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Duration of untreated psychosis

Introduction

The duration of untreated psychosis (DUP) is generally determined as the time from the onset of psychotic symptoms to initiation of treatment or first clinical presentation, when diagnosis of a first episode of psychosis (FEP) may be made. FEP is distinct from diagnosis of a first episode of schizophrenia, which requires particular symptoms to be present for a defined period, whereas FEP can refer to a number of different psychotic disorders. It has been proposed that untreated psychosis may have an inherently "toxic" effect, contributing to psychological deterioration and possibly adverse neural processes with longer DUP being associated with poorer prognosis. DUP is also thought to be a predictor of the likelihood and extent of recovery in first-episode schizophrenia. Consequently, understanding the effects of DUP is particularly important because it is potentially modifiable, and thereby altering prognosis. Topics included in this table include how DUP is measured and reported and how the length of DUP differs across regions. See the table DUP and relationship with outcomes for the impact of DUP on clinical and social outcomes.

Method

We have included only systematic reviews (systematic literature search, detailed methodology with inclusion/exclusion criteria) published in full text, in English, from the year 2000 that report results separately for people with a diagnosis of schizophrenia, schizoaffective disorder, schizophreniform disorder or first-episode schizophrenia. Reviews were identified by searching the databases MEDLINE, EMBASE, CINAHL, Current Contents, PsycINFO and the Cochrane library. Hand searching reference lists of identified reviews was also conducted. When multiple copies of reviews were found, only the most recent version was included. Reviews with pooled data are prioritised for inclusion.

Review reporting assessment was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist that describes a preferred way to present a meta-analysis[1]. Reviews with less than 50% of items checked have been excluded from the library. The PRISMA flow diagram is a suggested way of providing information about studies included and excluded with reasons for exclusion. Where no flow diagram has been presented by individual reviews, but identified studies have been described in the text, reviews have been checked for this item. Note that early reviews may have been guided by less stringent reporting checklists than the PRISMA, and that some reviews may have been limited by journal guidelines.

Evidence was graded using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group approach where high quality evidence such as that gained from randomised controlled trials (RCT) may be downgraded to moderate or low if review and study quality is limited, if there is inconsistency in results, indirect comparisons, imprecise or sparse data and high probability of reporting bias. It may also be downgraded if risks associated with the intervention or other matters under review are high. Conversely, low quality evidence such as that gained from observational studies may be upgraded if effect sizes are large, there is a dose dependent response or if results are reasonably consistent, precise and direct with low associated risks (see end of table for an explanation of these terms)[2]. The resulting table represents an objective summary of the available evidence, although the conclusions are solely the opinion of staff of NeuRA (Neuroscience Research Australia).

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Results

We found nine systematic reviews that met our inclusion criteria[3-11].

- Moderate to high quality evidence indicates the presence of obligatory dangerousness criterion for compulsory treatment is associated with longer DUP in those regions.
- Moderate quality evidence indicates longer DUP is found in low/middle income countries compared to high income countries.
- Moderate quality evidence indicates people with Black African groups have shorter DUP than White groups, while Black Caribbean groups have longer DUP than White groups (both small effects).
- Moderate quality evidence suggests people with schizophrenia have a longer DUP (~28 weeks) than people with an affective psychotic disorder, regardless of age and sex.
- Moderate quality evidence indicates there is a consistent definition of DUP in the literature; the time interval from emergence of psychotic symptoms to initiation of treatment, however, the exact criteria for onset and endpoint varies.
- Moderate quality evidence suggests good inter-rater reliability and small predictive validity for tools assessing duration of untreated psychosis, psychosis and treatment onset and outcomes.
- Moderate to low quality evidence indicates emergency services and inpatient units are associated with shorter DUP than community services pathways to care.
- Moderate quality evidence suggests long-term, widespread educational campaigns covering multiple domains such as advertising, distribution of brochures, visits to GPs and schools, training seminars, and follow-up contact may reduce the duration of untreated psychosis. A one-dimensional campaign approach, such as solely educating GPs, may not be as effective.

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Duration of untreated psychosis

Anderson KK, Fuhrer R, Malla AK

The pathways to mental health care of first episode psychosis patients: a systematic review

Psychological Medicine 2010; 40(10): 1585-1597

View review abstract online

Comparison	**Pathways to care and DUP following a first episode of psychosis (FEP).** **Note: some studies included patients with affective psychoses.**
Summary of evidence	**Moderate to low quality evidence (unclear sample size, unable to assess consistency or precision, direct) indicates emergency services and inpatient units are associated with the shortest DUP, and community services (including non-physicians) are associated with longer DUP.**
Pathways to care and DUP	
3 of 5 studies found significant associations between the referral source and the duration of untreated psychosis (DUP), such that emergency services and inpatient units were associated with the shortest DUP, and community services (including non-physicians) associated with longer DUP.	
Consistency in results‡	Unable to assess, but results appear inconsistent.
Precision in results§	Unable to assess; no measure of precision is reported.
Directness of results‖	Direct

Cascio MT, Cella M, Preti, A, Meneghelli A, Cocchi A.

Gender and duration of untreated psychosis: A systematic review and meta-analysis

Early Intervention in Psychiatry 2012; 6(2): 115-127

View review abstract online

Comparison	**Gender differences in DUP and age at first contact with treatment for patients with a schizophrenia spectrum disorder.**

Duration of untreated psychosis

Summary of evidence	**Moderate to high quality evidence (large sample, inconsistent, precise, direct) suggests no sex differences in the length of DUP.**
DUP, sex, and age at first episode	
27 studies, N = 4,721 *A significant, medium-sized effect of more males than females in FEP samples;* 23 samples, OR = 2.1, 95%CI 1.6 to 2.9, *p* = 0.0001 *No differences were found between males and females in the length of DUP;* DUP by any definition: 23 samples, *g* = -0.05, 95%CI -0.23 to 0.13, *p* = 0.58 DUP defined as the start of psychotic symptoms to first treatment: 13 samples, *g* = -0.11 95%CI -0.41 to 0.18, *p* = 0.45 Samples from Western countries: 20 samples, *g* = -0.06, 95%CI -0.28 to 0.16, *p* = 0.60 Samples from non-Western countries: 10 samples, *g* = -0.03, 95%CI -0.20 to 0.14, *p* = 0.76 *Males had a younger age at first contact with a mental health professional, but only in studies using 'any definition' of DUP, and only in samples from Western countries;* DUP by any definition: 16 samples, *g* = -0.18, 95%CI -0.37 to 0.001, *p* = 0.051 DUP defined as the start of psychotic symptoms to first treatment: 7 samples, *g* = -0.11, 95%CI -0.41 to 0.20), *p* = 0.49 Samples from Western countries: 15 samples, *g* = -0.37, 95%CI -0.56 to -0.17, *p* = 0.0001 Samples from non-Western countries: 7 samples, *g* = -0.08, 95%CI -0.33 to 0.11, *p* = 0.54	
Consistency in results	Authors state that heterogeneity was > 60% in all analyses.
Precision in results	Mostly precise
Directness of results	Direct

Compton MT, Carter T, Bergner E, Franz L, Stewart T, Trotman H, McGlashan TH, McGorry PD

Defining, operationalizing and measuring the duration of untreated psychosis: Advances, limitations and future directions

Early Intervention in Psychiatry 2007; 1(3): 236-250

View review abstract online

Duration of untreated psychosis

Comparison	Description of definition of DUP, operational criteria for the construct, and measures of DUP reported in the literature.
Summary of evidence	**Moderate (large sample, some inconsistency, unable to assess precision, direct) suggests studies apply a consistent definition of DUP; the time interval from emergence of psychotic symptoms to initiation of treatment, however, the exact criteria for onset and endpoint varies.** **No conclusions can be drawn regarding the use of measurement instruments - more research is needed to compare reliability and validity of the various measures used.**
Definition of DUP	
N = 7,290, 48 studies Consistent definition; the time interval from the emergence of psychotic symptoms to the initiation of treatment. This does not take into account frequency or severity of symptoms and assumes that psychosis was persistent since onset.	
Operationalisation of DUP	
N = 7,290, 48 studies Variable onset of DUP; when the patient became psychotic (emergence of mostly positive symptoms), to broad criteria of 'prodromal' symptoms. Variable endpoint of DUP; antipsychotic treatment, hospitalisation and/or treatment response.	
Preferred measurement tools	
IRAOS: 5 studies, N = 607, inter-rater reliability reported as 'acceptable'. Semi-structured interview designed to date and order temporally the onset of signs/symptoms - administered to patients and informants, plus data from medical charts and clinicians. RPMIP: 4 studies, N = 846, inter-rater reliability > 0.60. Instrument designed to measure mode of onset, psychopathology and diagnostic spectrum. CASH: 2 studies, N = 230, inter-rater and test–retest reliability reported as 'excellent'. Structured interview designed to measure premorbid functioning, current and past symptoms, course of illness and socio-demographic variables guide for applying diagnostic criteria. CORS: 1 study, N = 66, no reliability statistics reported. Semi-structured interview designed to measure status and willingness to engage in treatment assessed from both patient and informant perspectives. Followed by the Topography of Psychotic Episode instrument - semi-structured interview that focuses on a specific psychotic episode.	

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Symptom Onset in Schizophrenia: 1 study, N = 191, no reliability statistics reported. Inventory, interview guide and rating scale measuring severity and onset of 15 prodromal and 4 psychotic symptoms. Lifelong symptoms are considered premorbid and not prodromal, although premorbid symptoms that substantially worsen with time are rated as prodromal. Inter-rater reliability and symptom duration agreement reported as 'good to excellent'.	
Consistency in results	Consistent for definition of DUP, inconsistent for onset and endpoint.
Precision in results	Unable to assess; no measure of precision is reported.
Directness of results	Direct

Large MM, Nielssen O, Ryan CJ, Hayes R

Mental health laws that require dangerousness for involuntary admission may delay the initial treatment of schizophrenia

Social Psychiatry and Psychiatric Epidemiology 2008; 43(3): 251-256

View review abstract online

Comparison	**Differences in the average duration of untreated psychosis between countries with and without obligatory dangerousness criterion (assessed as being dangerous to themselves or to others) for involuntary treatment.**
Summary of evidence	**Moderate to high quality evidence (large sample, unable to assess consistency, precise, direct) indicates longer DUP is associated with the presence of obligatory dangerousness criterion.** **Authors conclude that it is likely that at least some of the increase in DUP in regions with an obligatory dangerousness criterion is a direct result of differences in mental health law.**
DUP and obligatory dangerousness criterion	
47 studies, N = 5,849 The weighted mean and mean DUP in samples from jurisdictions with an obligatory dangerousness criterion (ODC) was significantly longer. Median values are not significant due to skewed mean data. Obligatory dangerousness criterion; mean 79.5 weeks, 95%CI 63.5 to 95.4, weighted mean 77.7 weeks. Average median DUP in ODC jurisdictions: 27.5 weeks, 95%CI 17.3 to 37.3 weeks, median 28 weeks.	

No obligatory dangerousness criterion; mean 55.6 weeks, 95%CI 43.4 to 68.8 weeks, weighted mean 55.7 weeks. Average median DUP in non-ODC jurisdictions: 19.9 weeks, 95%CI 12.9 to 26.9 weeks, median 16 weeks.	
Consistency in results	Unable to assess; no measure of precision is reported.
Precision in results	Precise (CIs close to mean values).
Directness of results	Direct

Large M, Farooq S, Nielssen O, Slade T

Relationship between gross domestic product and duration of untreated psychosis in low- and middle-income countries

The British Journal of Psychiatry 2008; 193: 272-278

View review abstract online

Comparison	**Differences in DUP (defined as the period between the onset of definite psychotic symptoms and the beginning of adequate treatment - including initiation of treatment and contact with mental health services) between low- and middle-income countries and high-income countries based on per capita gross domestic product [GDP] in international dollars).**
Summary of evidence	**Moderate quality evidence (large sample, unable to assess consistency, imprecise, direct) indicates that longer DUP is found in low- and middle-income countries than in high income countries.**

DUP and GDP

The mean DUP was significantly longer in studies from low- and middle-income countries than in studies from high-income countries;

N = 13,809, 98 studies, 157 samples

Low- and middle-income countries; mean weeks (SD) = 125.0 (176.3), 95%CI 69.2 to 180.5

High income countries; mean weeks (SD) = 63.4 (53.3), 95%CI 53.2 to 73.6

$t = 2.56$, $p = 0.012$

Median values were not significantly different;

Low- and middle-income countries; average median weeks (SD) = 33.2 (62.1) 95%CI 0 to 66.3 High income countries; average median weeks (SD) = 18.6 (15.0) 95%CI 15.1 to 22.0 *For every $1000 of additional per capita GDP purchasing power parity, mean DUP in low- and middle-income countries fell by 9 weeks;* B = -0.009, SE = 0.0023, t = -4.212, p = 0.001 r = 0.644, r^2 = 0.415, SE of the estimate = 268.1 *For every $1000 of additional per capita GDP purchasing power parity, mean DUP in high-income countries rose by 3 weeks;* B = 0.003, SE = 0.001, t = 2.567, p = 0.012 r = 0.243, r^2 = 0.059 These findings were non-significant when the model included regions with obligatory dangerousness criterion as an explanatory variable.

Consistency in results	Unable to assess; no measure of consistency is reported.
Precision in results	Imprecise (CIs are very wide).
Directness of results	Direct

Large M, Nielssen O, Slade T, Harris A

Measurement and reporting of the duration of untreated psychosis

Early Intervention in Psychiatry 2008; 2: 201-211

View review abstract online

Comparison	**Differences between DUP in people with schizophrenia vs. affective psychoses.**
Summary of evidence	**Moderate quality evidence (large sample, unable to assess consistency, imprecise, direct) indicates people with schizophrenia or a non-affective psychosis have a longer DUP (~28 weeks) than people with an affective psychosis, regardless of age and sex.**
DUP and diagnosis	
A longer DUP was reported in samples that included only people with schizophrenia or non-affective psychosis compared to affective psychosis;	

75 samples, N ~9,870, *B* = 27.81, SE = 8.90, 95%CI 10.36 to 45.26 Random effects meta-regression results with age, sex and diagnosis in the model found diagnosis was the only significant predictor - samples comprising mostly patients with schizophrenia (compared to affective disorder) had a mean DUP that was 27.8 weeks longer.

Consistency in results	Unable to assess; no measure of consistency is reported.
Precision in results	Imprecise; CIs are very wide.
Directness of results	Direct

Lloyd-Evans B, Crosby M, Stockton S, Pilling S, Hobbs L, Hinton M, Johnson S

Initiatives to shorten duration of untreated psychosis: systematic review

The British Journal of Psychiatry 2011; 198: 256-263

View review abstract online

Comparison	**Assessment of campaigns to improve awareness of symptoms of early psychosis and to encourage early treatment, compared with standard care.**
Summary of evidence	**Moderate quality evidence (large population-level samples, unable to assess consistency and precision, direct) suggests long-term widespread educational campaigns covering multiple domains such as advertising, distribution of brochures, visits to GPs and schools, training seminars, and follow-up contact may reduce the duration of untreated psychosis. A one-dimensional campaign approach, such as solely educating GPs, may not be as effective.**

Duration of Untreated Psychosis

2 of 4 multi-focus campaigns reported significant reductions in mean or median DUP;

1 four-year study reported significant reductions in mean or median DUP, and less severe symptoms, and that patients were significantly more likely to self-refer and less likely to be referred via the police. Early intervention teams were established, brochures were delivered to 110,000 households, newspaper, radio, television and cinema advertising campaigns, visits twice a term to schools, education about symptoms and how to contact services to teachers and pupils, 3- to 4-hour training seminar to health professionals and 6-monthly follow-up letter to GPs.

1 two-year study reported significant reductions in mean or median DUP. Radio, newspaper and poster advertising was conducted, a mass postcard distribution, television docudrama and radio

features about psychosis were conducted, there was celebrity endorsement of the campaign, public forums, website and telephone hotline were set up, bi-monthly newsletter was distributed to GPs and school counselors, and talks and workshops were conducted with primary health professionals.

2 of 4 multifocus campaigns reported no significant reductions in mean or median DUP;

1 one-year study established a mobile assessment team, conducted 12 educational sessions delivered to staff and pupils in 6 schools, promoting help-seeking and describing signs and symptoms, a video was sent to 300 GPs, a mail out occurred every 6 months, 3 workshops were run with 90 GPs on education about psychosis, similar links were made with school counselors and youth workers. This study reported that patients from areas exposed to the intervention were found to have significantly less severe symptoms than those from comparison groups.

1 two-year study used a public poster and leaflet campaign, showed a film on television and university campus cinemas, clinicians attended schools and conducted counselling meetings monthly, pamphlets were sent and telephone contact was made with GPs.

No significant differences in mean or median DUP were found in 3 campaigns aimed at GP education or one study assessing changes in service configuration;

One eight-month study changed service configuration by establishing an early intervention team and conducted networking and community education activities.

One 27-month study conducted a workshop involving a 10-minute video and a 15-minute presentation provided to GP practices.

One 30-month study conducted a workshop involving a 17-minute video and a 15-minute question and answer session provided to GP practices, and a refresher video session was conducted 6 months later.

One 20-month study provided an information pack about early intervention service, and signs and symptoms, and conducted a 45-minute workshop involving presenting information, question and answer, and case vignettes delivered to GPs.

All 3 studies of GP education initiatives reported that GPs receiving education were more likely to refer people with first-episode psychosis to mental health services than GPs in a comparison group.

Consistency in results	Unable to assess; no measure of consistency is reported.
Precision in results	Unable to assess; no measure of precision is reported.
Directness of results	Not applicable

Register-Brown K, Hong LE

Reliability and validity of methods for measuring the duration of untreated psychosis: A quantitative review and meta-analysis

Duration of untreated psychosis

Schizophrenia Research 160; 2014: 20-26 View review abstract online	
Comparison	**Reliability and validity of assessment tools that measure the duration of untreated psychosis, psychosis and treatment onset and outcomes.**
Summary of evidence	**Moderate quality evidence (medium to large samples, some inconsistencies, unable to assess precision, direct) suggests good inter-rater reliability and small predictive validity for tools assessing duration of untreated psychosis, psychosis and treatment onset and outcomes.**
Overall inter-rater reliability for measuring DUP	
Authors state that all scales had good inter-rater reliability; Clinical Interview: 55 studies, N = 10,089, DUP ICC = 0.7 to 1.0 Chart Review: 6 studies, N = 497, DUP ICC = 0.73 Beiser Scale: 11 studies, N = 786, DUP ICC = 0.79 to 0.98, Psychosis onset ICC = 0.94 to 0.98, Treatment onset ICC = 0.95 Comprehensive Assessment of Symptoms and History: 4 studies, N = 337, DUP ICC = 0.87 to 1.00, Psychosis onset ICC = 0.96, Treatment onset ICC = 0.96 to 1.00 Circumstances of Onset and Relapse Schedule: 7 studies, N = 259, DUP ICC= 0.71 to 0.98 Interview for the Retrospective Assessment of the Onset of Schizophrenia: 11 studies, N = 1,089, DUP k = 0.6 to 0.95, Psychosis onset PA = 77%, Treatment onset PA = 80 to 100% Nottingham Onset Schedule: 2 studies, N = 1,740, DUP ICC = 0.95 to 0.99, Psychosis onset PA = 70% Positive and Negative Syndrome Scale for Schizophrenia (modified): 18 studies, N = 1,969, DUP ICC = 0.9 to 0.99 Psychiatric and Personal History Schedule: 4 studies, N = 277, DUP ICC = 0.90 Royal Park Multidiagnostic Instrument for Psychosis: 6 studies, N = 661, DUP k = 0.79, Psychosis onset k = 0.79 Symptom Onset in Schizophrenia Inventory: 7 studies, N = 937, DUP ICC = 0.99, Psychosis onset ICC = 1.0	
Predictive validity	
Authors report small effect sizes overall, and that no instrument had clearly larger effect sizes across different categories of outcomes or when all outcomes were grouped together. *All scales combined had significant predictive value for;*	

Duration of untreated psychosis

All outcomes combined: 132 studies, z = 0.18, $p < 0.001$

Treatment adherence: 6 studies, z = 0.14, $p < 0.001$

Overall functioning: 49 studies, z = 0.22, $p < 0.001$

Imaging outcomes: 14 studies, z = 0.25, $p < 0.001$

Negative symptoms: 32 studies, z = 0.21, $p < 0.001$

Positive symptoms: 27 studies, z = 0.22, $p < 0.001$

Neurocognition: 19 studies, z = 0.20, $p < 0.001$

Relapse risk: 29 studies, z = 0.21, $p < 0.001$

Suicidality/ violence: 15 studies, z = 0.084, $p < 0.001$

Clinical interview had significant predictive value for;

All outcomes combined: 55 studies, z = 0.17, $p < 0.001$

Treatment adherence: 3 studies, z = 0.15, $p < 0.05$

Overall functioning: 18 studies, z = 0.21, $p < 0.001$

Imaging outcomes: 8 studies, z = 0.32, $p < 0.001$

Negative symptoms: 11 studies, z = 0.19, $p < 0.001$

Positive symptoms: 9 studies, z = 0.24, $p < 0.001$

Neurocognition: 8 studies, z = 0.29, $p < 0.001$

Relapse risk: 12 studies, z = 0.22, $p < 0.001$

But not for;

Suicidality/ violence: 5 studies, z = 0.07, $p > 0.05$

Chart review had significant predictive value for;

All outcomes combined: 6 studies, z = 0.32, $p < 0.001$

Relapse risk: 2 studies, z = 0.37, $p < 0.05$

But not for;

Imaging outcomes: 1 study, z = 0.27, $p > 0.05$

Suicidality/ violence: 2 studies, z = 0.03, $p > 0.05$

Overall functioning: 3 studies, z = 0.14, $p > 0.05$

Basel Interview had no significant predictive value for;

Neurocognition: 1 study, z = 0.19, $p > 0.05$

Beiser Scale had significant predictive value for;

All outcomes combined: 11 studies, z = 0.20, $p < 0.001$

Overall functioning: 5 studies, z = 0.30, $p < 0.05$

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Negative symptoms: 2 studies, z = 0.33, $p < 0.001$

Positive symptoms: 3 studies, z = 0.28, $p < 0.001$

Neurocognition: 1 study, z = 0.44, $p < 0.05$

Suicidality/ violence: 2 studies, z = 0.16, $p < 0.05$

But not for;

Treatment adherence: 2 studies, z = 0.05, $p > 0.05$

Relapse risk: 2 studies, z = 0.02, $p > 0.05$

Comprehensive Assessment of Symptoms and History had significant predictive value for;

All outcomes combined: 4 studies, z = 0.12, $p < 0.05$

Overall functioning: 2 studies, z = 0.14, $p < 0.05$

Imaging outcomes: 2 studies, z = 0.14, $p < 0.05$

But not for;

Negative symptoms: 1 study, z = 0.02, $p > 0.05$

Positive symptoms: 1 study, z = 0.12, $p > 0.05$

Neurocognition: 1 study, z = 0.15, $p > 0.05$

Circumstances of Onset and Relapse Schedule had significant predictive value for;

All outcomes combined: 7 studies, z = 0.006, $p < 0.05$

Overall functioning: 2 studies, z = 0.19, $p < 0.001$

Imaging outcomes: 1 study, z = 0.22, $p < 0.05$

Negative symptoms: 3 studies, z = 0.18, $p < 0.05$

Positive symptoms: 2 studies, z = 0.22, $p < 0.001$

But not for;

Neurocognition: 2 studies, z = 0.19, $p > 0.05$

Relapse risk: 2 studies, z = 0.11, $p > 0.05$

Interview for the Retrospective Assessment of the Onset of Schizophrenia had significant predictive value for;

All outcomes combined: 11 studies, z = 0.17, $p < 0.001$

Overall functioning: 5 studies, z = 0.17, $p < 0.001$

Negative symptoms: 5 studies, z = 0.10, $p < 0.05$

Positive symptoms: 4 studies, z = 0.15, $p < 0.05$

Neurocognition: 2 studies, z = 0.26, $p < 0.05$

But not for:

Relapse risk: 4 studies, z = 0.14, $p > 0.05$

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Nottingham Onset Schedule had significant predictive value for;

Imaging outcomes: 1 study, z = 0.68, $p < 0.001$

But not for;

Suicidality/ violence: 1 study, z = -0.02, $p > 0.05$

Overall functioning: 2 studies, z = 0.12, $p > 0.05$

Positive and Negative Syndrome Scale for Schizophrenia (modified) had significant predictive value for;

All outcomes combined: 18 studies, z = 0.16, $p < 0.001$

Treatment adherence: 1 study, z = 0.19, $p < 0.05$

Overall functioning: 10 studies, z = 0.20, $p < 0.001$

Negative symptoms: 7 studies, z = 0.20, $p < 0.05$

Relapse risk: 5 studies, z = 0.15, $p < 0.05$

Suicidality/ violence: 3 studies, z = 0.19, $p < 0.001$

But not for;

Positive symptoms: 6 studies, z = 0.11, $p > 0.05$

Neurocognition: 1 study, z = 0.10, $p > 0.05$

Psychiatric and Personal History Schedule had significant predictive value for;

All outcomes combined: 4 studies, z = 0.23, $p < 0.05$

Imaging outcomes: 1 study, z = 0.35, $p < 0.05$

But not for;

Neurocognition: 1 study, z = 0.03, $p > 0.05$

Overall functioning: 2 studies, z = 0.45, $p > 0.05$

Royal Park Multi-diagnostic Instrument for Psychosis had significant predictive value for;

All outcomes combined: 6 studies, z = 0.20, $p < 0.001$

Overall functioning: 3 studies, z = 0.33, $p < 0.001$

Negative symptoms: 2 studies, z = 0.29, $p < 0.001$

Positive symptoms: 2 studies, z = 0.31, $p < 0.05$

Neurocognition: 1 study, z = 0.38, $p < 0.001$

Relapse risk: 1 study, z = 0.33, $p < 0.001$

But not for;

Suicidality/ violence: 1 study, z = 0.02, $p > 0.05$

Symptom Onset in Schizophrenia Inventory had significant predictive value for;

All outcomes combined: 7 studies, z = 0.16, $p < 0.001$

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Negative symptoms: 1 study, z = 0.27, $p < 0.001$ Relapse risk: 1 study, z = 0.28, $p < 0.001$ *But not for;* Overall functioning: 2 studies, z = 0.16, $p > 0.05$ Neurocognition: 1 study, z = -0.09, $p > 0.05$ Suicidality/ violence: 1 study, z = 0.01, $p > 0.05$ Additional meta-analyses of DUP measured by any specialized instrument vs. generic clinical interviews revealed no difference in effect size on any outcome. Authors report no evidence of publication bias.

Consistency in results	Unable to assess inter-rater reliability, authors report moderate to high heterogeneity for predictive validity.
Precision in results	Unable to assess; no measure of precision is reported.
Directness of results	Direct

Schoer N, Huang CW, Anderson KK

Differences in duration of untreated psychosis for racial and ethnic minority groups with first-episode psychosis: an updated systematic review and meta-analysis

Social Psychiatry and Psychiatric Epidemiology 2019; 54: 1295-8

View review abstract online

Comparison	**Racial differences in DUP in people with first-episode psychosis.**
Summary of evidence	**Moderate quality evidence (small samples, some inconsistency, precise, direct) indicates people with Black African groups have shorter DUP than White groups, while Black Caribbean groups have longer DUP than White groups (both small effects).**

Racial differences
Small effect shows Black African groups had a shorter DUP than White groups; 3 studies, N = 212, SMD = -0.23, 95%CI -0.40 to -0.06, $p < 0.05$, $I^2 = 0\%$, $p = 0.64$ *Small effect shows Black Caribbean groups had a longer DUP than White groups;* 3 studies, N = 186, SMD = 0.16, 95%CI -0.01 to 0.34, $p = 0.05$, $I^2 = 69\%$, $p = 0.04$

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Duration of untreated psychosis

Consistency in results	Consistent for Black African analysis, inconsistent for Black Caribbean analysis
Precision in results	Precise
Directness of results	Direct

Explanation of acronyms

b, B = beta coefficient, CASH = Comprehensive Assessment of Symptoms and History, CI = confidence interval, CORS = Circumstances of Onset and Relapse Schedule, DUP = duration of untreated psychosis, FEP = first-episode psychosis, GAF = Global Assessment of Functioning, GAS = Global Assessment Scale, GDP = gross domestic product, GP = general practitioner, IRAOS = Interview for the Retrospective Assessment of the Onset of Schizophrenia, MPAS = Modified Premorbid Adjustment Scale, N = number of participants, ODC = obligatory dangerousness criterion, *p* = statistical probability of obtaining that result ($p < 0.05$ generally regarded as significant), PAS = Premorbid Adjustment Scale, Phillips = Abbreviated Phillips Premorbid Functioning Scale, PSA = Premorbid Social Adjustment Scale, PSST = Premorbid Schizoid and Schizotypal Trait Scale, *r, R* = correlation coefficient, SE = standard error, *t* = two sample t-test, SMD = standardised mean difference, vs. = versus

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Duration of untreated psychosis

Explanation of technical terms

*Bias has the potential to affect reviews of both RCT and studies. Forms of bias include; reporting bias – selective reporting of results; publication bias - trials that are not formally published tend to show less effect than published trials, further if there are statistically significant differences between groups in a trial, these trial results tend to get published before those of trials without significant differences; language bias – only including English language reports; funding bias - source of funding for the primary research with selective reporting of results within primary studies; outcome variable selection bias; database bias - including reports from some databases and not others; citation bias - preferential citation of authors. Trials can also be subject to bias when evaluators are not blind to treatment condition and selection bias of participants if trial samples are small[12].

† Different effect measures are reported by different reviews.

Correlation coefficients (eg, r) indicate the strength of association or relationship between variables. They are an indication of prediction, but do not confirm causality due to possible and often unforseen confounding variables. An r of 0.10 represents a weak association, 0.25 a medium association and 0.40 and over represents a strong association. Unstandardised (*b*) regression coefficients indicate the average change in the dependent variable associated with a 1 unit change in the dependent variable, statistically controlling for the other independent variables. Standardised regression coefficients represent the change being in units of standard deviations to allow comparison across different scales.

Prevalence refers to how many existing cases there are at a particular point in time. Incidence refers to how many new cases there are per population in a specified time period. Incidence is usually reported as the number of new cases per 100,000 people per year. Alternatively some studies present the number of new cases that have accumulated over several years against a person-years denominator. This denominator is the sum of individual units of time that the persons in the population are at risk of becoming a case. It takes into account the size of the underlying population sample and its age structure over the duration of observation.

Reliability and validity refers to how accurate the instrument is. Sensitivity is the proportion of actual positives that are correctly identified (100% sensitivity = correct identification of all actual positives) and specificity is the proportion of negatives that are correctly identified (100% specificity = not identifying anyone as positive if they are truly not).

Weighted mean difference scores refer to mean differences between treatment and comparison groups after treatment (or occasionally pre to post treatment) and in a randomised trial there is an assumption that both groups are comparable on this measure prior to treatment. Standardised mean differences are divided by the pooled standard deviation (or the standard deviation of one group when groups are homogenous) that allows results from different scales to be combined and compared. Each study's mean difference is then given a weighting depending on the size of the sample and the variability in the data. 0.2 represents a small effect, 0.5 a medium effect, and 0.8 and over represents a large effect[12].

Odds ratio (OR) or relative risk (RR) refers to the probability of a reduction (< 1) or an increase (> 1) in a particular outcome in a

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treatment group, or a group exposed to a risk factor, relative to the comparison group. For example, a RR of 0.75 translates to a reduction in risk of an outcome of 25% relative to those not receiving the treatment or not exposed to the risk factor. Conversely, an RR of 1.25 translates to an increased risk of 25% relative to those not receiving treatment or not having been exposed to a risk factor. An RR or OR of 1.00 means there is no difference between groups. A medium effect is considered if RR > 2 or < 0.5 and a large effect if RR > 5 or < 0.2[13]. lnOR stands for logarithmic OR where a lnOR of 0 shows no difference between groups. Hazard ratios measure the effect of an explanatory variable on the hazard or risk of an event.

‡ Inconsistency refers to differing estimates of treatment effect across studies (i.e. heterogeneity or variability in results) which is not explained by subgroup analyses and therefore reduces confidence in the effect estimate. I^2 is the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance) - 0% to 40%: heterogeneity might not be important, 30% to 60%: may represent moderate heterogeneity, 50% to 90%: may represent substantial heterogeneity and 75% to 100%: considerable heterogeneity. I^2 can be calculated from Q (chi-square) for the test of heterogeneity with the following formula;

$$I^2 = \left(\frac{Q - df}{Q}\right) \times 100\%$$

§ Imprecision refers to wide confidence intervals indicating a lack of confidence in the effect estimate. Based on GRADE recommendations, a result for continuous data (standardised mean differences, not weighted mean differences) is considered imprecise if the upper or lower confidence limit crosses an effect size of 0.5 in either direction, and for binary and correlation data, an effect size of 0.25. GRADE also recommends downgrading the evidence when sample size is smaller than 300 (for binary data) and 400 (for continuous data), although for some topics, this criteria should be relaxed[14].

‖ Indirectness of comparison occurs when a comparison of intervention A versus B is not available but A was compared with C and B was compared with C that allows indirect comparisons of the magnitude of effect of A versus B. Indirectness of population, comparator and or outcome can also occur when the available evidence regarding a particular population, intervention, comparator, or outcome is not available so is inferred from available evidence. These inferred treatment effect sizes are of lower quality than those gained from head-to-head comparisons of A and B.

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