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#### Pathways to care

#### Introduction

The help-seeking efforts made by an individual and their families when symptoms of psychosis are apparent, and the clinical services made available as a result of these efforts, are collectively known as 'pathways to care'. Pathways to care can also encompass service structures that have not been actively sought by the individual.

Understanding pathways to care may improve early intervention strategies and contribute to reducing the duration of untreated psychosis. This topic presents the current evidence on various pathways to care in relation to illness outcomes. It also includes evidence regarding rates of, and possible reasons for, transition to psychosis in help-seeking individuals who report early symptoms of psychosis.

#### 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 а diagnosis of schizophrenia, schizoaffective schizophreniform disorder. 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 given priority 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<sup>1</sup>. 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 (RCTs) 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 matter under review are high. Conversely, low quality evidence such as that gained from observational studies may be upgraded if effect sizes are large or if there is a dose dependent response. We have also taken into account sample size and whether results are consistent, precise and direct with low associated risks (see end of table for an explanation of these terms)<sup>2</sup>. 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).

#### Results

We found nine reviews that met inclusion criteria<sup>3-11</sup>.

 Moderate to low quality evidence suggest young people have around three contracts

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before receiving specific services for firstepisode psychosis. General practitioners are the most common first contact, followed by specialised services. psychiatrists or emergency or inpatient units, family or friends then social workers. Contacts with counsellors or courts led to longer duration of untreated psychosis, which was shortest following referrals from emergency services or general practitioners. Contact with the criminal justice system, emergency or inpatient units were associated with poor patient experiences, disengagement, and high costs, despite sometimes resulting in reduced treatment delays.

- Moderate quality evidence suggests having a sense of being different or not normal and characterising this difference negatively can lead to fewer pathways to care for people with first-episode psychosis or at-risk mental Anticipating and experiencing states. negative reactions from self or others, employing strategies to avoid these negative reactions (such as nondisclosure of symptoms), lack awareness and understanding of mental illness, and having a negative opinion of services also impacts on pathways to care.
- Moderate quality evidence suggests perceived stigma about mental illness is associated with more negative help-seeking attitudes towards treatment (psychotherapy and medication). Service-related stigma is a reason for opposing psychiatric treatment, and shame is the main reason for nondisclosure of symptoms. Care-givers' concern that loved ones experiencing firstepisode psychosis would be labelled as 'mad' was a frequent reason for relatives not contacting psychiatric services.
- Moderate to high quality evidence suggests having a diagnosis of a psychotic disorder was associated with more involuntary than voluntary psychiatric admission, which was a stronger association than for bipolar disorder or organic disorder. Being unemployed, on

- welfare, single, and having previous involuntary admissions were related to a higher risk of involuntary admissions.
- Moderate quality evidence shows a small effect of increased compulsory psychiatric admissions in migrant groups compared to native groups. Compared to white ethnic groups, there were small effects compulsory increased psychiatric admissions in Black Caribbean, Black African, South Asian, East Asian, and other Authors report that the minority groups. most common explanations for increased risk of detainment in these groups included psychotic symptoms, perceived risk of violence, having police contact, absence of or mistrust of general practitioners, and ethnic disadvantages.
- Moderate quality evidence indicates black people in the U.K. may be more likely to have had compulsory hospital admissions compared to white people in the U.K, particularly those of African Caribbean or Black African ethnicity. Black people in the UK are less likely to be hospitalised on first presentation, or to be referred to specialist services, and police are more likely to have been involved during admission.
- Moderate quality evidence indicates there may be fewer compulsory admissions for Asians with first-episode psychosis in Canada than for Whites, Blacks, or those of other ethnic backgrounds.
- Moderate quality evidence suggests the worldwide voluntary admission rate is around 62%, while the involuntary admission rate is around 43%.

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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 following a first episode of psychosis, including first contact with services and sources of primary referrals to care.
Summary of evidence	Moderate quality evidence (large samples, appears inconsistent, unable to assess precision, direct) indicates physicians are the most likely first point of contact and the most common referral source is emergency services.

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First contact with mental health services;

13 of 21 (total N = 1,674) studies reported that a physician was the point of first contact (8 were European studies, none from USA). 3 studies found a similar proportion of patients first accessed a physician or the emergency services. 3 studies found that the majority (52–66%) were admitted to emergency services, and 2 found that the majority (62–63%) of patients approached a non-physician (counsellors, social workers, private clinical or religious agencies).

7 of 10 studies found significant associations between the first service contact and the duration of untreated psychosis (DUP), such that non-physicians were associated with the longest DUP.

Referral source on the pathway to care;

9 of 22 (total N = 3,130) studies reported emergency services were the most common referral source for further care. 8 studies reported that a physician was the main referral source and 4 studies reported referrals from a non-physician. A physician was the main source of referral for the largest proportion of patients in 6 of 8 European studies, while 6 of 7 North American studies reported greater referrals from the emergency services. 4 of 5 Asian studies found that the largest proportion of patients used a non-physician as their referral source.

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.

Five of six studies found no evidence for a relationship between socio-economic status and pathways to care.

No consistent relationships were reported between differences in pathways to care and differences



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in sex or ethnicity.	
Consistency in results <sup>‡</sup> Appears inconsistent.	
Precision in results§ Unable to assess; no measure of precision is reported.	
Directness of results	Direct

Barnett P, Mackay E, Matthews H, Gate R, Greenwood H, Ariyo K, Bhui K, Halvorsrud K, Pilling S, Smith S

Ethnic variations in compulsory detention under the Mental Health Act: a systematic review and meta-analysis of international data

The Lancet Psychiatry 2019; 6: 305-17

View review abstract online

Comparison	Ethnic variations in compulsory psychiatric admissions.
Summary of evidence	Moderate quality evidence (large samples, mostly inconsistent, imprecise, direct) shows a small effect of increased compulsory psychiatric admissions in migrant groups compared to native groups. Compared to white ethnic groups, there were small effects of increased compulsory psychiatric admissions in Black Caribbean, Black African, South Asian, East Asian, and other minority groups. Authors report that the most common explanations for the increased risk of detainment in these groups included psychotic symptoms, perceived risk of violence, having police contact, absence of or mistrust of general practitioners, and ethnic disadvantages.

#### **Hospital admissions**

71 studies, N = 1,953,135

A small effect showed migrant groups in general were more likely to be compulsorily admitted to hospital than native groups;

OR = 12 studies, 1.50, 95%CI 1.21 to 1.87, p = 0.0003,  $I^2 = 87\%$ 

Small effects showed Black Caribbean, Black African, South Asian, East Asian, and other minority ethnicity patients were more likely to be compulsorily admitted to hospital than white ethnic groups;

Black Caribbean: 25 studies, OR = 2.53, 95%Cl 2.03 to 3.16, p < 0.0001,  $l^2 = 72\%$ 



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Black African: 10 studies, OR = 2.27, 95%Cl 1.62 to 3.19, p < 0.0001,  $l^2 = 71\%$ 

South Asian: 20 studies, OR = 1.33, 95%CI 1.07 to 1.65, p = 0.0091,  $I^2 = 83\%$ 

East Asian: 3 studies, OR = 2.17, 95%Cl 1.47 to 3.22, p = 0.0001,  $l^2 = 9\%$ 

Other minority groups: 13 studies, OR = 1.66, 95%CI 1.29 to 2.14, p < 0.0001, 81%

A small effect showed black Caribbean patients were also more likely to be readmitted to hospital than white ethnic groups;

OR = 7 studies, 2.30, 95%CI 1.22 to 4.34, p = 0.0102,  $I^2 = 82\%$ 

Authors report that the most common explanations for the increased risk of detainment in these groups included psychotic symptoms, perceived risk of violence, having police contact, absence of or mistrust of general practitioners, and ethnic disadvantages.

Subgroup analyses showed UK-based studies reported increased odds of compulsory admission in black ethnic groups compared with international studies.

More women in the samples was also a significant predictor of compulsory admission to hospital in black, unspecified, and black Caribbean groups.

Recent publication date was a significant predictor of compulsory admission to hospital only in black Caribbean groups.

There were no moderating effects of age, study quality, or whether data were adjusted.

Consistency in results	Mostly inconsistent
Precision in results	Imprecise
Directness of results	Direct

Bhui K, Stansfeld S, Hull S, Priebe S, Mole F, Feder G

Ethnic variations in pathways to and use of specialist mental health services in the UK. Systematic review

British Journal of Psychiatry 2003; 182: 105-116

View review abstract online

Comparison	Ethnic variations in access to care, continuity of contact, and voluntary and compulsory psychiatric in-patient admissions.
Summary of evidence	Moderate to low quality evidence (unclear sample size, unable to assess consistency, imprecise or unable to assess, direct) indicates black people may be more likely to have had compulsory hospital admissions than white people. Black



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	people are also less likely to be referred to specialist services,
	and police are more likely to have been involved during hospital
	admission.

#### Pathways to care in the UK

One study reported that compared with white patients, black patients had more complex routes to specialist care, including contact with multiple carers before access to a specialist. A greater proportion of black patients had some contact with a helping agency the week before psychiatric service contact (1 study), and hospital admission was more likely to follow a home visit (1 study).

Compared with white and South Asian patients who visited their GP, black people were less likely to be referred to specialist services (3 studies). However, among patients presenting to general practice who are recognised to have a mental health problem, black patients were more likely to be found in specialist services (2 studies). The police were more likely to be involved in admissions or readmissions of black people (3 studies), though police involvement before admission was explained by a lack of GP involvement rather than ethnic origin of the patients (1 study).

Black people were most likely to present in crisis, often seeing the duty psychiatrist as a first point of contact with services (2 studies).

Specialist referral following primary care assessments appeared to be equally common among white and South Asian patients (1 West London study), but hospital admission was more likely among South Asians following a home visit (2 studies). South Asians had the highest community rates of mental disorder, were the most frequent consulters in primary care but were less likely than white people to have their mental disorder recognised (2 Birmingham studies).

#### Continuity of contact in the UK

Compared with white patients, services were less likely to maintain contact with black and South Asian people in one part of south London (Norwood, 1 study) but not in other areas of London (2 studies), suggesting variation in local service provision.

Compared with white people, black people were more likely to be in contact with services at 5- and 18year follow-up, respectively (2 studies).

#### Hospital admissions in the UK

Meta-analysis showed increased odds of compulsory hospital admission in black people compared to white people;

12 studies, N = 6753, OR = 4.31, 95% CI 3.33 to 5.58, p = not reported

Consistency in results Unable to assess; no measure of consistency is reported.	
Precision in results	
Directness of results	Direct

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Gronholm PC, Thornicroft G, Laurens KR, Evans-Lacko S

Mental health-related stigma and pathways to care for people at risk of psychotic disorders or experiencing first-episode psychosis: a systematic review

Psychological Medicine 2017; Feb 15: 1-13. doi: 10.1017/S0033291717000344.

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Comparison	Relationship between stigma and pathways to care in people with first-episode psychosis or people with at-risk mental states.
Summary of evidence	Moderate quality evidence (overall large samples, unable to assess consistency or precision, direct) from qualitative studies suggests the following themes related stigma to lower levels of pathways to care; a sense of being different or not normal, characterising this difference negatively, anticipating and experiencing negative reactions from self or others, employing strategies to avoid these negative reactions, a lack of awareness and understanding of mental illness, and having a negative opinion of services.
	Quantitative studies report increased perceived stigma was associated with more negative help-seeking attitudes towards treatment (psychotherapy and medication). Service-related stigma was a reason for opposing psychiatric treatment, and shame was the main reason for nondisclosure of symptoms. Care-givers' concern that loved ones experiencing first-episode psychosis would be labelled as 'mad' and was a frequent reason for relatives not contacting psychiatric services.

#### Pathways to care

Qualitative studies, N = 541

Themes relating stigma to pathways to care;

#### Sense of difference

The impression that something is wrong or not normal, a general conceptualisation of mental illness, and specific thoughts on particular diagnoses and symptoms.

#### Characterising difference negatively

Stigmatising labels like mad, crazy, or mental, and thoughts around a person being dangerous, violent, unpredictable, stupid, incapable or lazy.



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#### Negative reactions (anticipated and experienced)

Negative and judgemental reactions from self or others, social distancing, sense of stigma, feelings of shame, embarrassment, or guilt, and fear that experiences would worry or upset others.

#### **Strategies**

Peoples' attempts to avoid negative reactions, including non-disclosure, concealment efforts, denying, ignoring, not accepting or admitting the situation, normalising and rationalising experiences, and social withdrawal.

#### Lack of knowledge and understanding

Stigma related factors contributed towards a limited awareness and understanding of mental illness.

#### Service-related factors

Feeling labelled, judged, and treated differently by service providers prejudiced attitudes towards, and fear of, mental health services and led to belief that services break families apart. This theme also described facilitative experiences where positive interaction with services contributed to diminished stigma by normalising mental health, providing a destigmatising peer-environment, and normalising impact of treatment.

#### Quantitative findings, N = 692

1 study (N = 67) reported increased perceived stigma among people at risk of psychosis was significantly associated with more negative help-seeking attitudes towards psychotherapy at the 1 year follow-up assessment. Conversely, 1 study (N = 172) reported lower stigma stress was significantly associated with more positive help-seeking attitudes towards both psychotherapy and psychiatric medication at baseline.

1 study (N = 56) reported service-related stigma was a reason for opposing psychiatric treatment among people with first-episode psychosis, and shame was the main reason for nondisclosure of symptoms.

1 study (N = 34) reported care-givers' concern that loved ones experiencing first-episode psychosis would be labelled 'mad' and was a frequent reason for relatives not contacting psychiatric services.

1 mixed-methods study (N = 63) found health professionals left young people who hear voices feeling 'not normal'.

1 study (N = 288) found that people at risk of psychosis reported reduced internalised stigma regardless of whether or not they received cognitive therapy over standard care.

Consistency in results	Unable to assess; no measure of consistency is reported.	
Precision in results Unable to assess; no fmeasure of precision is reported.		
Directness of results	Direct	

#### MacDonald K, Fainman-Adelman N, Anderson KK, Iyer SN



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Pathways to mental health services for	voung people: a s	systematic review
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Social psychiatry and psychiatric epidemiology 2018; 53: 1005-38.

View review abstract online

Comparison	Pathways to care for young people (≤30 years) with first-episode psychosis or other mental illness. The majority of the studies included people with psychosis.
Summary of evidence	Moderate to low quality evidence (unclear sample sizes, unable to assess consistency or precision, direct) suggest young people have around three contracts before receiving specific services for first-episode psychosis. General practitioners are the most common first contact, followed by psychiatrists or specialised services, emergency or inpatient units, family or friends then social workers. Contacts with counsellors or courts led to longer duration of untreated psychosis, which was shortest following referrals from emergency services or general practitioners. Contact with the criminal justice system, emergency or inpatient units were associated with poor patient experiences, disengagement and high costs, despite sometimes resulting in reduced treatment delays.

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#### **Contacts**

28 studies (N unclear) reported the number of contacts before receiving specific services ranged averaged 2.9 contacts (range; 0 to 15). Contacts involved included medical professionals (general practitioners, psychiatrists); non-medical professionals (psychologists, social workers, counsellors, school teachers, rural healthcare workers); informal sources of help (family, friends, employers, colleagues); healthcare institutions (emergency services, inpatient units, walk-in clinics); criminal or justice system (police, prisons, lawyers, courts); traditional or faith-based healers (prayer houses, priests, herbalists, clergy); and technology-enabled contacts (websites, helplines, crisis lines).

14 of 29 studies (N unclear) reported general practitioners were the most common first contact followed by psychiatrists or specialised services (5/29); faith or traditional healers (4/29); ERs/inpatient units (3/29); family or friends (2/29) and social workers (1/29).

8 of 22 studies (N unclear) reported the successful contact (contact that resulted in obtaining the correct service) was an ER/inpatient unit. 6 studies reported self-referrals (referrals made by youths themselves or family/carers) were the most frequent successful contact. Other prominent successful contacts included general practitioners, general hospitals, helplines, and outpatient units.

#### Impact of pathways to care on treatment delays

7 studies found that contacts with counsellors or courts led to longer duration of untreated



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psychosis (DUP), and DUP was shorter following referrals from emergency services. DUPs were also shorter if the first contact was with general practitioners compared to psychiatrists and psychologists, although 1 study reported longer referral delays following contact with primary care, albeit such contact resulted in fewer negative pathways to care (e.g., emergency or inpatient services).

#### Factors influencing pathways to care

12 studies found that families and friends influenced whether participants had sought mental healthcare.

#### Negative pathways to care

4 studies reported that negative pathways involved contact with the criminal justice system, emergency or inpatient units, and were associated with poor patient experiences, disengagement and high costs, despite sometimes resulting in reduced treatment delays.

#### Costs

1 Canadian study reported inpatient units were 18.5 times costlier than pathways with no inpatient unit involvement. This was attributable to the greater involvement of police and emergency services.
 1 Indian study reported the median monetary cost of an individual's pathway to care was more than half the average family's monthly income.

#### Study quality

Authors report that common study limitations were insufficient reporting on sample size determination; low participation rates or inadequate differentiation between participants and non-participants; and non-standardised ascertainment of pathways to care.

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	Direct

#### Mann F, Fisher HL, Johnson S

A systematic review of ethnic variations in hospital admission and compulsory detention in first-episode psychosis

Journal of Mental Health 2014; 23(4): 205-211

View review abstract online

Comparison	Rates of hospital admissions and involuntary admissions in
	people with first-episode psychosis in ethnic minority vs. native populations.



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#### **Summary of evidence**

Moderate quality evidence (overall large sample, unable to assess consistency or precision, direct) indicates African Caribbean men, and Black African people with first-episode psychosis in the UK may be more likely to have compulsory hospital admissions than white people with first-episode psychosis. White people in the UK are more likely to be hospitalised on first presentation than Black people or those of other ethnic backgrounds. There may be fewer compulsory admissions for Asians with first-episode psychosis in Canada than for Whites, Blacks or those of other ethnic backgrounds.

#### Hospital admissions and involuntary admissions

- 1 English study (N = 93) showed Whites were six times more likely to be hospitalized at first presentation compared with Black people and "others". Another English study (N = 462) reported African Caribbean men had over 3.5 times the odds, and Black African people had 4 times the odds of being compulsorily detained than White people. However, 2 English studies (N = 100 and 93) reported no differences in rates of compulsory detention between Whites, Blacks (incl. African Caribbeans) Asians or others.
  - 1 Dutch study (N = 257) reported no overall differences in rates of compulsory detention between Whites, Moroccan, Surinamese, Turkish or Antellean people, although Surinamese women were more likely to be detained.
- 1 Canadian study (N = 81) reported fewer compulsory admissions for Asians compared with Whites, Blacks or 'Others'. This study reported no differences in rates of hospitalisation according to ethnic groupings.
  - 1 New Zealand study (N = 200) showed no differences in rates of hospitalisations in Maori compared with non-Maori service users.

Authors report that the majority of studies scored weak to moderate on quality ratings.

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	Direct

Walker S, Mackay E, Barnett P, Sheridan Rains L, Leverton M, Dalton-Locke C, Trevillion K, Lloyd-Evans B, Johnson S

Clinical and social factors associated with increased risk for involuntary psychiatric hospitalisation: a systematic review, meta-analysis, and



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The Lancet Psychiatry 2019; 6: 1039-53

View review abstract online

Comparison	Factors associated with involuntary vs. voluntary hospitalisation in people with schizophrenia or other psychiatric disorders.
Summary of evidence	Moderate to high quality evidence (overall large sample, inconsistent, precise, direct) suggests having a diagnosis of a psychotic disorder was associated with involuntary admission, which was a stronger association than for bipolar disorder or organic disorder. Being unemployed, on welfare, single, and having previous involuntary admissions were related to a higher risk of involuntary admissions.

#### Clinical and social factors

77 studies, N = 975,004

A diagnosis of a psychotic disorder showed a medium-sized association with involuntary admission compared to voluntary admission;

Psychosis: 37 studies, N not reported, OR = 2.18, 95%CI 1.95 to 2.44,  $I^2 = 95\%$ 

Bipolar disorder and organic disorder also showed an increased risk of involuntary admission, although the effect sizes were small.

Having a diagnosis of depression, anxiety, other mood disorders, personality disorder, or neurosis showed reduced likelihood of involuntary admission.

Across all diagnoses, being unemployed, on welfare, being single, and having previous involuntary admissions were related to involuntary admissions.

Consistency in results	Inconsistent
Precision in results	Precise
Directness of results	Direct

Yang Y, Li W, An FR, Wang YY, Ungvari GS, Balbuena L, Xiang YT

**Voluntary and Involuntary Admissions for Severe Mental Illness in China:** 



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A Systematic Review and Meta-Analysis  Psychiatric services 2020; 71: 83-6	
Comparison	Prevalence of involuntary and voluntary admissions in people with schizophrenia living in China.
Summary of evidence	Moderate quality evidence (large sample, inconsistent, imprecise, direct) suggests the involuntary admission rate was higher than the voluntary admission rate in people with schizophrenia living in China.
	Prevalence
	14 studies, N = 94,305
Voluntary admissions: 19.6%, 95%Cl 14.09% to 26.54%, $I^2 = 96\%$	
Involuntary admissions: $44.3\% 95\%CI 5.98\%$ to $90.88\%$ , $I^2 = 100\%$	
Consistency in results	Inconsistent
Precision in results	Appears imprecise

Yang Y, Li W, Lok KI, Zhang Q, Hong L, Ungvari GS, Bressington DT, Cheung T, Xiang YT

Voluntary admissions for patients with schizophrenia: A systematic review and meta-analysis

Asian Journal of Psychiatry 2020; 48: 101902

Direct

View review abstract online

**Directness of results** 

Comparison	Worldwide prevalence of involuntary and voluntary admissions in people with schizophrenia.
Summary of evidence	Moderate quality evidence (large sample, inconsistent, some imprecision, direct) suggests the worldwide voluntary admission rate is around 62%, while the involuntary admission



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rate is around 43%.

#### **Prevalence**

35 studies, N = 134,100

Voluntary admissions: 61.9%, 95%Cl 52.3% to 70.7%,  $I^2 = 99.75$ % Involuntary admissions: 43.0%, 95%Cl 34.8% to 51.7%,  $I^2 = 99.50$ %

Subgroup analyses showed patients in Europe had significantly higher voluntary admission rates, while their North American counterparts were more likely admitted involuntarily.

Papers published prior to 2008 reported higher involuntary admission rates.

Meta-regression analyses showed that higher male percentage and higher study quality were significantly associated with higher voluntary admission rate.

Consistency in results	Inconsistent
Precision in results	Appears precise for voluntary admissions and imprecise for involuntary admissions.
Directness of results	Direct

#### Explanation of acronyms

 $\beta$  = Beta coefficient, CI = confidence interval, DSM = Diagnostic and Statistical Manual of Mental Disorders, I² = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance), ICD = The International Statistical Classification of Diseases, N = number of participants, OR = odds ratio, p = statistical probability of obtaining that result (p < 0.05 generally regarded as significant), Q = Q statistic for the test of heterogeneity, Q<sub>w</sub> = test for within group differences (heterogeneity in study results within a group of studies – measure of study consistency), Q<sub>B</sub> = test for between group differences (heterogeneity between groups of studies for an outcome of interest). R² = coefficient of determination.

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#### Explanation of technical terms

\* Bias has the potential to affect reviews of both RCT and observational 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.

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 Standardised mean prior to treatment. 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. Less than 0.4 represents a small effect, around 0.5 a medium effect, and over 0.8 represents a large effect.<sup>12</sup>

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 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, a 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. A 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  $< 0.2^{13}$ . InOR stands for logarithmic OR where a InOR of 0 shows no difference between groups. Hazard ratios

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measure the effect of an explanatory variable on the hazard or risk of an event.

Correlation coefficients (eg, r) indicate the strength of association or relationship between variables. They can provide an indirect 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 а strong association. Unstandardised (b) regression coefficients indicate the average change in the dependent variable associated with a 1 unit change in the independent variable, statistically controlling for the other independent Standardised variables. regression coefficients represent the change being in units of standard deviations to comparison across different scales.

‡ Inconsistency refers to differing estimates of effect across studies (i.e. heterogeneity or variability in results) is not explained by subgroup analyses and therefore reduces confidence in the effect estimate. I2 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 considerable heterogeneity and over this is considerable heterogeneity. I<sup>2</sup> can calculated from Q (chi-square) for the test of heterogeneity with the following formula;12

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

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, these 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 Indirectness versus B. of population, comparator and/or outcome can also occur when the available evidence regarding a particular population, intervention. comparator, or outcome is not available and is therefore inferred from available evidence. These inferred treatment effect sizes are of lower quality than those gained from head-tohead comparisons of A and B.

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#### Pathways to care

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