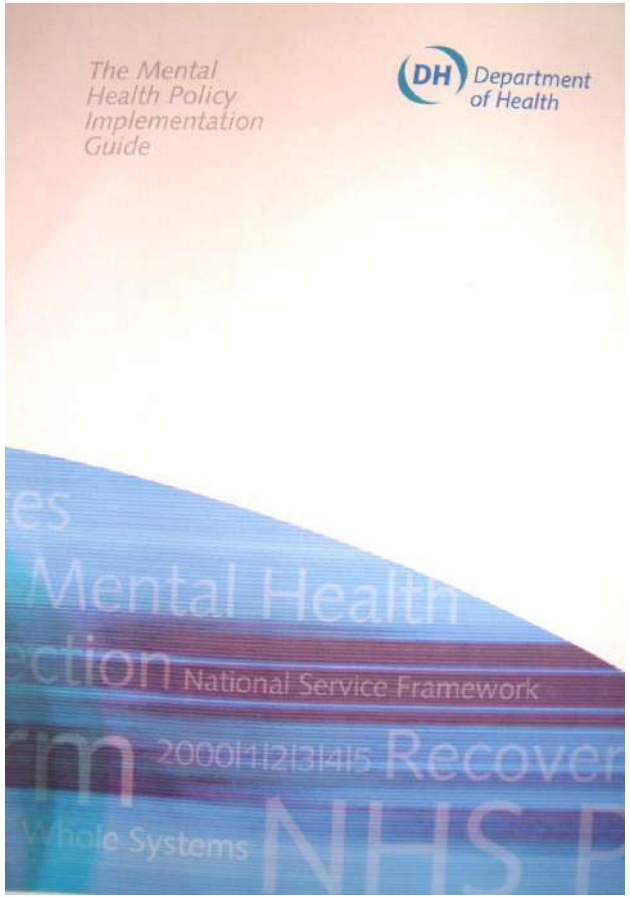
Method
We conducted a systematic review and meta-analysis to assess pooled prevalence rates of remission and recovery in FEP in longitudinal studies with more than 1 year of follow-up data, and conducted meta-regression analyses to investigate potential moderators.

Results
Seventy-nine studies were included representing 19 072 patients with FEP. The pooled rate of remission among 12 301 individuals with FEP was 58% (60 studies, mean follow-up 5.5 years). Higher remission rates were moderated by studies from more recent years. The pooled prevalence of recovery among 9642 individuals with FEP was 38% (35 studies, mean follow-up 7.2 years). Recovery rates were higher in North America than in other regions.

Conclusions
Remission and recovery rates in FEP may be more favourable than previously thought. We observed stability of recovery rates after the first 2 years, suggesting that a progressive deteriorating course of illness is not typical. Although remission rates have improved over time recovery rates have not, raising questions about the effectiveness of services in achieving improved recovery.

Declaration of interest
None.

Sustaining engagement and intervention through the ‘Critical Period’ with specialised teams

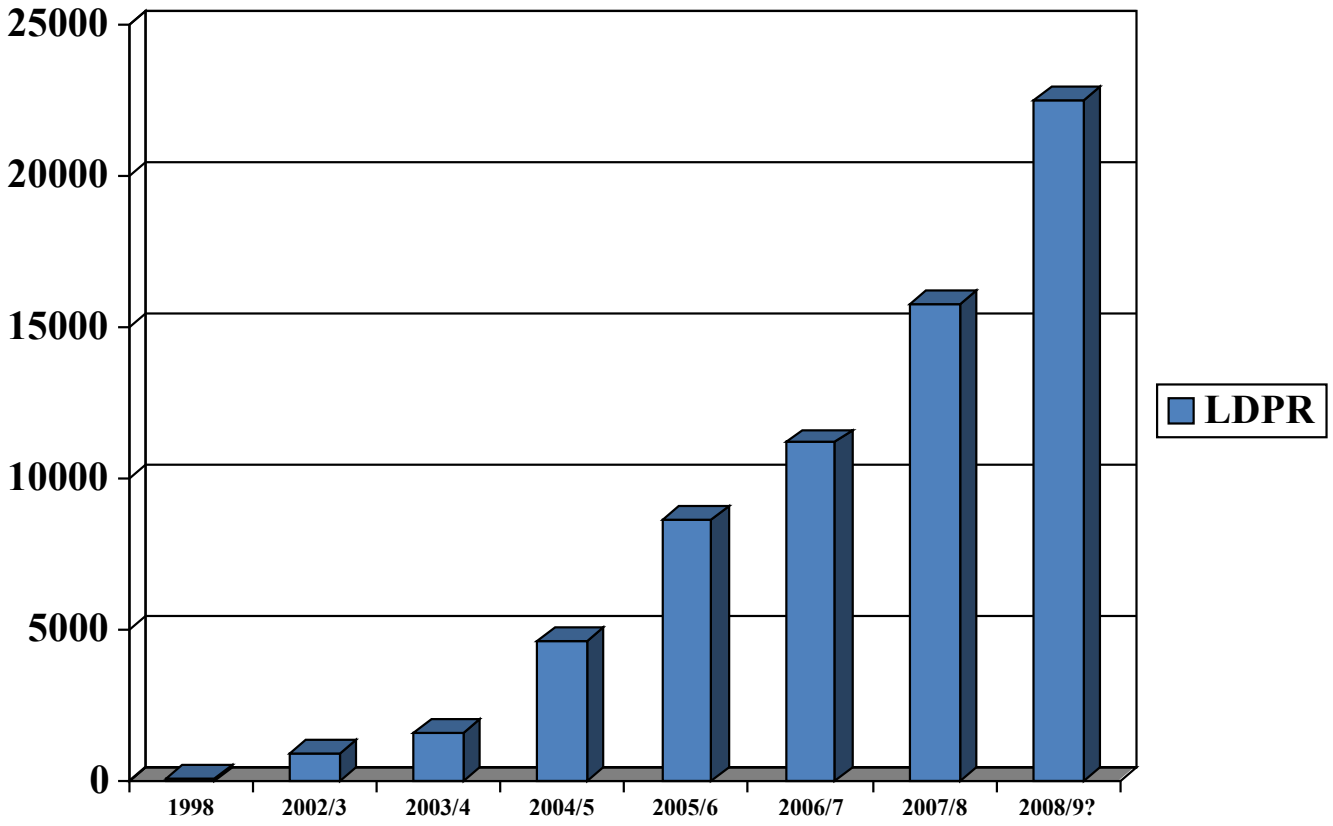


EIS model was a ‘best guess’ in 2001.

Progenitor service, 1994- : Birmingham.

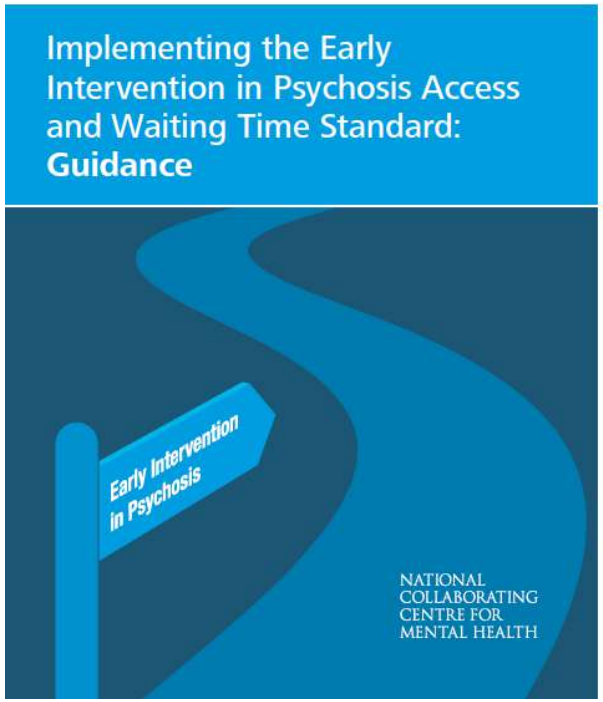
- Adapted ACT model
- 1:15 case ratio
- 3 years
- Emphasis on psychosocial
  + vocation interventions
- Engagement in low stigma channels
- Youth sensitive and youth co-designed

EI provision across England



NICE National Institute for Health and Care Excellence

NHS England

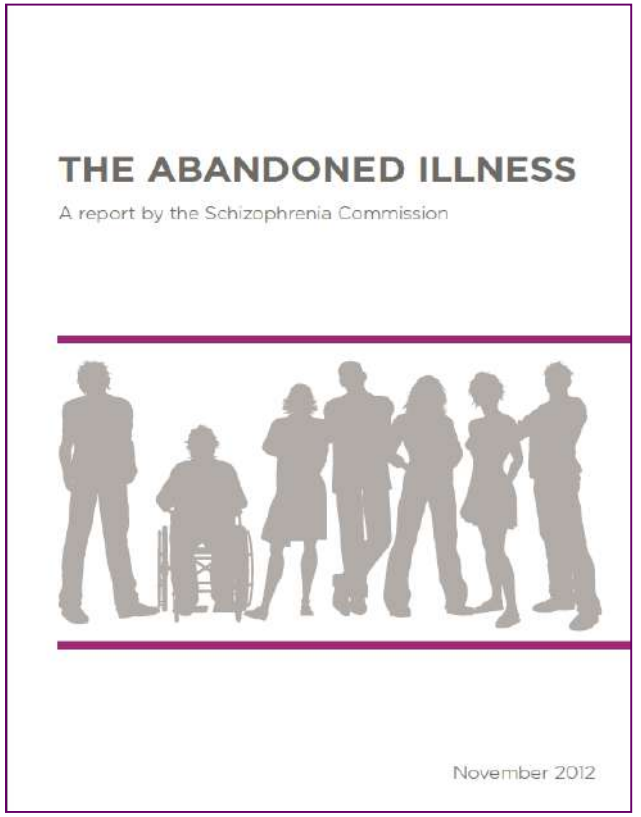


2 teams 24 teams 41teams 109 teams 127 teams 160 teams 145services

Early intervention is crucial to improving outcomes. The Commission's view is that Early Intervention in Psychosis (EIP) has been the most positive development in mental health services since the beginning of community care.

We recommend that all Clinical Commissioning Groups commission Early Intervention in Psychosis services with sufficient resources to provide fidelity to the service model. It is crucial that the NHS Commissioning Board holds local commissioners to account for this and we recommend that early intervention services are included in the NHS Commissioning Outcomes Framework.

"We can be really proud of our early intervention services which are popular and have been shown to work. Now we need to build on that success by extending the approach to cover the whole service."
Liz Meek, Member of the Commission



The Abandoned Illness
The Schizophrenia Commission, Nov 2012

www.schizophreniacommission.org.uk
Chair: Prof Sir Robin Murray

Phase 2: Trials

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.

Editorial page 545
Supplemental content

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Published online May 2, 2018.

The Lambeth Early Onset (LEO) Team: randomised controlled trial of the effectiveness of specialised care for early psychosis

Tom K J Craig, Philippa Garety, Paddy Power, Nikola Rahaman, Susannah Colbert, Miriam Fornells-Ambrojo, Graham Dunn

Abstract

Objective To evaluate the effectiveness of a service for early psychosis.
Design Randomised controlled clinical trial.
Setting Community mental health teams in one London borough.
Participants 144 people aged 16-40 years presenting to mental health services for the first or second time with non-organic, non-affective psychosis.
Interventions Assertive outreach with evidence based biopsychosocial interventions (specialised care group) and standard care (control group) delivered by community mental health teams.
Primary outcome measures Rates of relapse and readmission to hospital.
Results Compared with patients in the standard care group, those in the specialised care group were less likely to relapse (odds ratio 0.46, 95% confidence interval 0.22 to 0.97), were readmitted fewer times (β 0.39, 0.10 to 0.68), and were less likely to drop out of the study (odds ratio 0.35, 0.15 to 0.81). When rates were adjusted for sex, previous psychotic episode, and ethnicity, the difference in relapse was no longer significant (odds ratio 0.55, 0.24 to 1.26); only total number of readmissions (β 0.36, 0.04 to 0.66) and dropout rates (β 0.28, 0.12 to 0.73) remained significant.
Conclusions Limited evidence shows that a team delivering specialised care for patients with early psychosis is superior to standard care for maintaining contact with professionals and for reducing readmissions to hospital. No firm conclusions can, however, be drawn owing to the modest sample size.

We investigated whether a specialist team could achieve better outcomes for people with early non-affective psychotic disorders than existing services. We hypothesised that, over an 18 month period, people receiving specialised care would have more frequent contact with mental health services, fewer relapses, and fewer readmissions to hospital than patients receiving standard care.

Methods

We considered all people aged 16-40 years living in the London borough of Lambeth and presenting to mental health services for the first time with non-affective psychosis (schizophrenia, schizotypal, and delusional disorders, F20-29; international classification of diseases, 10th revision). We also considered people who had presented once but had subsequently disengaged without treatment from routine community services. We excluded those with organic psychosis or a primary alcohol or drug addiction. Non-English speakers were not excluded, but we did exclude asylum seekers who were liable to enforced dispersal.

Lambeth is the seventh most deprived of the 376 local authority boroughs in England and Wales.[12] It has a sizeable population from ethnic minority groups and unemployment is around twice the national average (2001 census). Community mental health services are provided through five multiprofessional teams.

Interventions

Assertive outreach for early psychosis

The Lambeth Early Onset (LEO) Team is a community team comprising 10 members of staff (team leader, part time consultant psychiatrist, trainee psychiatrist, half time clinical psycholo-

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A randomised multicentre trial of integrated versus standard treatment for patients with a first episode of psychotic illness

Lone Petersen, Pia Jeppesen, Anne Thorup, Maj-Britt Abel, Johan Øhlenschlæger, Torben Østergaard Christensen, Gertrud Krarup, Per Jørgensen, Merete Nordentoft

Abstract

Objectives To evaluate the effects of integrated treatment for patients with a first episode of psychotic illness.
Design Randomised clinical trial.
Setting Copenhagen Hospital Corporation and Psychiatric Hospital Aarhus, Denmark.
Participants 547 patients with first episode of schizophrenia spectrum disorder.
Interventions Integrated treatment and standard treatment. The integrated treatment lasted for two years and consisted of assertive community treatment with programmes for family involvement and social skills training. Standard treatment offered contact with a community mental health centre.
Main outcome measures Psychotic and negative symptoms (each scored from 0 to a maximum of 5) at one and two years' follow-up.
Results At one year's follow-up, psychotic symptoms changed favourably to a mean of 1.09 (standard deviation 1.27) with an estimated mean difference between groups of −0.31 (95% confidence interval −0.55 to −0.07, $P = 0.02$) in favour of integrated treatment. Negative symptoms changed favourably with an estimated difference between groups of −0.36 (−0.54 to −0.17, $P < 0.001$) in favour of integrated treatment. At two years' follow-up the estimated mean difference between groups in psychotic symptoms was −0.32 (−0.58 to −0.06, $P = 0.02$) and in negative symptoms was −0.45 (−0.67 to −0.22, $P < 0.001$), both in favour of integrated treatment. Patients who received integrated treatment had significantly less comorbid substance misuse, better adherence to treatment, and more satisfaction with treatment.
Conclusion Integrated treatment improved clinical outcome and adherence to treatment. The improvement in clinical outcome was consistent at one year and two year follow-ups.

patients who had experienced a first episode of psychosis? The null hypothesis investigated was that there would be no differences between integrated treatment and standard treatment with regard to psychotic and negative symptoms, treatment adherence, admissions, use of bed days, substance abuse, accommodation status, labour market affiliation, and user satisfaction.

Participants and methods

Patients

Patients were included from all inpatient and outpatient mental health services in Copenhagen (Copenhagen Hospital Corporation) and Aarhus County. From January 1998 until December 2000, 547 patients aged 18-45 years with a diagnosis in the schizophrenia spectrum (ICD-10 codes in the F2 category) and who had not been given antipsychotic drugs for more than 12 weeks of continuous treatment were included in the trial.

Randomisation

The included patients were centrally randomised to integrated treatment or standard treatment. In Copenhagen, randomisation was carried out through centralised telephone randomisation at the Copenhagen Trial Unit. The allocation sequence was computer generated, 1:1, in blocks of six, and stratified for each of five centres. In Aarhus, the researchers contacted a secretary by telephone when they had finished the entry assessment of each patient. The secretary then drew one lot from among five red and five white lots out of a black box. When the block of 10 was used, the lots were redrawn. Block sizes were unknown to the investigators.

Interventions

The trial was pragmatic, comparing integrated treatment defined by a set of protocols with treatment as usual.[5]

Feasibility and Effectiveness of a Multi-Element Psychosocial Intervention for First-Episode Psychosis: Results From the Cluster-Randomized Controlled GET UP PIANO Trial in a Catchment Area of 10 Million Inhabitants

Mirella Ruggeri[w,1,2], Chiara Bonetto[1], Antonio Lasalvia[1,2], Angelo Fioritti[3], Giovanni de Girolamo[4], Paolo Santonastaso[5], Francesca Pileggi[3], Giovanni Neri[6,7], Daniela Ghigi[8], Franco Giubilini[9], Maurizio Miceli[10], Silvio Searone[11], Angelo Cocchi[12], Stefano Torresani[13], Carlo Faravelli[14], Carla Cremonese[15], Paolo Scocco[16], Emanuela Leuci[9], Fausto Mazzi[17], Michela Pratelli[8], Francesca Bellini[8], Sarah Tosato[1,2], Katia De Santi[1,2], Sarah Bissoli[1], Sara Poli[1], Elisa Ira[1], Silvia Zoppei[1], Paola Rucci[3,7], Laura Bislenghi[12], Giovanni Patelli[12], Doriana Cristofalo[1], Anna Meneghelli[12], and The GET UP Group[18]

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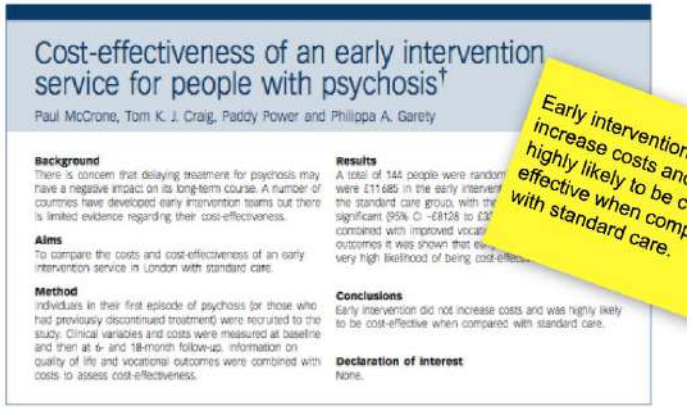
Cost Economic Data: EI vs Standard CMHT Care



Cost-effectiveness of an early intervention service for people with psychosis†

Paul McCrone, Tom K. J. Craig, Paddy Power and Philippa A. Garety

Background
There is concern that delaying treatment for psychosis may have a negative impact on its long-term course. A number of countries have developed early intervention teams but there is limited evidence regarding their cost-effectiveness.

Aims
To compare the costs and cost-effectiveness of an early intervention service in London with standard care.

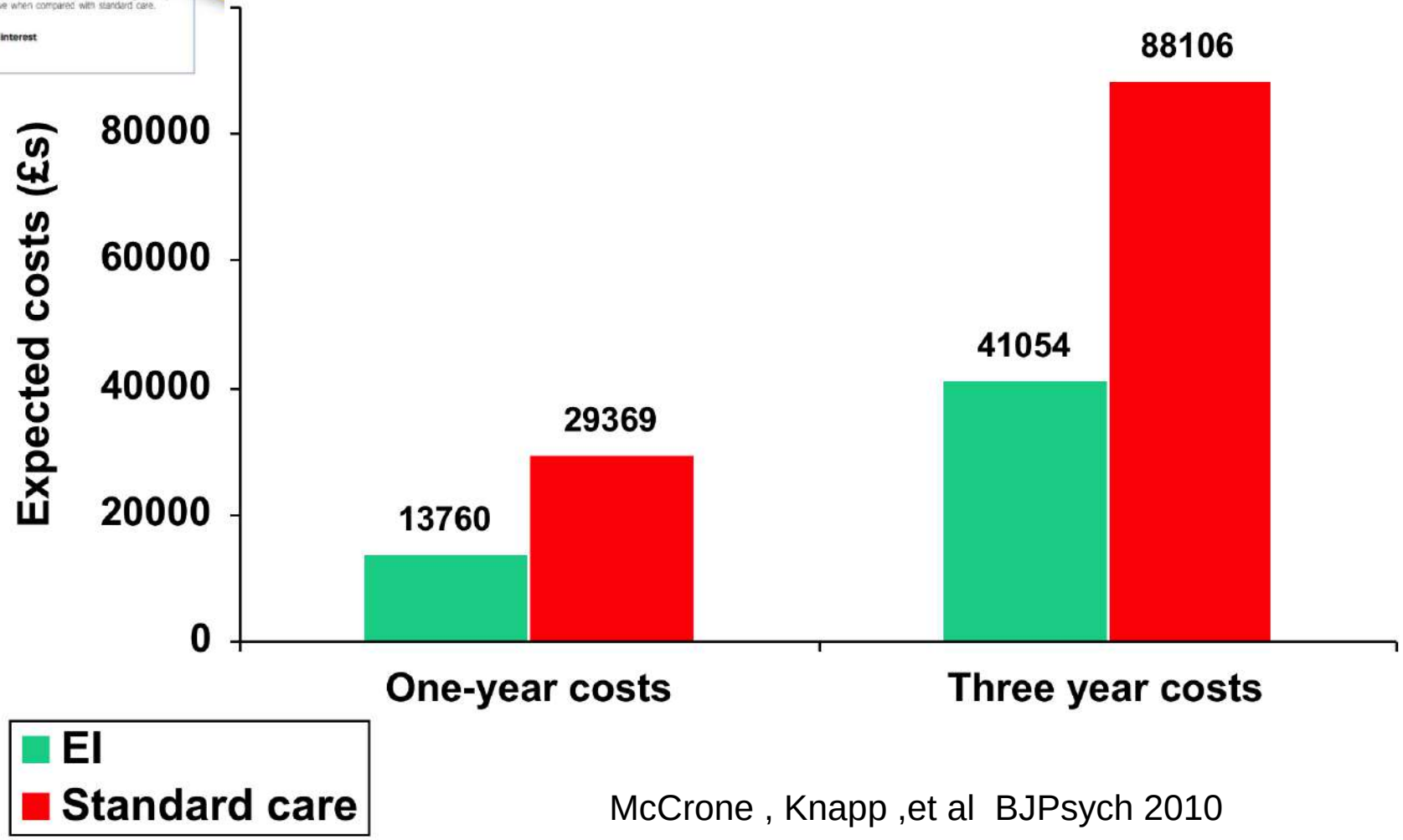
Method
Individuals in their first episode of psychosis (or those who had previously discontinued treatment) were recruited to the study. Clinical variables and costs were measured at baseline and then at 6- and 18-month follow-up. Information on quality of life and vocational outcomes were combined with costs to assess cost-effectiveness.

Results
A total of 144 people were random
were £11 685 in the early intervent
the standard care group, with the
significant (95% CI −£8128 to £3
combined with improved vocati
outcomes it was shown that ea
very high likelihood of being cost-effect

Conclusions
Early intervention did not increase costs and was highly likely to be cost-effective when compared with standard care.

Declaration of interest
None.

Early intervention
increase costs an
highly likely to be c
effective when comp
with standard care.



McCrone , Knapp ,et al BJPsych 2010

Early intervention teams most effective when DUP is low

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

John M. Kane, M.D., Delbert G. Robinson, M.D., Nina R. Schooler, Ph.D., Kim T. Mueser, Ph.D., David L. Penn, Ph.D., Robert A. Rosenheck, M.D., Jean Addington, Ph.D., Mary F. Brunette, M.D., Christoph U. Correll, M.D., Sue E. Estroff, Ph.D., Patricia Marcy, B.S.N., James Robinson, M.Ed., Piper S. Meyer-Kalos, Ph.D., L.P., Jennifer D. Gottlieb, Ph.D., Shirley M. Glynn, Ph.D., David W. Lynde, M.S.W., Ronny Pipes, M.A., L.P.C.-S., Benji T. Kurian, M.D., M.P.H., Alexander L. Miller, M.D., Susan T. Azrin, Ph.D., Amy B. Goldstein, Ph.D., Joanne B. Severe, M.S., Haiqun Lin, M.D., Ph.D., Kyaw J. Sint, M.P.H., Majnu John, Ph.D., Robert K. Heinssen, Ph.D., A.B.P.P.

Objective: The primary aim of this study was to compare the impact of NAVIGATE, a comprehensive, multidisciplinary, team-based treatment approach for first-episode psychosis designed for implementation in the U.S. health care system, with community care on quality of life.

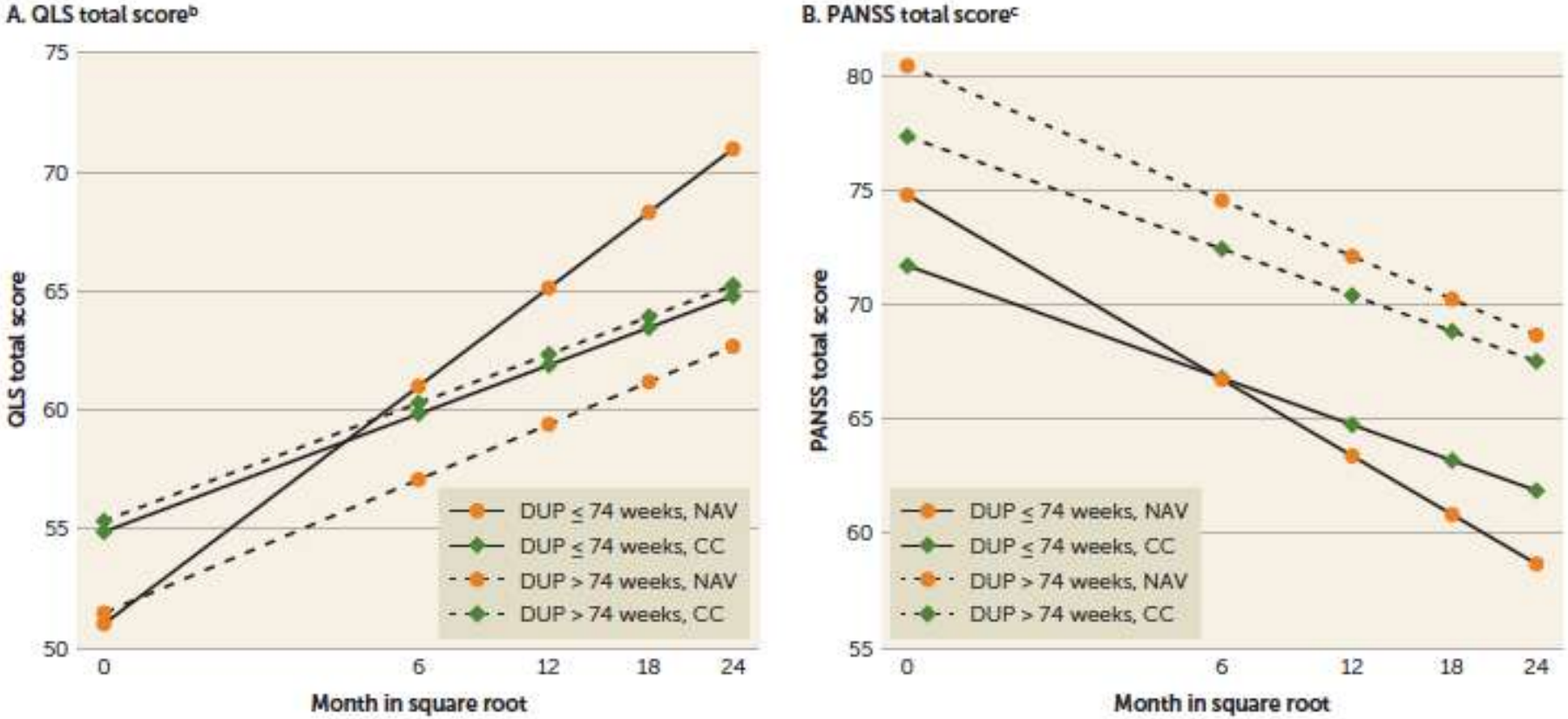
Method: Thirty-four clinics in 21 states were randomly assigned to NAVIGATE or community care. Diagnosis, duration of untreated psychosis, and clinical outcomes were assessed via live, two-way video by remote, centralized raters masked to study design and treatment. Participants (mean age, 23) with schizophrenia and related disorders and ≤6 months of antipsychotic treatment (N=404) were enrolled and followed for ≥2 years. The primary outcome was the total score of the Heinrichs-Carpenter Quality of Life Scale, a measure that includes sense of purpose, motivation, emotional and social interactions, role functioning, and engagement in regular activities.

Results: The 223 recipients of NAVIGATE remained in treatment longer, experienced greater improvement in quality of life and psychopathology, and experienced greater involvement in work and school compared with 181 participants in community care. The median duration of untreated psychosis was 74 weeks. NAVIGATE participants with duration of untreated psychosis of <74 weeks had greater improvement in quality of life and psychopathology compared with those with longer duration of untreated psychosis and those in community care. Rates of hospitalization were relatively low compared with other first-episode psychosis clinical trials and did not differ between groups.

Conclusions: Comprehensive care for first-episode psychosis can be implemented in U.S. community clinics and improves functional and clinical outcomes. Effects are more pronounced for those with shorter duration of untreated psychosis.

Am J Psychiatry 2016; 173:362–372; doi: 10.1176/appi.ajp.2015.15050632

FIGURE 3. Heinrichs-Carpenter Quality of Life (QLS) Total Score and PANSS Total Score: Effects of Shorter or Longer Duration of Untreated Psychosis (DUP) Based on a Model With Square Root Transformation of Months[a]



[a] In the model, DUP and DUP by square root of time by treatment terms were included as covariates in addition to the covariates listed in Table 2. The DUP by square root of time term was found not to be significant for either outcome. PANSS=Positive and Negative Syndrome Scale; CC=Community Care; NAV=NAVIGATE.

[b] DUP by treatment by square root of time interaction, $p=0.003$.

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

Are gains from intensive early intervention maintained?

ORIGINAL ARTICLE

Five-Year Follow-up of a Randomized Multicenter Trial of Intensive Early Intervention vs Standard Treatment for Patients With a First Episode of Psychotic Illness

The OPUS Trial

Mette Bertelsen, MSc; Pia Jeppesen, MD, PhD; Lone Petersen, PhD; Anne Thorup, MD, PhD; Johan Øhlenschlæger, MD, PhD; Phuong le Quach, MD; Torben Østergaard Christensen, PhD; Gertrud Krarup, MD; Per Jørgensen, MD; Merete Nordentoft, MD, PhD, MPH

Table 5. Remission and Relapse During Last 2 Years Before 5-Year Follow-up[a]

	5-Year Follow-up, No. (%)		
	Intensive Early-Intervention Program (n=151)	Standard Treatment (n=150)	Differences in Percentages (95% CI)
Episodic course of illness[b]	21 (14)	19 (13)	–2 (–0.06 to 0.1)
Continuous course of illness[c]	67 (45)	65 (44)	–2 (–0.12 to 0.1)
Not psychotic[d]	62 (41)	64 (43)	2 (–0.13 to 0.09)

Abbreviation: CI, confidence interval

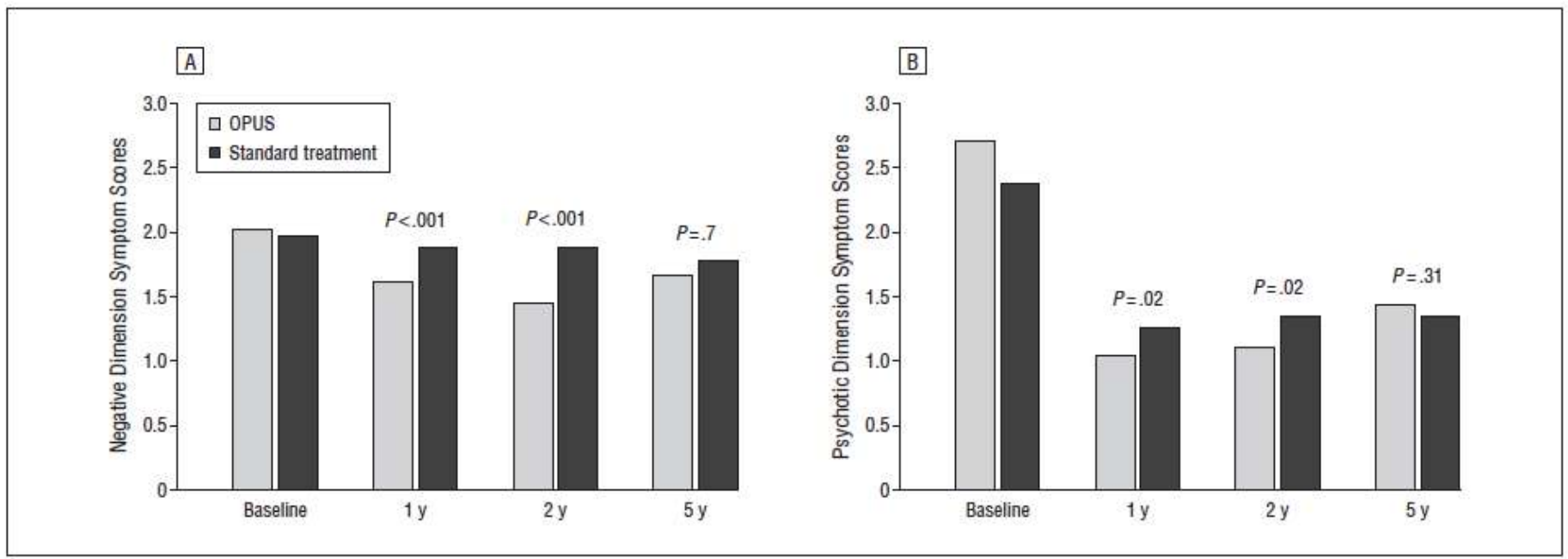


Figure 2. Mean symptom values for patients in the intensive early-intervention program (OPUS) vs standard treatment, according to the Scale for Assessment of Psychotic Symptoms and Scale for Assessment of Negative Symptoms[25] at baseline, 2-year follow-up, and 5-year follow-up for the negative (A) and psychotic (B) dimensions. Values range from 0 to 5.

How do we maintain gains from early intervention?

RESEARCH REPORT

Comparing three-year extension of early intervention service to regular care following two years of early intervention service in first-episode psychosis: a randomized single blind clinical trial

Ashok Malla[1,2], Ridha Joober[1,2], Srividya Iyer[1,2], Ross Norman[3], Norbert Schmitz[1,4], Thomas Brown[1,4], Danyael Lutgens[1,2], Eric Jarvis[1,5], Howard C. Margolese[1,6], Nicola Casacalenda[1,5], Amal Abdel-Baki[7], Eric Latimer[1,4], Sally Mustafa[2], Sherezad Abadi[2]

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This study aimed to determine if, following two years of early intervention service for first-episode psychosis, three-year extension of that service was superior to three years of regular care. We conducted a randomized single blind clinical trial using an urn randomization balanced for gender and substance abuse. Participants were recruited from early intervention service clinics in Montreal. Patients (N=220), 18-35 years old, were randomized to an extension of early intervention service (EEIS; N=110) or to regular care (N=110). EEIS included case management, family intervention, cognitive behaviour therapy and crisis intervention, while regular care involved transfer to primary (community health and social services and family physicians) or secondary care (psychiatric outpatient clinics). Cumulative length of positive and negative symptom remission was the primary outcome measure. EEIS patients had a significantly longer mean length of remission of positive symptoms (92.5 vs. 63.6 weeks, $t=4.47$, $p<0.001$), negative symptoms (73.4 vs. 59.6 weeks, $t=2.84$, $p=0.005$) and both positive and negative symptoms (66.5 vs. 56.7 weeks, $t=2.25$, $p=0.03$) compared to regular care patients. EEIS patients stayed in treatment longer than regular care patients (mean 131.7 vs. 105.3 weeks, $t=3.98$, $p<0.001$ through contact with physicians; 134.8 ± 37.7 vs. 89.8 ± 55.2, $t=6.45$, $p<0.0001$ through contact with other health care providers) and received more units of treatment (mean 74.9 vs. 39.9, $t=4.21$, $p<0.001$ from physicians, and 57.3 vs. 28.2, $t=4.08$, $p<0.001$ from other health care professionals). Length of treatment had an independent effect on the length of remission of positive symptoms ($t=2.62$, $p=0.009$), while number of units of treatment by any health care provider had an effect on length of remission of negative symptoms ($t=-2.70$, $p=0.008$) as well as total symptoms ($t=-2.40$, $p=0.02$). Post-hoc analysis showed that patients randomized to primary care, based on their better clinical profile at randomization, maintained their better outcome, especially as to remission of negative symptoms, at the end of the study. These data suggest that extending early intervention service for three additional years has a positive impact on length of remission of positive and negative symptoms compared to regular care. This may have policy implications for extending early intervention services beyond the current two years.

Key words: First-episode psychosis, extension of early intervention service, regular care, positive symptoms, negative symptoms, outcome, remission

(World Psychiatry 2017;16:278–286)

Impact of extended EIP?

- Patients in the E-EIP: remission of positive symptoms for ~50% longer period than CMHT care (mean 92.5 vs. 63.6 weeks, standardized beta 50.34, t=54.47, p<0.001).

- Extending EIP for three additional years has a positive impact on length of remission of positive and negative symptoms compared to regular care.

- NB. Not differentiated by need. ‘Maintenance dose’?

How does it work?: More interventions delivered

Table 2 Clinical care received during follow-up

	Number of interventions (mean ± SD)		Length of treatment (weeks, mean ± SD)	
	EEIS	**Regular care**	**EEIS**	**Regular care**
Physicians	74.9 ± 43.6*	39.9 ± 69.1	131.7 ± 37.4*	105.3 ± 51.5
Other health care providers	57.3 ± 37.3*	28.2 ± 59.6	134.8 ± 37.7**	89.8 ± 55.2

EEIS – extended early intervention service

*p<0.001, **p<0.0001

How does it work?: Better satisfaction, more engagement

Received: 6 January 2020 | Revised: 15 April 2020 | Accepted: 24 May 2020
DOI: 10.1111/eip.13004

BRIEF REPORT

WILEY

Patient satisfaction with random assignment to extended early intervention for psychosis vs regular care: Relationship with service engagement

Srividya N. Iyer[1,2] | Sally S. Mustafa[2] | Sherezad Abadi[3] | Ridha Joober[1,2] | Amal Abdel-Baki[4] | Eric Jarvis[1,5] | Eric Latimer[1,3] | Howard C. Margolese[1,6] | Nicola Casacalenda[1,7] | Norbert Schmitz[1,3] | Thomas Brown[1,3] | Ashok Malla[1,2]

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[2]Prevention and Early Intervention Program for Psychosis (PEPP), Douglas Mental Health University Institute, Quebec, Canada
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[4]Department of Psychiatry, University of Montreal, Centre hospitalier de l'Université de Montréal, Quebec, Canada
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Correspondence
Srividya N. Iyer, PhD, Douglas Mental Health University Institute, 6875 boulevard LaSalle, Montréal, QC, Canada H4H 1R3.
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Funding information
The project was funded by the Canadian Institutes of Health Research, Grant/Award Numbers: MCT 94189, CCT-NAPN-18590; Ashok Malla is funded by the Canada Research Chairs Program; Srividya N. Iyer has received salary awards from Fonds de recherche du Québec – Santé (FRQS) and the Canadian Institutes of Health Research (CIHR)

Abstract

Aim: We investigated whether individuals varied in their satisfaction with being randomized to an extension of early intervention (EI) for psychosis or regular care after 2 years of EI, and whether satisfaction was associated with service engagement 3 years later.

Methods: Following randomization, patients (N = 220) indicated if they were happy with, unhappy or indifferent to their group assignment. Follow-up with service providers was recorded monthly.

Results: Patients randomized to extended EI were more likely to express satisfaction with their group assignment than those in the regular care group (88.2% vs 31.5%, $\chi^2 = 49.96$, $P < .001$). In the extended EI group, those happy with their assigned group were likelier to continue seeing their case manager for the entire five-year period than those who were unhappy/indifferent ($\chi^2 = 5.61$, $P = .030$).

Conclusions: Perceptions about EI, indicated by satisfaction with being assigned to extended EI, may have lasting effects on service engagement.

KEYWORDS
early intervention services, engagement, first-episode psychosis, randomization, satisfaction

Acta Psychiatrica Scandinavica

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DOI: 10.1111/acps.13083

ACTA PSYCHIATRICA SCANDINAVICA

Short duration of untreated psychosis enhances negative symptom remission in extended early intervention service for psychosis

Dama M, Shah J, Norman R, Iyer S, Joober R, Schmitz N, Abdel-Baki A, Malla A. Short duration of untreated psychosis enhances negative symptom remission in extended early intervention service for psychosis

Objective: To test whether duration of untreated psychosis (DUP) < 3 months, recommended by the World Health Organization/ International Early Psychosis Association, enhances the effects of an extended early intervention service (EEIS) on symptom remission.
Method: We examined data from a randomized controlled trial in which patients who received 2 years of treatment in EIS for psychosis were subsequently randomized to either 3 years of EEIS or 3 years of regular care (RC). Using a DUP cut-off ≤ 12 weeks (approximately < 3 months), patients were split into two groups. Length of positive, negative and total symptom remission were the outcomes.
Results: Patients ($N = 217$) were mostly male (68%) with schizophrenia spectrum disorder (65%); 108 (50%) received EEIS (58 had DUP ≤12 weeks; 50 had DUP >12 weeks). Interaction between treatment condition (EEIS vs. RC) and DUP cut-off ≤ 12 weeks was only significant in multiple linear regression model examining length of negative symptom remission as the outcome (adjusted $\beta = 36.88$ [SE = 15.88], $t = 2.32$, $P = 0.02$). EEIS patients with DUP ≤12 weeks achieved 25 more weeks of negative symptom remission than EEIS patients with DUP >12 weeks.
Conclusion: Having a short DUP may be critical in deriving long-term benefits from EIS for psychosis, including EEIS settings. This work empirically supports policy recommendations of reducing DUP <3 months.

M. Dama[1], J. Shah[2], R. Norman[3], S. Iyer[2], R. Joober[2], N. Schmitz[2], A. Abdel-Baki[4], A. Malla[2]

[1]Prevention and Early Intervention Program for Psychosis (PEPP-Montreal), Douglas Mental Health University Institute, Montreal, QC, Canada, [2]Department of Psychiatry, McGill University, Montreal, QC, Canada, [3]Departments of Psychiatry and Epidemiology & Biostatistics, Western University, London, ON, and [4]Department of Psychiatry, Universite de Montreal, Montreal, QC, Canada

Key words: psychotic disorders; schizophrenia; young adult; early intervention; health services accessibility

Ashok Malla, ACCESS Open Minds, 6625 Blvd Lasalle, Montréal, QC H4H 1R3, Canada. E-mail: ashok.malla@mcgill.ca

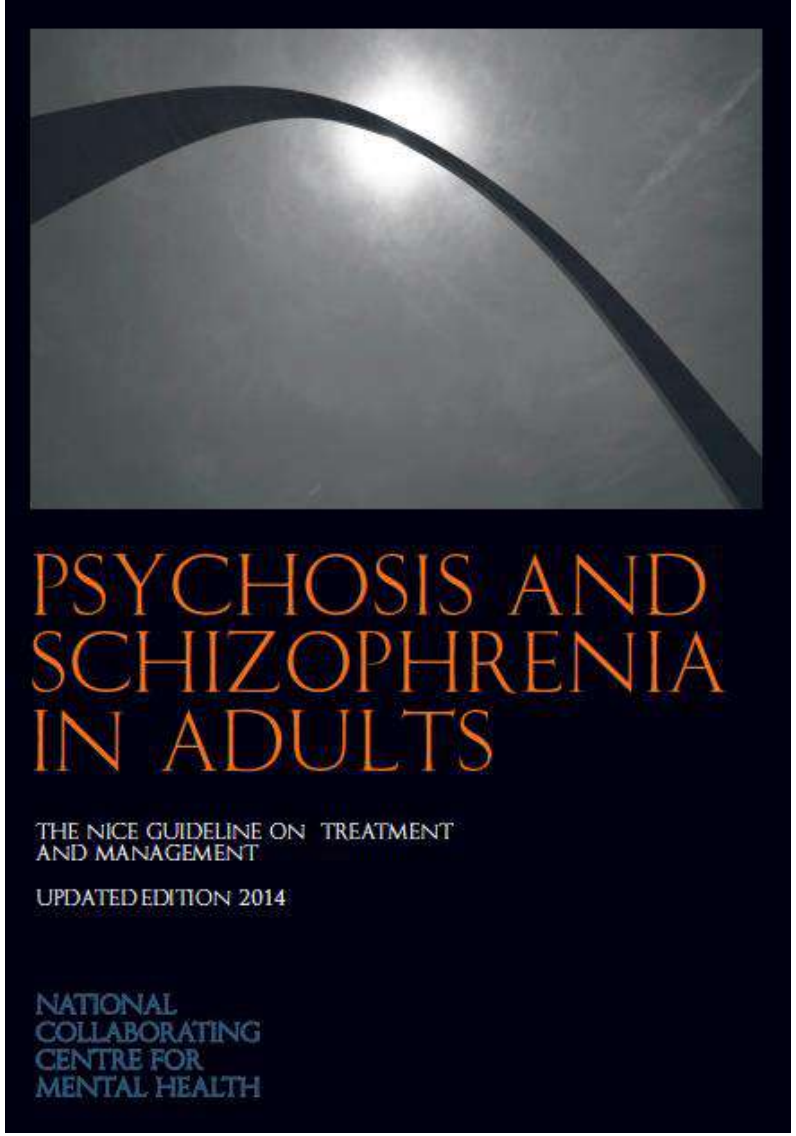
Trial registration: ISRCTN Registry, ISRCTN11889876

Accepted for publication April 3, 2019

Significant outcomes

- Having a short DUP of 12 weeks or less may increase the length of negative symptom remission by 25 more weeks among patients receiving treatment in an extended early intervention service for psychosis
- These results are independent of known confounds including the age at onset of psychosis, premorbid functioning, having a diagnosis of schizophrenia spectrum disorder and the severity of negative symptoms at the time of randomization
- This work provides important empirical support for the World Health Organization and International Early Psychosis Association's recommendation of having a DUP of less than 3 months in early intervention services for psychosis

BUT, it won't work well if DUP is long



14.3 FIRST EPISODE PSYCHOSIS

14.3.1 Early intervention in psychosis services

14.3.1.1 Early intervention in psychosis services should be accessible to all people with a first episode or first presentation of psychosis, irrespective of the person's age or the duration of untreated psychosis. [new 2014]

14.3.1.2 People presenting to early intervention in psychosis services should be assessed without delay. If the service cannot provide urgent intervention for people in a crisis, refer the person to a crisis resolution and home treatment team (with support from early intervention in psychosis services). Referral may be from primary or secondary care (including other community services) or a self- or carer-referral. [new 2014]

14.3.1.3 Early intervention in psychosis services should aim to provide a full range of pharmacological, psychological, social, occupational and educational interventions for people with psychosis, consistent with this guideline. [2014]

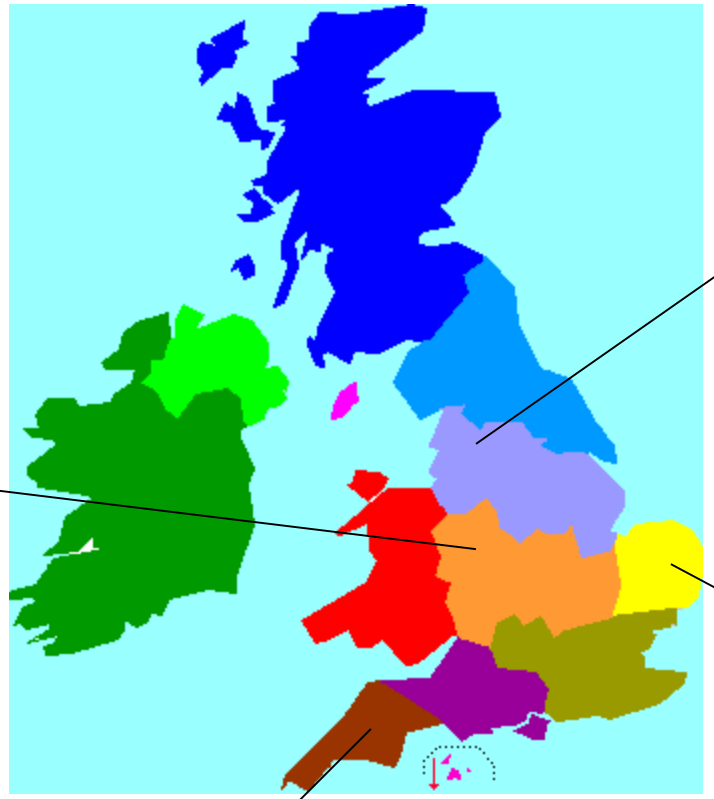
14.3.1.4 Consider extending the availability of early intervention in psychosis services beyond 3 years if the person has not made a stable recovery from psychosis or schizophrenia. [new 2014]

Phase 3: Implementation studies: DUP; EIP ‘non-responders’; fidelity and cost-effectiveness.

The National/SUPER EDEN sites

Lancashire + Wirral
5 teams
(Marshall/Lewis/Sharma)

Birmingham
5 teams
(Birchwood/Lester)



East Anglia
4 teams
(Jones/Fowler)

Cornwall 2 teams
(Amos/Harrison)

Schizophrenia Research 159 (2014) 1–6

Contents lists available at ScienceDirect

Schizophrenia Research

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

Impact of early intervention services on duration of untreated psychosis: Data from the National EDEN prospective cohort study

Max Marshall [a,*], Nusrat Husain [a], Natalie Bork [a], Imran B. Chaudhry [a], Helen Lester [b], Linda Everard [b], Swaran P. Singh [c], Nick Freemantle [d], Vimal Sharma [e], Peter B. Jones [f], David Fowler [g], Tim Amos [h], Barbara Tomenson [a], Max Birchwood [b]

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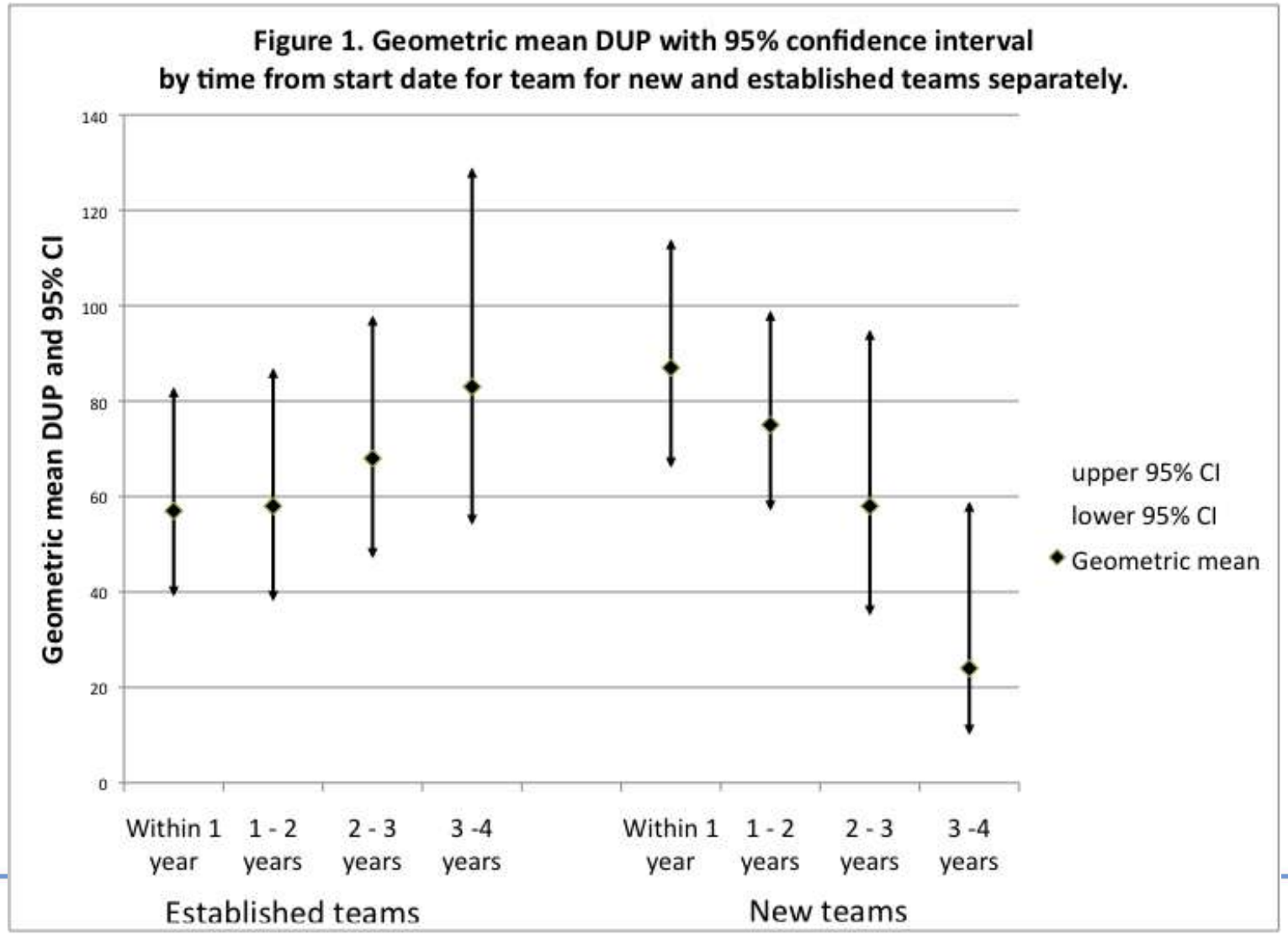
[f] Department of Psychiatry, University of Cambridge, Cambridge, United Kingdom
[g] School of Medicine, University of East Anglia, United Kingdom
[h] Academic Unit of Psychiatry, University of Bristol, Bristol, United Kingdom



Marshall, Birchwood et al Schiz Res, 2014

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.

Introduction

Prolonged duration of untreated psychosis (DUP) predicts worse symptoms of all types and poorer social functioning and quality of life for 2 years[1–3] after presentation or longer.[4,5] Earlier detection improved outcomes in the quasi-experimental TIPS study,[6] as did introduction of specialist early intervention services,[7,8] spurring introduction of early treatment services worldwide. Yet the mechanism by which delayed treatment might cause harm remains unclear. Evidence of direct neurotoxicity is inconsistent.[9,10,11]

Symptoms could simply accumulate over time, worsening presentation. In the TIPS trial, for patients in the control areas that had longer DUP, psychosis and excitement were increased only at presentation, while depression and disorganisation were worse only at follow-up, in proportion to their greater severity at presentation. Additionally, if exacerbation of one symptom worsens others, depending on which symptoms are primary, early monotherapy with antipsychotics, antidepressants, or lithium might mitigate a range of later problems.

DUP and outcome might be associated only via some unmeasured patient characteristic or residual

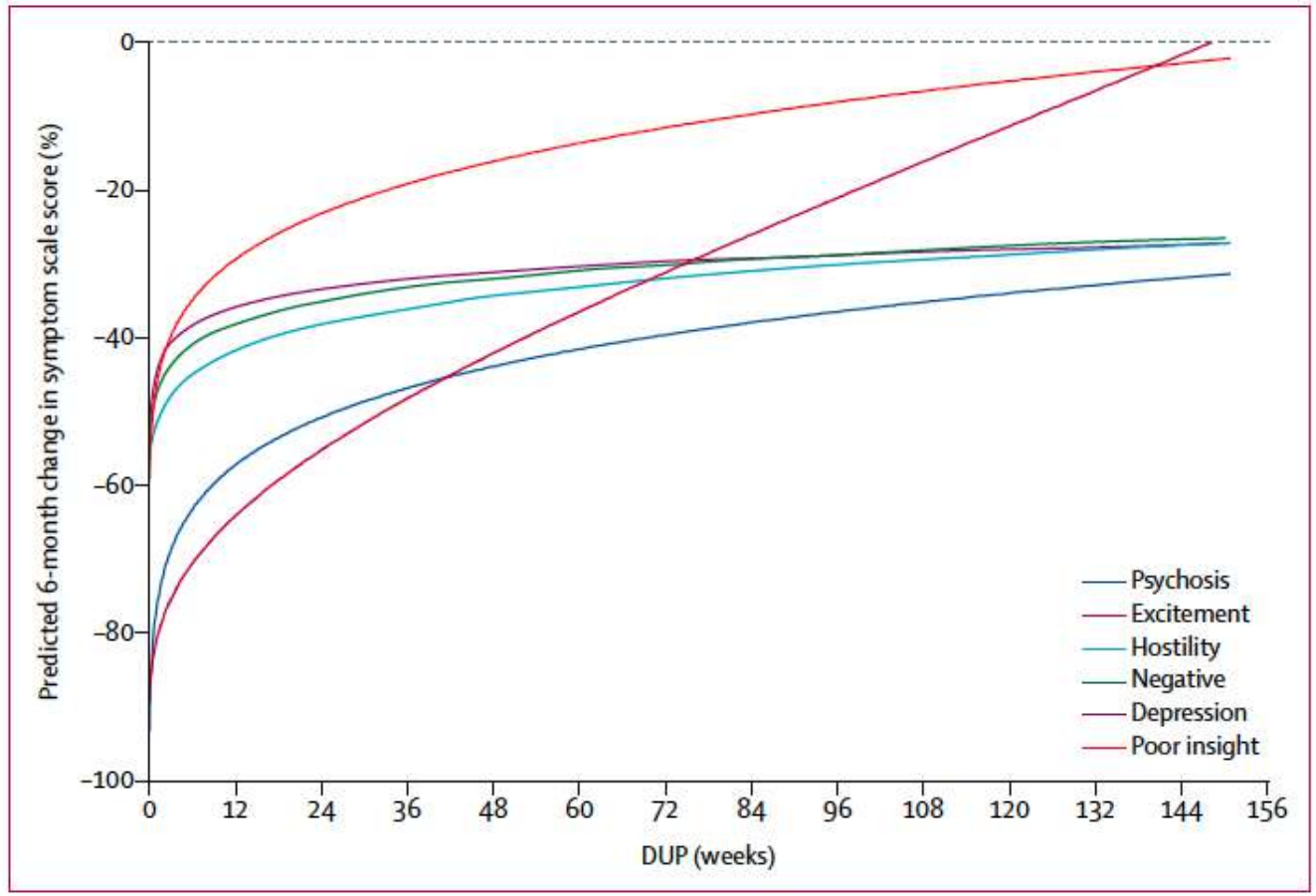


Figure 2: **Predicted change in untransformed symptom scale scores over 6 months as a proportion of baseline, against DUP**

Symptom change was calculated from natural log-transformed scores adjusted for centre, drug use, and demographics. Only the first 3 years of DUP are shown. DUP=duration of untreated psychosis.

DUP: 2 key messages

- Harm incurred by treatment delay is greatest in the early weeks of psychosis
- The effect size for a ten-times increase in DUP appeared comparable to that for placebo versus antipsychotic implying that: this increase in the delay before receiving treatment predicts a difference in symptoms comparable to placebo versus antipsychotics.

DUP in UK (the National EDEN study)

Table 4
Duration of untreated psychosis in days for each EIS.

	n	Min	Max	Median	Mean	95% CI for mean	Geometric mean	95% CI for geometric mean	Number and percentage of patients with DUP under 6 months
Established EIS									
Birmingham Central	66	0	2905	45	237	127 to 346	40	22 to 72	47 (71.2%)
Birmingham East	67	0	2022	141	296	195 to 398	85	51 to 142	37 (55.2%)
East Anglia Norfolk	146	0	5652	102	385	252 to 518	90	66 to 124	90 (61.6%)
CAMEO South	98	0	4748	47	257	130 to 384	43	28 to 66	72 (73.5%)
Wirral	27	0	3598	113	322	47 to 596	69	28 to 165	17 (63.0%)
West Cheshire	18	0	298	73	93	52 to 133	52	25 to 109	16 (88.9%)
East Cheshire	11	5	783	133	261	67 to 455	73	15 to 347	6 (54.5%)
All established teams	435	0	5652	77	300	240 to 361	64	53 to 78	285 (65.8%)
New EIS									
Lancashire	189	0	5435	146	438	333 to 544	133	103 to 173	100 (52.9%)
Birmingham BEN	98	0	4821	34	208	94 to 321	24	15 to 40	76 (77.6%)
Birmingham South	79	0	1900	141	307	217 to 397	100	66 to 154	43 (54.4%)
Norfolk Kings Lynn	11	0	1471	12	300	−18 to 617	15	1 to 157	7 (63.6%)
Solihull	31	3	2807	87	357	144 to 569	92	45 to 187	19 (61.3%)
CAMEO North	23	0	857	110	200	100 to 299	68	29 to 159	13 (56.5%)
Cornwall	122	0	6185	67	272	141 to 402	57	40 to 82	82 (67.2%)
All new teams	556	0	6185	89	325	271 to 378	72	60 to 86	340 (61.5%)
All teams	986	0	6185	82	314	274 to 354	68	60 to 78	625 (63.4%)

Still late intervention (DUP>6 months) for ~ 1/3

Why is DUP still so long?

Reducing duration of untreated psychosis: care pathways to early intervention in psychosis services

Max Birchwood, Charlotte Connor, Helen Lester, Paul Patterson, Nick Freemantle, Max Marshall, David Fowler, Shon Lewis, Peter Jones, Tim Amos, Linda Everard and Swaran Singh

Background
Interventions to reduce treatment delay in first-episode psychosis have met with mixed results. Systematic reviews highlight the need for greater understanding of delays within the care pathway if successful strategies are to be developed.

Aims
To document the care-pathway components of duration of untreated psychosis (DUP) and their link with delays in accessing specialised early intervention services (EIS). To model the likely impact on efforts to reduce DUP of targeted changes in the care pathway.

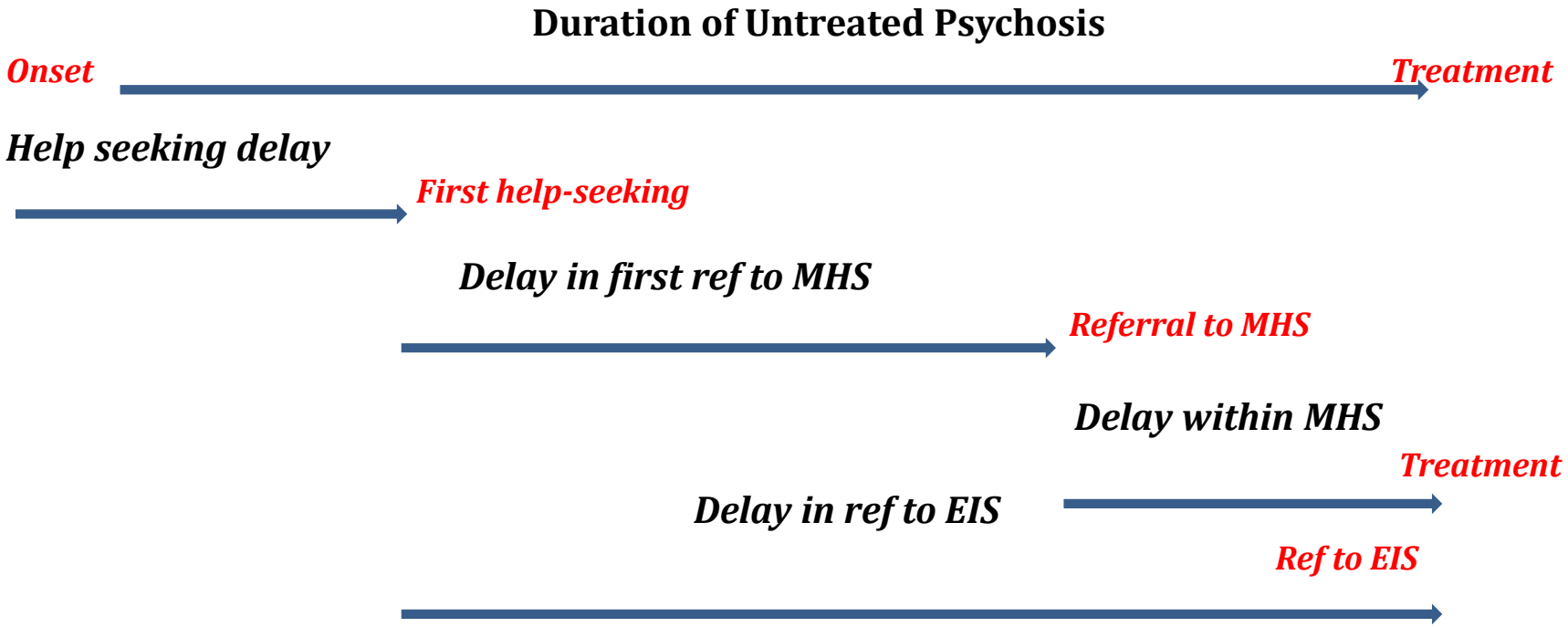
Method
Data for 343 individuals from the Birmingham, UK lead site of the National EDEN cohort study were analysed.

Results
One-third of the cohort had a DUP exceeding 6 months. The greatest contribution to DUP for the whole cohort came from delays within mental health services, followed by help-seeking delays. It was found that delay in reaching EIS was strongly correlated with longer DUP.

Conclusions
Community education and awareness campaigns to reduce DUP may be constrained by later delays within mental health services, especially access to EIS. Our methodology, based on analysis of care pathways, will have international application when devising strategies to reduce DUP.

Declarations of interest
None.

Duration of Untreated Psychosis – component delays



1/3 still have long DUP (> 6 months)

Table 1 Duration of untreated psychosis (DUP) and component delays

	DUP		Delay in help-seeking		Delay in referral to mental health services		Delay within mental health services		Delay reaching EIS (T_1) (first help-seeking to EIS acceptance)		Delay reaching EIS (T_2) (first mental health referral to EIS acceptance)	
	Mean (s.d.)	Median	Mean (s.d.)	Median	Mean (s.d.)	Median	Mean (s.d.)	Median	Mean (s.d.)	Median	Mean (s.d.)	Median
All patients ($n = 343$)	260.3 (472.5)	50	93.8 (274.1)	0.00	58.1 (228.9)	0.00	108.7 (308.9)	8	353.7 (607.0)	111	187.5 (353.4)	49
Patients with DUP <6 months ($n = 228$)	36.6 (44.7)	19	12.7 (27.9)	0.00	8.2 (55.32)	0.00	15.7 (28.2)	1	267.7 (493.1)	66.5	144.2 (246.9)	36
Patients with DUP >6 months ($n = 115$)	704.2 (603.3)	518	254.6 (429.7)	66	157.0 (375.9)	4	292.6 (482.1)	141	510.1 (760.1)	212	273.3 (492)	87

EIS, early intervention services.

1/3 still have long DUP (> 6 months)

Mostly accounted for by delays *within* mental health services

Table 1 Duration of untreated psychosis (DUP) and component delays

	DUP		Delay in help-seeking		Delay in referral to mental health services		Delay within mental health services		Delay reaching EIS (T_1) (first help-seeking to EIS acceptance)		Delay reaching EIS (T_2) (first mental health referral to EIS acceptance)	
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EIS, early intervention services.

Impact of the first mental health contact

CAMHS/CMHTs linked to longer DUP

Table 2 Delays associated with first mental health service contact

First mental health service contact	Mean (s.d.)		
	Delay within mental health services	Delay reaching early intervention services	Duration of untreated psychosis
Community mental health team ($n = 164$)	174.37 (411.04)	469.23 (727.76)	367.70 (579.41)
Child and adolescent mental health services ($n = 22$)	205.95 (326.58)	360.36 (376.23)	283.82 (334.63)
Home treatment team ($n = 84$)	21.52 (62.22)	173.30 (299.30)	129.05 (238.45)
Psychiatric hospital ($n = 43$)	36.25 (97.03)	313.79 (639.75)	166.82 (423.64)

Why does first contact with CMHT/CAMHS prolong DUP?

Premature discharge from CMHT common → lengthens DUP

Table 4 Community mental health team response, mental health service delay and duration of untreated psychosis

Outcome	Mental health service delay		Duration of untreated psychosis	
	Mean (s.d.)	Median	Mean (s.d.)	Median
Referred to home treatment team	92 (233.5)	13	306 (501.3)	68
Discharged	482.9 (784.8)	172	631 (848.7)	299
Referred to early intervention services	91 (139.7)	52	420 (508.1)	203

Why?
Delays access to EIS, which prolongs DUP

Table 1 Duration of untreated psychosis (DUP) and component delays

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EIS, early intervention services.

2 months or more after EIS acceptance. The delay in reaching criteria treatment within mental health services was strongly correlated ($r=0.68$, $P<0.001$) with delay in accessing EIS (T_2), following referral to mental health services when psychotic.

NICE National Institute for Health and Care Excellence

NHS England

Implementing the Early Intervention in Psychosis Access and Waiting Time Standard: **Guidance**

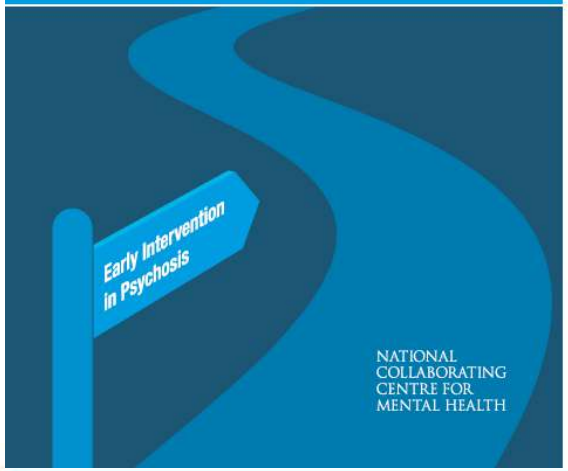


Table 5 Modelling the impact of reducing component delays on duration of untreated psychosis (DUP)

Delay	365 days	180 days	90 days	60 days	30 days
Delay in mental health services					
DUP					
Mean (s.d.)	220.9 (377.9)	198.6 (366.1)	183.8 (361.5)	175.3 (359.6)	167 (358.5)
Median	49	49	49	49	32
n (%) with DUP >6 months	115 (33.5)	115 (33.5)	115 (33.5)	78 (22.7)	74 (21.5)
Delay in help-seeking					
DUP					
Mean (s.d.)	223.5 (403.9)	204.6 (392.6)	191.1 (388.7)	184.2 (387.6)	177.0 (386.8)
Median	49	49	49	49	37
n (%) with DUP >6 months	115 (33.5)	115 (33.5)	93 (27)	89 (26)	83 (24)

Reducing treatment delay within mental health services and impact on DUP

Connor et al. BMC Psychiatry (2016) 16:127
DOI 10.1186/s12888-016-0816-7

BMC Psychiatry

RESEARCH ARTICLE Open Access

Don't turn your back on the symptoms of psychosis: the results of a proof-of-principle, quasi-experimental intervention to reduce duration of untreated psychosis

Charlotte Connor[1*], Max Birchwood[1], Nick Freemantle[2], Colin Palmer[1], Sunita Channa[1], Clare Barker[3], Paul Patterson[4] and Swaran Singh[1]

Abstract

Background: No evidence based approach to reduce duration of untreated psychosis (DUP) has been effective in the UK. Existing interventions have many components and have been difficult to replicate. The majority of DUP in Birmingham, UK is accounted for by delays within mental health services (MHS) followed by help-seeking delay and, we hypothesise, these require explicit targeting. This study examined the feasibility and impact of an intervention to reduce DUP, targeting help-seeking and MHSs delays.

Methods: A dual-component intervention, comprising a direct care pathway, for 16-25 year olds, and a community psychosis awareness campaign, using our youth-friendly website as the central hub, was implemented, targeting the primary sources of care pathway delays experienced by those with long DUP. Evaluation, using a quasi-experimental, design compared DUP of cases in two areas of the city receiving early detection vs detection as usual, controlling for baseline DUP in each area.

Results: DUP in the intervention area was reduced from a median 71 days (mean 285) to 39 days (mean 104) following the intervention, with no change in the control area. Relative risk for the reduction in DUP was 0.74 (95 % CI 0.35 to 0.89; $p = .004$). Delays in MHSs and help-seeking were also reduced.

Conclusions: Our targeted approach appears to be successful in reducing DUP and could provide a generalizable methodology applicable in a variety of healthcare contexts with differing sources of delay. More research is needed, however, to establish whether our approach is truly effective.

Trial registration: ISRCTN45058713 - 30 December 2012.

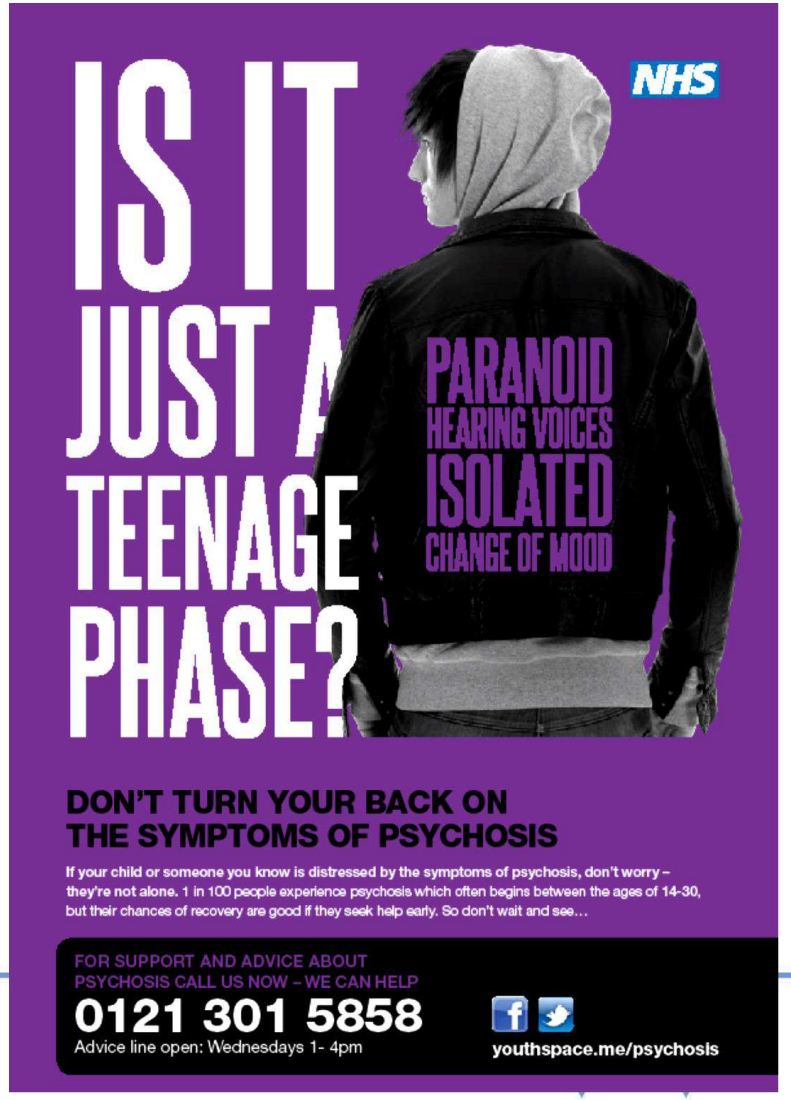


Table 5 DUP for EIS clients in intervention and control areas during trial (July 2011 – Dec 2013)

		Help-seeking delay	Delay within MHSs	Delay in reaching EIS	DUP	*N* = 151
Control area	Mean	**116.97**	**124.19**	162.30	**216.43**	74
	Median	11.50	21.00	44.00	79.50	
	St Dev	229.02	216.45	242.84	335.86	
Intervention area	Mean	**41.49**	**42.32**	130.57	**103.82**	77
	Median	1.50	6.50	40.50	39.00	
	St Dev	105.93	86.74	225.89	155.00	

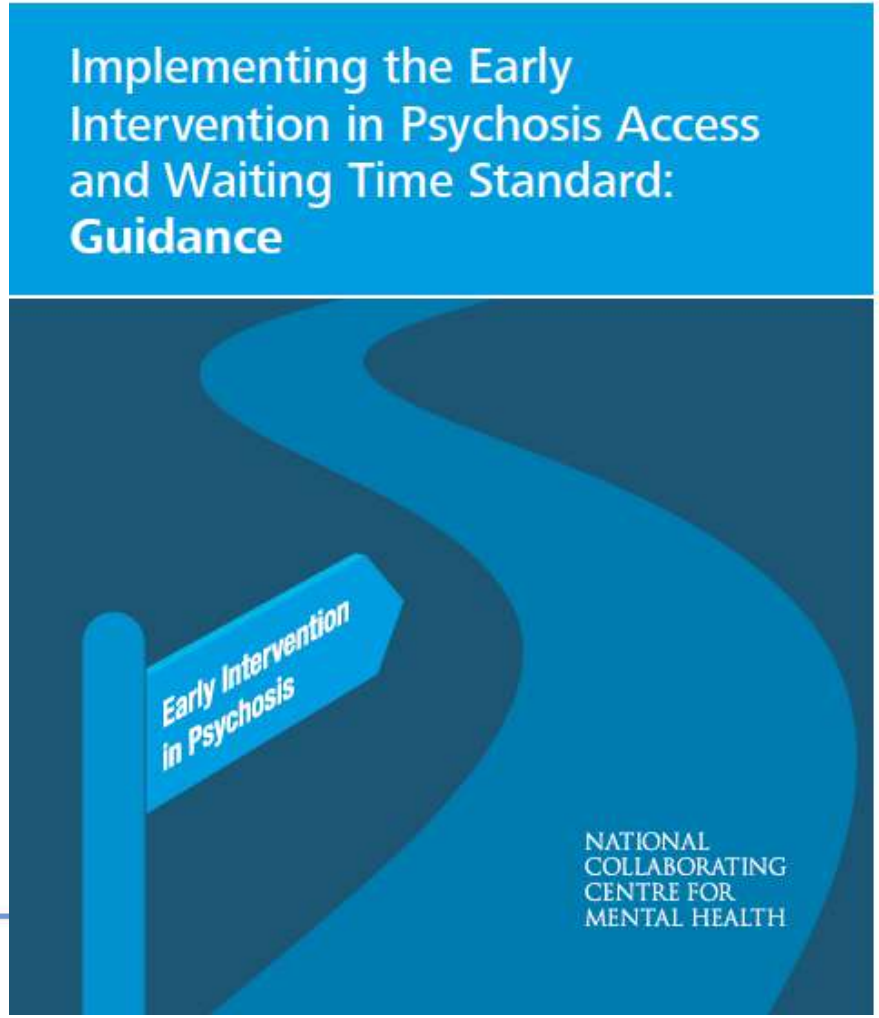
The bold text is to highlight the mean scores

Relative risk for the reduction in DUP = 0.736 (95% CI 0.350 to 0.893; p=.0039)

Phase 4: National standards and monitoring.

NICE National Institute for Health and Care Excellence

NHS England



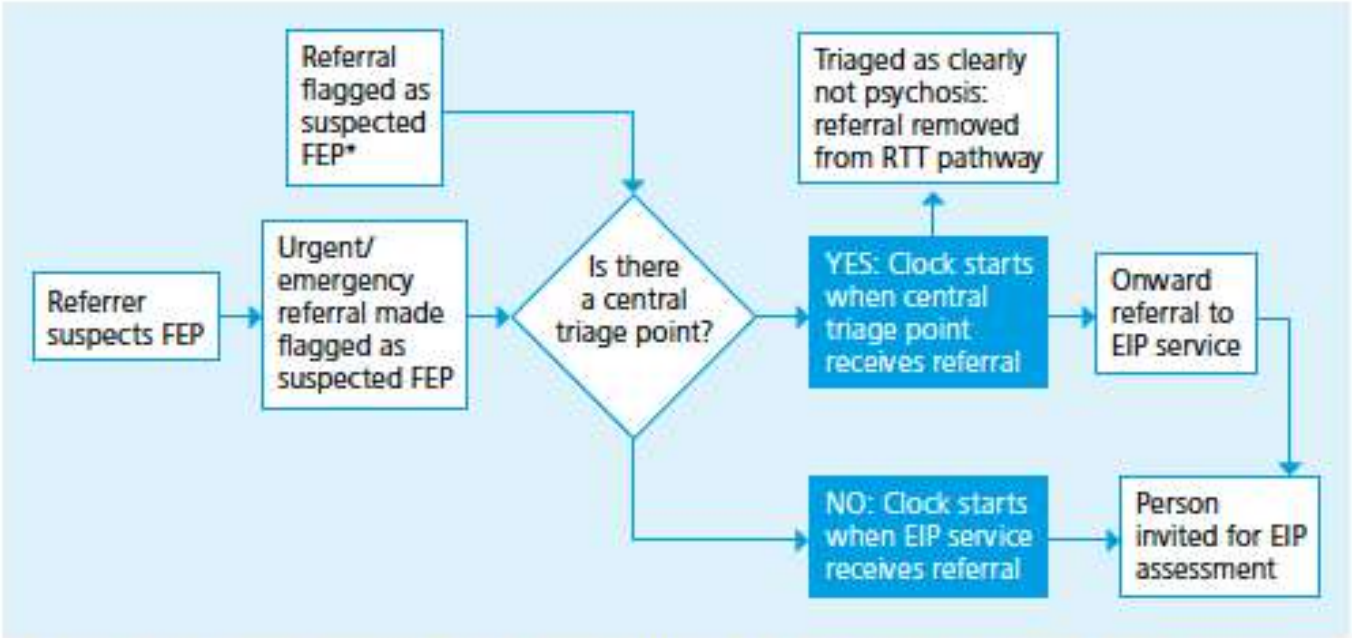
5. The standard requires that, from 1 April 2016, more than 50% of people experiencing first episode psychosis commence a National Institute for Health and Care Excellence (NICE)-recommended package of care within two weeks of referral. Treatment will be deemed to have commenced when the person:
   a. has had an initial assessment; AND
   b. has been accepted on to the caseload of an EIP service capable of providing a full package of NICE-recommended care; AND
   c. has been allocated to and engaged with by an EIP care coordinator.

4.2 Measuring and reporting performance against the referral to treatment (RTT) waiting time requirement

4.2.1 Measuring the clock start: referral, recognition and initial assessment

Referral and recognition

Fig 1: Referral to clock start



*If assessed by the central triage point as suspected FEP this referral should be flagged and moved on to the first episode pathway, and the clock will start on the day the central triage received the referral.

Key: FEP = first episode psychosis; RTT = referral to treatment

Title: **Early Intervention in Psychosis Waiting Times**
Summary: Waiting times for patients started treatment for Early Intervention in Psychosis.

Period: **December 2015 - March 2019**
Source: SDCS Data Collection - First Episode Psychosis
Basis: Commissioner
Published: 9th May 2019
Revised: N/A
Status: Published
Contact: England.eip-data@nhs.net

National Level Data

	The number of patients started treatment by week since referral					
Period	>0-2 weeks	>2-6 weeks	>6-12 weeks	12 plus	Total number of completed pathways (all)	% within 2 weeks
December 2015	523	232	70	61	886	59.0%
January 2016	530	251	86	41	908	58.4%
February 2016	687	261	78	26	1,052	65.3%
March 2016	720	281	96	21	1,118	64.4%
April 2016	782	288	102	32	1,204	65.0%
May 2016	788	278	62	34	1,162	67.8%
June 2016	863	236	51	27	1,177	73.3%
July 2016	938	245	54	20	1,257	74.6%
August 2016	875	198	51	18	1,142	76.6%
September 2016	921	206	43	19	1,189	77.5%
October 2016	963	221	48	25	1,257	76.6%
November 2016	935	216	34	20	1,205	77.6%
December 2016	816	234	37	10	1,097	74.4%
January 2017	853	190	66	10	1,119	76.2%
February 2017	887	168	36	15	1,106	80.2%
March 2017	920	272	40	16	1,248	73.7%
April 2017	674	201	39	16	930	72.5%
May 2017	886	205	34	11	1,136	78.0%
June 2017	873	193	39	22	1,127	77.5%
July 2017	824	226	36	14	1,100	74.9%
August 2017	816	207	45	16	1,084	75.3%
September 2017	818	187	47	15	1,067	76.7%
October 2017	836	178	50	18	1,082	77.3%
November 2017	787	230	50	22	1,089	72.3%
December 2017	699	198	39	19	955	73.2%
January 2018	722	238	65	17	1,042	69.3%
February 2018	807	185	36	24	1,052	76.7%
March 2018	795	178	49	26	1,048	75.9%
April 2018	783	204	44	21	1,052	74.4%
May 2018	840	210	47	12	1,109	75.7%
June 2018	829	190	47	17	1,083	76.5%
July 2018	819	210	37	13	1,079	75.9%
August 2018	809	234	30	15	1,088	74.4%
September 2018	766	171	60	10	1,007	76.1%
October 2018	952	197	45	18	1,212	78.5%
November 2018	872	213	45	14	1,144	76.2%
December 2018	763	169	42	21	995	76.7%
January 2019	811	206	49	13	1,079	75.2%
February 2019	745	171	53	31	1,000	74.5%
March 2019	759	171	46	20	996	76.2%

Phase 5: Improving outcomes from Early Intervention

EIP ‘non-responders’

- Clients of early intervention services for 12–30 months
- Low levels of structured activity following 1 year in EIS (defined as ≤30 hrs/week on the Time Use Survey.

Investigating trajectories of social recovery in individuals with first episode psychosis: a latent class growth analysis

Jo Hodgekins, Max Birchwood, Rose Christopher, Max Marshall, Sian Coker, Linda Everard, Helen Lester,* Peter Jones, Tim Amos, Swaran Singh, Vimal Sharma, Nick Freemantle and David Fowler

Background
Social disability is a hallmark of severe mental illness yet individual differences and factors predicting outcome are largely unknown.

Aim
To explore trajectories and predictors of social recovery following a first episode of psychosis (FEP).

Method
A sample of 764 individuals with FEP were assessed upon entry into Early Intervention for Psychosis (EIP) services and followed up over 12 months. Social recovery profiles were examined using Latent Class Growth Analysis.

Results
Three types of social recovery profile were identified: Low Stable (66%), Moderate-Increasing (27%), and High-Decreasing (7%). Poor social recovery was predicted by male gender, ethnic minority status, younger age at onset of psychosis, increased negative symptoms, and poor premorbid adjustment.

Conclusion
Social disability is prevalent in FEP, although distinct recovery profiles are evident. Where social disability is present upon entry into EIP services it can remain stable, highlighting a need for targeted intervention.

Declaration of interest
None.

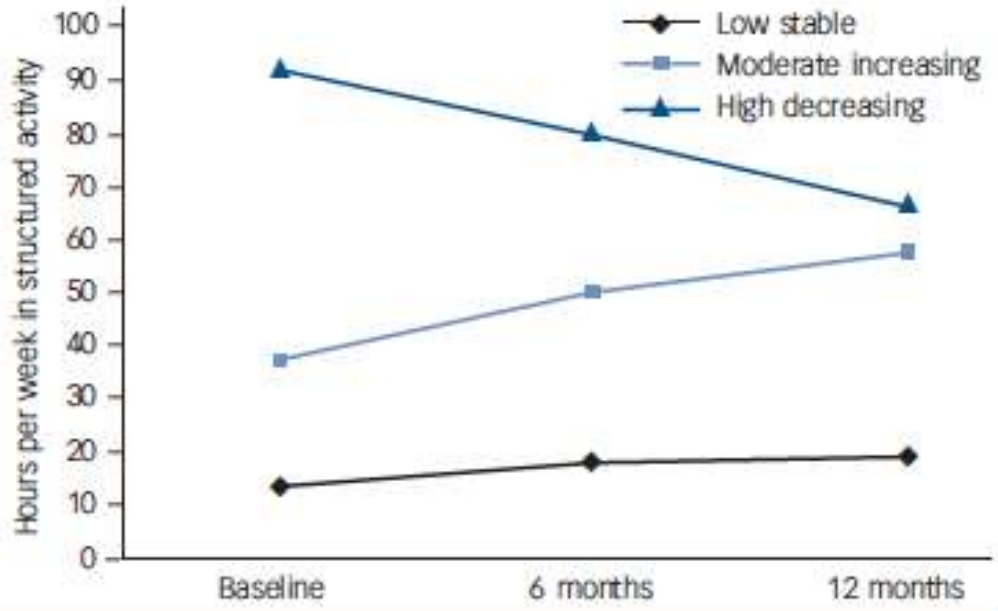


Fig. 1 LCGA model with three social recovery trajectories.

Social Recovery orientated Cognitive Behavioural Therapy (SR-CBT)

- Identify hopes and expectations as a young person
- Identify and overcome barriers to activity (eg. Hopelessness, social anxiety, family acceptance, stigma)
- Motivational interviewing: short and long term goals.
- Behavioural activation and coaching.
- Intensive outreach approach

Social recovery therapy in combination with early intervention services for enhancement of social recovery in patients with first-episode psychosis (SUPEREDEN3): a single-blind, randomised controlled trial

David Fowler, Jo Hodgekins, Paul French, Max Marshall, Nick Freemantle, Paul McCrone, Linda Everard, Anna Lavis, Peter B Jones, Tim Amos, Swaran Singh, Vimal Sharma, Max Birchwood

Summary

Background Provision of early intervention services has increased the rate of social recovery in patients with first-episode psychosis; however, many individuals have continuing severe and persistent problems with social functioning. We aimed to assess the efficacy of early intervention services augmented with social recovery therapy in patients with first-episode psychosis. The primary hypothesis was that social recovery therapy plus early intervention services would lead to improvements in social recovery.

Methods We did this single-blind, phase 2, randomised controlled trial (SUPEREDEN3) at four specialist early intervention services in the UK. We included participants who were aged 16–35 years, had non-affective psychosis, had been clients of early intervention services for 12–30 months, and had persistent and severe social disability, defined as engagement in less than 30 h per week of structured activity. Participants were randomly assigned (1:1), via computer-generated randomisation with permuted blocks (sizes of four to six), to receive social recovery therapy plus early intervention services or early intervention services alone. Randomisation was stratified by sex and recruitment centre (Norfolk, Birmingham, Lancashire, and Sussex). By necessity, participants were not masked to group allocation, but allocation was concealed from outcome assessors. The primary outcome was time spent in structured activity at 9 months, as measured by the Time Use Survey. Analysis was by intention to treat. This trial is registered with ISRCTN, number ISRCTN61621571.

Findings Between Oct 1, 2012, and June 20, 2014, we randomly assigned 155 participants to receive social recovery therapy plus early intervention services (n=76) or early intervention services alone (n=79); the intention-to-treat population comprised 154 patients. At 9 months, 143 (93%) participants had data for the primary outcome. Social recovery therapy plus early intervention services was associated with an increase in structured activity of 8·1 h (95% CI 2·5–13·6; p=0·0050) compared with early intervention services alone. No adverse events were deemed attributable to study therapy.

Interpretation Our findings show a clinically important benefit of enhanced social recovery on structured activity in patients with first-episode psychosis who received social recovery therapy plus early intervention services. Social recovery therapy might be useful in improving functional outcomes in people with first-episode psychosis, particularly in individuals not motivated to engage in existing psychosocial interventions targeting functioning, or who have comorbid difficulties preventing them from doing so.

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See Comment page 3

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Primary hypothesis

The social recovery intervention will lead to improvements in the time spent in structured activity.

Design

- Single blind, ITT pragmatic trial
- 9 month treatment envelope
- Follow up at 9 months (primary outcome) and 15 months.

Design

- Single blind, ITT pragmatic trial
- 9 month treatment envelope
- Follow up at 9 months (primary outcome) and 15 months.

At baseline

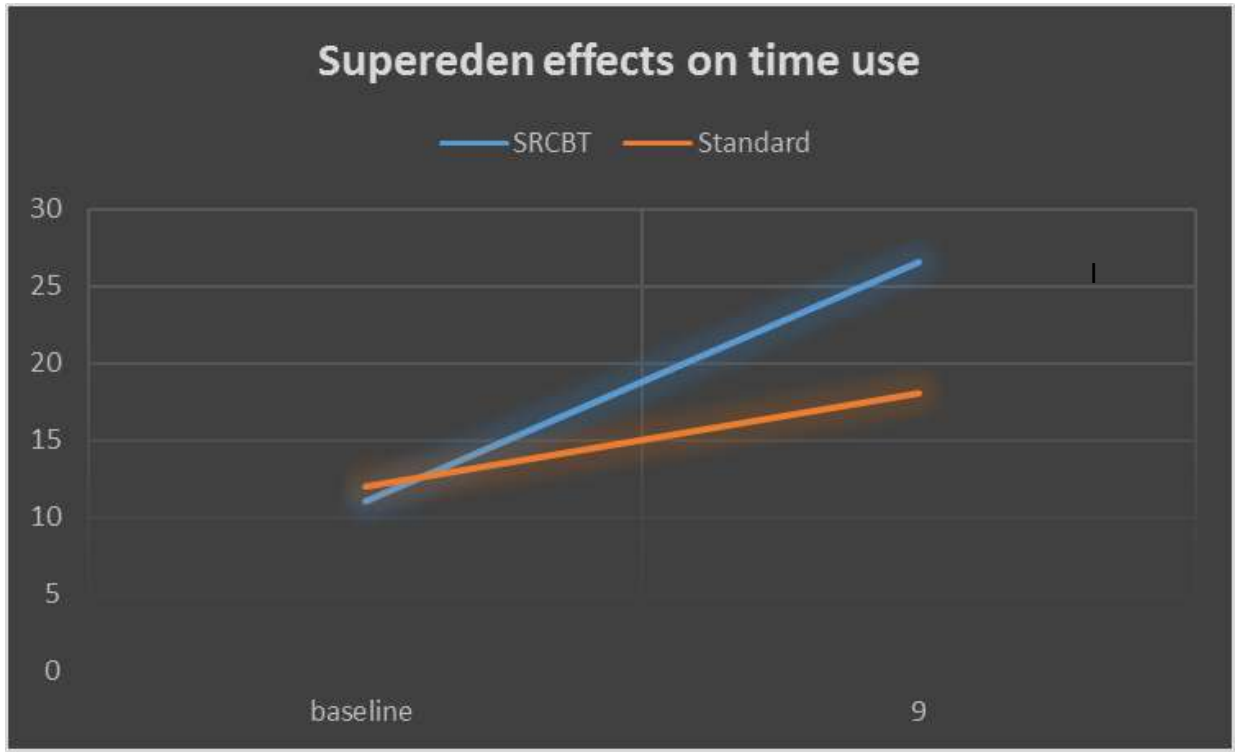
10/155 in some level of paid employment.

Mean 7.45 hour/week of structured activity (1.5-15)

Results

Impact on primary outcome: time spent in ‘structured activities’.

Social recovery therapy + EIS was associated with an increase in structured activity of 8·1 hrs/week (95% CI 2·5–13·6; p=0·0050) compared with EIS alone.



	Effect size (95% CI)	p value (intervention vs control)*	Missing data		p value‡
			Early intervention services alone (n=79)	Social recovery therapy plus early intervention services (n=75)†	
Primary outcomes					
Structured activity at 9 months	8·080 (2·502 to 13·657)	0·0050	9 (11%)	2 (3%)	0·011
Constructive economic activity at 9 months	5·859 (0·790 to 10·928)	0·024	9 (11%)	2 (3%)	0·034
Secondary outcomes					
Structured activity at 15 months	0·054 (−5·154 to 5·262)	0·98	19 (24%)	7 (9%)	0·037
Constructive economic activity at 15 months	−0·506 (−5·048 to 4·036)	0·83	19 (24%)	7 (9%)	0·046
Positive PANSS 9 months	0·306 (−1·228 to 1·840)	0·69	22 (28%)	9 (12%)	0·068
Negative PANSS 9 months	−1·020 (−2·662 to 0·622)	0·22	22 (28%)	9 (12%)	0·032
General PANSS 9 months	−1·014 (−3·514 to 1·486)	0·42	22 (28%)	9 (12%)	0·043
Positive PANSS 15 months	1·219 (−0·632 to 3·071)	0·19	32 (41%)	18 (24%)	0·071
Negative PANSS 15 months	−0·629 (−2·411 to 1·152)	0·49	32 (41%)	18 (24%)	0·073
General PANSS 15 months	−0·084 (−3·031 to 2·862)	0·96	33 (42%)	18 (24%)	0·081
SANS total at 9 months	9·713 (−14·568 to 33·994)	0·43	20 (25%)	11 (15%)	0·17
SANS total at 15 months	16·798 (−10·553 to 44·147)	0·23	32 (41%)	18 (24%)	0·035
BDI at 9 months	−1·567 (−4·840 to 1·706)	0·35	24 (30%)	13 (17%)	0·10
BDI at 15 months	0·748 (−3·261 to 4·757)	0·71	36 (46%)	20 (27%)	0·067
SIAS at 9 months	−2·559 (−6·964 to 1·846)	0·25	26 (33%)	11 (15%)	0·016
SIAS at 15 months	1·490 (−4·132 to 7·111)	0·60	36 (46%)	19 (25%)	0·10
BHS at 9 months	−1·464 (−3·282 to 0·354)	0·11	33 (42%)	16 (21%)	0·020
BHS at 15 months	−1·451 (−3·257 to 0·355)	0·11	37 (47%)	19 (25%)	0·022
ATHS total score 9 months	2·214 (−1·504 to 5·931)	0·24	33 (42%)	21 (28%)	0·15
ATHS total score 15 months	3·860 (−0·266 to 7·987)	0·066	39 (49%)	22 (29%)	0·0060
MLQ total score 9 months	2·193 (−1·496 to 5·883)	0·24	33 (42%)	19 (25%)	0·12
MLQ total score 15 months	0·782 (−3·196 to 4·759)	0·70	39 (49%)	23 (31%)	0·043

Data are n (%), unless otherwise specified. This approach assumes that loss to follow-up is associated with poor performance on the scale of interest. PANSS=Positive and Negative Symptom Scales. SANS=Scale for Assessment of Negative Symptoms. BDI=Beck Depression Inventory. SIAS=Social Interaction Anxiety Scale. BHS=Beck Hopelessness Scale. ATHS=Adult Trait Hope Scale. MLQ=Meaning in Life Questionnaire. *p value from completer case analysis. †Minus one participant who withdrew and requested that their data be removed. ‡p value from joint modelling (multivariate) analyses done to account for missing data.

Table 3: **Prespecified outcome analysis and joint models for primary and secondary outcomes**

Secondary outcomes:

- Negative symptoms ✓
- Social anxiety, ✓
- Hopelessness ✓
- Hope ✓
- Meaning in life ✓

- Depression X
- Positive symptoms X

Phase 6: Phase-specific interventions.

Vocational intervention in first-episode psychosis: individual placement and support *v.* treatment as usual

Eóin Killackey, Henry J. Jackson and Patrick D. McGorry

Background

Unemployment is a major problem for people with first-episode psychosis and schizophrenia. This has repercussions for the economy, social functioning and illness prognosis.

Aims

To examine whether a vocational intervention – individual placement and support (IPS) – which has been found to be beneficial in populations with chronic schizophrenia, was a useful intervention for those with first-episode psychosis.

Method

A total of 41 people with first-episode psychosis were randomised to receive either 6 months of IPS + treatment as usual (TAU) (n=20) or TAU alone (n=21).

Results

The IPS group had significantly better outcomes on level of employment (13 *v.* 2, $P<0.001$), hours worked per week (median 38 *v.* 22.5, P=0.006), jobs acquired (23 *v.* 3) and longevity of employment (median 5 weeks *v.* 0, P=0.021). The IPS group also significantly reduced their reliance on welfare benefits.

Conclusions

Individual placement and support has good potential to address the problem of vocational outcome in people with first-episode psychosis. This has economic, social and health implications.

Declaration of interest

This research was supported by a National Health and Medical Research Council Program Grant (ID: 350241) and an unrestricted study grant from Bristol Myers Squibb. ORYGEN Research Centre is supported by the Colonial Foundation.

ADEPP

The ADEPP study is a randomised controlled trial with an internal pilot looking at the use of antidepressant for the prevention of depression following first episode psychosis.

The aim of the ADEPP trial is to establish the effectiveness and cost effectiveness of an antidepressant medication (sertraline) for the prevention of a depressive episode following first episode psychosis.

This page explains the ADEPP study for researchers who are taking part in the study, or who are considering doing so. A summary for participants is here.

In 'ADEPP'

- Information for patients
- Privacy
- **ADEPP**
- Trial documentation
- Recruitment and participating centres
- Contact us

The Early Youth Engagement in first episode psychosis (EYE-2) study

- Cluster randomized controlled trial of effectiveness, cost effectiveness and implementation of the team-based motivational engagement intervention

- evaluated with respect to disengagement & routinely collected outcome data (HoNOS, QPR and DIALOG) in 1059 new FEP service users aged 14-35 in 5 sites across the UK.

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The traumatic experience of first-episode psychosis: A systematic review and meta-analysis

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ABSTRACT

Introduction: A psychotic episode may be sufficiently traumatic to induce symptoms of post-traumatic stress disorder (PTSD), which could impact outcomes in first-episode psychosis (FEP). The objectives of this systematic review and meta-analysis were to estimate the prevalence of PTSD symptoms in relation to psychosis in FEP and to identify risk factors for the development of PTSD symptoms.
Methods: We searched electronic databases and conducted manual searching of reference lists and tables of contents to identify relevant studies. Quantitative studies were included if the population was experiencing FEP and if PTSD was measured in relation to psychosis. Prevalence of PTSD symptoms and diagnoses were meta-analyzed using a random effects model. Potential risk factors for PTSD symptoms were summarized qualitatively.
Results: Thirteen studies were included. Eight studies assessed PTSD symptoms, three studies assessed full PTSD, and two studies assessed both. The pooled prevalence of PTSD symptoms was 42% (95% CI 30%–55%), and the pooled prevalence of a PTSD diagnosis was 30% (95% CI 21%–40%). Exploratory subgroup analyses suggest that prevalence may be higher in affective psychosis and inpatient samples. Evidence from included studies implicate depression and anxiety as potential risk factors for PTSD symptoms.
Conclusions: Approximately one in two people experience PTSD symptoms and one in three experience full PTSD following a first psychotic episode. Evidence-based interventions to treat PTSD symptoms in the context of FEP are needed to address this burden and improve outcomes after the first psychotic episode. Further studies are needed to clarify the associated risk factors.

Original Investigation

Prolonged Exposure vs Eye Movement Desensitization and Reprocessing vs Waiting List for Posttraumatic Stress Disorder in Patients With a Psychotic Disorder

A Randomized Clinical Trial

David P. G. van den Berg, MSc; Paul A. J. M. de Bont, MSc; Berber M. van der Vleugel, MSc; Carlijn de Roos, MSc; Ad de Jongh, PhD; Agnes Van Minnen, PhD; Mark van der Gaag, PhD

IMPORTANCE The efficacy of posttraumatic stress disorder (PTSD) treatments in psychosis has not been examined in a randomized clinical trial to our knowledge. Psychosis is an exclusion criterion in most PTSD trials.

OBJECTIVE To examine the efficacy and safety of prolonged exposure (PE) therapy and eye movement desensitization and reprocessing (EMDR) therapy in patients with psychotic disorders and comorbid PTSD.

DESIGN, SETTING, AND PARTICIPANTS A single-blind randomized clinical trial with 3 arms (N = 155), including PE therapy, EMDR therapy, and waiting list (WL) of 13 outpatient mental health services among patients with a lifetime psychotic disorder and current chronic PTSD. Baseline, posttreatment, and 6-month follow-up assessments were made.

INTERVENTIONS Participants were randomized to receive 8 weekly 90-minute sessions of PE (n = 53), EMDR (n = 55), or WL (n = 47). Standard protocols were used, and treatment was not preceded by stabilizing psychotherapeutic interventions.

MAIN OUTCOMES AND MEASURES Clinician-rated severity of PTSD symptoms, PTSD diagnosis, and full remission (on the Clinician-Administered PTSD Scale) were primary outcomes. Self-reported PTSD symptoms and posttraumatic cognitions were secondary outcomes.

RESULTS Data were analyzed as intent to treat with linear mixed models and generalized estimating equations. Participants in the PE and EMDR conditions showed a greater reduction of PTSD symptoms than those in the WL condition. Between-group effect sizes were 0.78 ($P < .001$) in PE and 0.65 ($P = .001$) in EMDR. Participants in the PE condition (56.6%; odds ratio [OR], 3.41; $P = .006$) or the EMDR condition (60.0%; OR, 3.92; $P < .001$) were significantly more likely to achieve loss of diagnosis during treatment than those in the WL condition (27.7%). Participants in the PE condition (28.3%; OR, 5.79; $P = .01$), but not those in the EMDR condition (16.4%; OR, 2.87; $P = .10$), were more likely to gain full remission than those in the WL condition (6.4%). Treatment effects were maintained at the 6-month follow-up in PE and EMDR. Similar results were obtained regarding secondary outcomes. There were no differences in severe adverse events between conditions (2 in PE, 1 in EMDR, and 4 in WL). The PE therapy and EMDR therapy showed no difference in any of the outcomes and no difference in participant dropout (24.5% in PE and 20.0% in EMDR, $P = .57$).

CONCLUSIONS AND RELEVANCE Standard PE and EMDR protocols are effective, safe, and feasible in patients with PTSD and severe psychotic disorders, including current symptoms. A priori exclusion of individuals with psychosis from evidence-based PTSD treatments may not be justifiable.

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Trials

STUDY PROTOCOL Open Access

The CIRCuiTS study (Implementation of cognitive remediation in early intervention services): protocol for a randomised controlled trial

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Abstract

Background: Cognitive problems in people with schizophrenia predict poor functional recovery even with the best possible rehabilitation opportunities and optimal medication. A psychological treatment known as cognitive remediation therapy (CRT) aims to improve cognition in neuropsychiatric disorders, with the ultimate goal of improving functional recovery. Studies suggest that intervening early in the course of the disorder will have the most benefit, so this study will be based in early intervention services, which treat individuals in the first few years following the onset of the disorder. The overall aim is to investigate different methods of CRT.

Methods: This is a multicentre, randomised, single-blinded, controlled trial based in early intervention services in National Health Service Mental Health Trusts in six English research sites. Three different methods of providing CRT (intensive, group, and independent) will be compared with treatment as usual. We will recruit 720 service users aged between 16 and 45 over 3 years who have a research diagnosis of non-affective psychosis and will be at least 3 months from the onset of the first episode of psychosis. The primary outcome measure will be the degree to which participants have achieved their stated goals using the Goal Attainment Scale. Secondary outcome measures will include improvements in cognitive function, social function, self-esteem, and clinical symptoms.

Discussion: It has already been established that cognitive remediation improves cognitive function in people with schizophrenia. Successful implementation in mental health services has the potential to change the recovery trajectory of individuals with schizophrenia-spectrum disorders. However, the best mode of implementation, in terms of efficacy, service user and team preference, and cost-effectiveness is still unclear. The CIRCuiTS trial will provide guidance for a large-scale roll-out of CRT to mental health services where cognitive difficulties impact recovery and resilience.

Trial registration: ISRCTN, ISRCTN14678860, Registered on 6 June 2016.

Keywords: Cognition, Cognitive enhancement, Cognitive remediation, Cognitive training, Early psychosis, Implementation, Functioning, Psychological therapy, Recovery, Schizophrenia

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Social anxiety disorder in first-episode psychosis: incidence, phenomenology and relationship with paranoia

Maria Michail and Max Birchwood

Background
Social anxiety disorder constitutes a significant problem for people with psychosis. It is unclear whether this is a by-product of persecutory thinking.

Aims
To compare the phenomenology of social anxiety disorder in first-episode psychosis with that in a group without psychosis. The relationship between social anxiety and psychosis symptoms was investigated.

Method
A sample of people with first-episode psychosis (FEP group) was compared with a sample with social anxiety disorder without psychosis (SaD group).

Results
Of the individuals in the FEP group ($n=80$) 25% were diagnosed with an ICD–10 social anxiety disorder (FEP/SaD group); a further 11.6% reported severe difficulties in social encounters. The FEP/SaD and SaD groups reported comparable levels of social anxiety, autonomic symptoms, avoidance and depression. Social anxiety in psychosis was not related to the positive symptoms of the Positive and Negative Syndrome Scale (PANSS) including suspiciousness/persecution. However, a significantly greater percentage of socially anxious *v.* non-socially anxious individuals with psychosis expressed perceived threat from persecutors, although this did not affect the severity of social anxiety within the FEP/SaD group. The majority of those in the FEP/SaD group did not have concurrent persecutory delusions.

Conclusions
Social anxiety is a significant comorbidity in first-episode psychosis. It is not simply an epiphenomenon of psychotic symptoms and clinical paranoia, and it has more than one causal pathway. For a subgroup of socially anxious people with psychosis, anticipated harm is present and the processes that underlie its relationship with social anxiety warrant further investigation.

Declaration of interest
None.

25 years of EIP: what have we learned?

- Early phase of psychosis a ‘critical period’ for long term outcome.
- Assuring interventions engagement and hope via dedicated teams with youth ethos works; popular with young people; and cost-effective.
- For some the EIP approach may need to be extended to maintain gains.
- But EIP works best if DUP < 3 to 6 months. This needs careful audit in each setting.
- Generic CMHTs alienate young people and best avoided. No evidence base.
- There are EIP ‘non-responders’ esp wrt severe social disability. Need to adapt model with new interventions.
- Need for phase-specific interventions, esp severe disability and affective disorder.

Thank you

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