TECHNICAL COMMENTARY

Spatial variation

Introduction

Prevalence measures the proportion of individuals who have a disorder at a particular point in time (point prevalence) or during a specified period (annual prevalence, lifetime prevalence). It is distinct from incidence, which refers to how many new cases there are per population in a specified time period. Lifetime prevalence is the number of individuals in a population that at some point in their life have experienced schizophrenia compared to the total number of individuals. Annual prevalence is often used in conjunction with lifetime prevalence. This table summarizes the evidence examining how the prevalence of schizophrenia varies between regions.

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 given preference 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. 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, 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).

Results

We found five systematic reviews that met our inclusion criteria[3-7].

- High quality evidence suggests the *age-standardised* point prevalence in 2016 was 0.28%, with rates varying slightly across regions from 0.19% in Africa to 0.42% in East Asia. Rates were similar in all regions in 1990 and 2016.
- Moderate to high quality evidence indicates there is worldwide spatial variation in the prevalence of schizophrenia and

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schizophrenia-related disorders. There is increased prevalence of schizophrenia with higher latitudes and colder climates. At the same latitude, prevalence is higher for people with darker skin (African American, sub-Saharan Africa and southern Indian regions).

- Moderate quality evidence suggests decreased prevalence in least developed countries compared to developed countries.
- Moderate to high quality evidence suggests no differences in the prevalence of schizophrenia in urban, rural or mixed urban/rural areas.

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Charlson FJ, Ferrari AJ, Santomauro DF, Diminic S, Stockings E, Scott JG, McGrath JJ, Whiteford HA

Global Epidemiology and Burden of Schizophrenia: Findings From the Global Burden of Disease Study 2016

Schizophrenia Bulletin 2018; 44: 1195-203

View review abstract online

Comparison	**Spatial variation in the prevalence of schizophrenia.**
Summary of evidence	**High quality evidence (very large samples, appears consistent and precise, direct) suggests the age-standardised point prevalence in 1990 and 2016 was 0.28%, with rates varying slightly across regions, from 0.19% in Africa to 0.42% in East Asia.**

Prevalence of schizophrenia

Global

1990: 0.28%, 95%UI 0.25% to 0.31%

2016: 0.28%, 95%UI 0.24% to 0.31%

East Asia

1990: 0.42%, 95%UI 0.38% to 0.47%

2016: 0.42%, 95%UI 0.38% to 0.47%

Southeast Asia

1990: 0.26%, 95%UI 0.23% to 0.30%

2016: 0.27%, 95%UI 0.24% to 0.31%

Central Asia

1990: 0.20%, 95%UI 0.18% to 0.23%

2016: 0.20%, 95%UI 0.18% to 0.23%

Oceania

1990: 0.29%, 95%UI 0.25% to 0.33%

2016: 0.28%, 95%UI 0.25% to 0.32%

Australasia

1990: 0.33%, 95%UI 0.29% to 0.37%

2016: 0.33%, 95%UI 0.29% to 0.37%

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Central Europe 1990: 0.21%, 95%UI 0.18% to 0.25% 2016: 0.22%, 95%UI 0.18% to 0.26% *Eastern Europe* 1990: 0.20%, 95%UI 0.17% to 0.22% 2016: 0.20%, 95%UI 0.18% to 0.23% *Western Europe* 1990: 0.24%, 95%UI 0.22% to 0.27% 2016: 0.25%, 95%UI 0.22% to 0.27% *Latin America and Caribbean* 1990: 0.20%, 95%UI 0.18% to 0.23% 2016: 0.20%, 95%UI 0.18% to 0.23% *North Africa and Middle East* 1990: 0.18%, 95%UI 0.16% to 0.21% 2016: 0.19%, 95%UI 0.16% to 0.21% *Sub-Saharan Africa* 1990: 0.19%, 95%UI 0.17% to 0.21% 2016: 0.19%, 95%UI 0.17% to 0.21%	
Consistency in results‡	Authors report results are consistent.
Precision in results§	Appears precise.
Directness of results‖	Direct

Goldner EM, Hsu L, Waraich P, Somers JM

Prevalence and incidence studies of schizophrenic disorders: a systematic review of the literature

Canadian Journal of Psychiatry 2002; 47(9): 833-843

View review abstract online

Comparison	**Spatial variation in the prevalence of schizophrenia and schizophrenia-related disorders.**
Summary of evidence	**Moderate to high quality evidence (large samples, unable to assess precision, direct) indicates there is spatial variation in the**

	prevalence of schizophrenia and schizophrenia-related disorders.
Prevalence of schizophrenia diagnosed by ICD-9 or DSM-III and later criteria	
For all schizophrenia-related disorders (all rates are per 100): 10 population-level studies Canada, metropolitan Edmonton: 1 year = 0.4, lifetime = 0.6 Finland, national: lifetime = 2.2 Germany, former West Germany: lifetime = 0.71 (ICD-9 clinician diagnosis) and 0.72 (DIS diagnosis) Korea, Dong, Seoul (urban) and Eub, Myeon (rural): lifetime = 0.46 New Zealand, Christchurch, mostly urban: 1 year = 0.2, lifetime = 0.4 Puerto Rico, national: lifetime = 1.8 Sweden, city and rural areas of Uppsala: 1 year = 0.73 US, national: 1 year = 0.5, lifetime = 0.7 (clinical diagnosis) and 2.2 (CIDI diagnosis) US, 5 urban sites: 1 year = 1.0, lifetime = 1.5 *For schizophrenia diagnosis:* 14 population-level studies Canada, metropolitan Edmonton: 1 year = 0.3, lifetime = 0.6 Finland, national: lifetime = 1.3 Germany, former West Germany: lifetime; 0.6 Hong Kong, national: lifetime; 0.12 per 100 Korea, Dong, Seoul (urban) and Eub, Myeon (rural): lifetime = 0.4 Netherlands, national: 1 year = 0.2, lifetime; 0.4 New Zealand, Christchurch, mostly urban: 1 year = 0.2, lifetime = 0.3 Puerto Rico, national: lifetime = 1.6 Sweden: 1 year; 0.42 Taiwan, metropolitan Taipei: 1 year = 0.28, lifetime = 0.3 Taiwan, small towns: 1 year = 0.23, lifetime = 0.23 Taiwan, rural villages: 1 year = 0.2, lifetime = 0.23 US, national: lifetime = 0.15 (clinical diagnosis) and 1.1 (CIDI diagnosis) US, 5 urban sites: 1 year = 0.9, lifetime = 1.3 *For schizophreniform disorder diagnosis:* 10 population-level studies Canada, metropolitan Edmonton: 1 year = 0.0, lifetime = 0.1	

Germany, former West Germany: lifetime; 0.12 Hong Kongm national: lifetime; 0.06 per 100 Korea, Dong, Seoul (urban) and Eub, Myeon (rural): lifetime = 0.06 New Zealand, Christchurch, mostly urban: 1 year = 0.0, lifetime = 0.1 Puerto Rico, national: lifetime = 0.2 Taiwan, metropolitan Taipei: lifetime = 0.02 Taiwan, small towns: lifetime = 0.00 Taiwan, rural villages: lifetime = 0.00 US, 5 urban sites: 1 year = 0.1, lifetime = 0.2	
Consistency in results	Rates were expected to vary between countries; no within-country consistency is reported.
Precision in results	Unable to assess; no measure of precision is reported.
Directness of results	Direct

Kinney DK, Teixeira P, Hsu D, Napoleon SC, Crowley DJ, Miller A, Hyman W, Huang E

Relation of Schizophrenia Prevalence to Latitude, Climate, Fish Consumption, Infant Mortality, and Skin Color: A Role for Prenatal Vitamin D Deficiency and Infections?

Schizophrenia Bulletin 2009; 35(3): 582-595

View review abstract online

Comparison 1	**Comparison of regional prevalence of schizophrenia, latitude of study site and daily average minimum temperature in the coldest month of the year at the study site or nearest geographic site, 25 years prior to prevalence estimates (authors state that the average age of onset for schizophrenia is early to mid 20's).**
Summary of evidence	**Moderate to high quality evidence (large samples, unable to assess precision, direct) suggests a relationship between increased latitude, colder climate, and increased prevalence of schizophrenia.** **Prevalence is greatest for disadvantaged ethnic minority groups.**
Relationship between latitude/climate and regional prevalence of schizophrenia	

Spatial variation

Significant relationship between both latitude and climate and regional prevalence for schizophrenia: Worldwide; 49 prevalence studies (no control groups), N = 2,392,539 Latitude correlation with schizophrenia prevalence; r = 0.46, p < 0.001 Climate correlation with schizophrenia prevalence; r = -0.60, p < 0.001 *Similar correlations were observed within each major continental region with a minimum of 3 studies:* Latitude correlation range; r = 0.51 to 0.94 Climate correlation range; r = -0.51 to -0.99 *Prevalence ranged from 0.9 cases per 1,000 at Accra, Ghana and Jakarta, Indonesia to 28 cases per 1,000 at Oxford Bay, Canada* Major continental regions: *Africa;* Ethiopia, Botswana and Ghana *East Asia;* South Korea (rural and Seoul), China, Japan (Nagasaki), Taiwan (Taipei) and Hong Kong *South Asia;* India (New Delhi, Chandigarh rural and urban, West Bengal, Tamil Nadu, Vellore, Madras, Punjab, Lucknow slum) and Indonesia (Jakarta slum) *Europe;* Finland, Germany (Munich, Upper Bavaria), The Netherlands (Nijmegen), UK (Camden, Nottingham and Hampstead), Russia (Moscow), Iceland, Norway (fishing village), Denmark (Bornholm Island, Aarhus), Ireland (Dublin) *North America*; Canada (Oxford Bay, Alberta, Edmonton). US (Los Angeles, Baltimore, New Haven, Honolulu, subgroups of ethnic communities)
Relationship between disadvantaged ethnic minority groups, latitude and relative risk for schizophrenia
Significant relationship between increased prevalence for schizophrenia and disadvantaged ethnic minority groups from high latitude regions compared to disadvantaged ethnic minority groups from low latitude regions: 5 prevalence studies, N = 342,612, r = 0.98, p = 0.01 Regions included in analysis were Canada, USA, India and Taiwan

Consistency in results	Rates are expected to vary across regions; no measure of within region consistency is reported.
Precision in results	Unable to assess; no measure of precision is reported.
Directness of results	Direct
Comparison 2	**Relationship between skin colour (dark = African American, groups from sub-Saharan Africa and southern India, light for groups of European ancestry and all others intermediate, eg: East Asians) and regional prevalence of schizophrenia, controlling for latitude.**
Summary of evidence	**Moderate to high quality evidence (large samples, unable to assess precision, direct) suggests that at the same latitude, prevalence tends to be higher for groups with dark skin colour (African American, sub-Saharan Arica and southern Indian**

	regions).
Relationship between skin colour and regional prevalence of schizophrenia, controlling for latitude	
Prevalence increases with latitude for samples with darker skin colour as well as those with intermediate and lighter skin colour, although prevalence tends to be higher for samples with darker skin: 49 studies, N = 2,392,539, GLM main effects for skin colour; $F = 13.70$, $p = 0.0006$ Interaction not significant (statistics not reported)	
Consistency in results	Rates are expected to vary across groups; no within-group consistency is reported.
Precision in results	Unable to assess; no measure of precision is reported.
Directness of results	Direct

Saha S, Chant D, Welham J, McGrath J

A systematic review of the prevalence of schizophrenia

PLoS Medicine / Public Library of Science 2005; 2(5): e141

View review abstract online

Comparison 1	**Distribution rates of the prevalence of schizophrenia with influence of urbanicity.**
Summary of evidence	**Moderate to high quality evidence (large samples, unable to assess precision, direct) suggests no differences in the prevalence of schizophrenia in urban, rural or mixed urban/rural areas.**
Differences in prevalence rates for urban vs rural and mixed urban/rural place of residence	
132 observational studies in total (worldwide), population level data No difference prevalence of schizophrenia in urban vs. rural regions No difference in prevalence of schizophrenia in urban vs. mixed regions No difference in prevalence of schizophrenia in rural vs. mixed regions	
Consistency in results	Rates expected to vary across regions; no within-region consistency reported
Precision in results	Unable to assess; no measure of precision is reported.

Spatial variation

Directness of results	Direct
Comparison 2	**Distribution rates of the prevalence of schizophrenia with influence of socioeconomic status.**
Summary of evidence	**Moderate quality evidence (large samples, unable to assess precision, indirect) suggests decreased prevalence in least developed countries compared to developed countries.**
Differences in prevalence rates for developed vs. emerging vs. least developed countries	
Significantly lower prevalence of schizophrenia in least developed vs. developed countries: 85 observational studies, population level data Using per capita gross national product of the study site and World Bank definitions of mean income: < US$2995 per annum = least developed, US$2995 to $9266 = emerging economy, >US$9266 = developed Difference in harmonic means – all 3 groups; $F_{2,85} = 3.57$, $p = 0.03$ Difference in harmonic means – least developed vs. developed groups; $F_{1,74} = 6.55$, $p = 0.04$	
Consistency in results	Rates are expected to vary across groups; no within-group consistency is reported.
Precision in results	Unable to assess; no measure of precision is reported.
Directness of results	Indirect measure of socioeconomic status.

Saha S, Chant DC, Welham JL, McGrath JJ

The incidence and prevalence of schizophrenia varies with latitude

Acta Psychiatrica Scandinavica 2006; 114(1): 36-39

View review abstract online

Comparison 1	**Association of the prevalence of schizophrenia by latitude. Based on absolute latitude; low = 0 to 30°, medium = 30 to 60° and high = > 60°.**
Summary of evidence	**Moderate to high quality evidence (large samples, unable to assess precision, direct) suggests increased prevalence of schizophrenia with higher latitudes.**
Relationship between latitude and prevalence and of schizophrenia	

Spatial variation

94 prevalence studies (combined estimate), 35 countries worldwide, population level data

Low latitude countries = Botswana, China, Ethiopia, India, Iran, Micronesia, Puerto Rico, Taiwan, Tanzania,
& USA (Hawaii)
Medium latitude countries= Argentina, Bulgaria, Canada, Croatia, Denmark, France, Germany, Ghana, Greece, Ireland, Italy, Japan, New Zealand, Reunion Island, Russia, S. Africa, S. Korea, Sri Lanka, Sweden, the Netherlands, UK, USA & Yugoslavia
High latitude countries = Canada, Finland, Iceland, Norway & Sweden

For all persons, prevalence rates (adjusted for normality and within study clustering):
28 low latitude studies adjusted harmonic mean; 3.4, 95%CI 2.5 to 4.5
46 medium latitude countries adjusted harmonic mean; 3.2, 95%CI 2.5 to 4.0
10 high latitude countries adjusted harmonic mean; 8.2, 95%CI 4.9 to13.5

Significantly higher prevalence rates (log-transformed harmonic means) for all persons in higher latitudes, $F_{2,81} = 5.76$, $p = 0.005$

For males, prevalence rates (adjusted for normality and within study clustering):
12 low latitude studies adjusted harmonic mean; 2.9, 95%CI 1.9 to 4.3
26 medium latitude countries adjusted harmonic mean; 4.0, 95%CI 3.0 to 5.3
6 high latitude countries adjusted harmonic mean; 8.2, 95%CI 4.5 to14.7

Significantly higher prevalence rates (log-transformed harmonic means) for males in higher latitudes $F_{2,43} = 4.08$, $P = 0.02$

For females, prevalence rates (adjusted for normality and within study clustering)
13 low latitude studies adjusted harmonic mean; 2.9, 95%CI = 1.9 to 4.3
25 medium latitude countries adjusted harmonic mean; 3.2, 95%CI = 2.4 to 4.2
7 high latitude countries adjusted harmonic mean; 10.0, 95%CI = 5.5 to18.2

Significantly higher prevalence rates (log-transformed harmonic means) for males in higher latitudes, $F_{2,42} = 6.72$, $p = 0.003$

Consistency in results	Rates are expected to vary across regions; no within-region consistency is reported.
Precision in results	Unable to assess (harmonic means).
Directness of results	Direct

Explanation of acronyms

F = one-way ANOVA F-test for (harmonic) means, N = number of participants, *p* = statistical probability of obtaining that result ($p < 0.05$ generally regarded as significant), *r* = correlation

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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[8].

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† 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 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[8].

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[9]. 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.

Correlation coefficients (eg, r) indicate the strength of association or relationship

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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 independent 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.

‡ Inconsistency refers to differing estimates of treatment effect across studies (i.e. heterogeneity or variability in results) that 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[10].

‖ 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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