TECHNICAL COMMENTARY

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Incidence in migrants

Introduction

The incidence of schizophrenia refers to how many new cases there are per population in a specified time-period. It is different from prevalence, which refers to how many existing cases there are at a particular point in time. 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 developing schizophrenia. It takes into account the size of the underlying population sample and its age structure over the duration of observation.

Differences in the incidence of a disorder can provide clues to its possible causes. For example, a population register with information gained from consensus data helps to identify all adults who were born within a certain time-period (an age cohort) and where they were born. Cross linking this information with a mental health register can be used to identify those who received treatment for schizophrenia over particular time periods. This can provide information regarding the incidence of schizophrenia within different migrant groups.

The term “migrant” usually refers to first generation migrants - people with a foreign birthplace, however some studies also include locally born offspring, or second-generation migrants in their analyses. Any association observed between migrant status and increased incidence of schizophrenia has stimulated a great deal of research and explanatory hypotheses, including additional stress relating to migration and settling into a new country, and possible issues with discrimination. Other explanations include a tendency for at-risk individuals to migrate and underlying genetic variances across cultures.

Method

We have included only systematic reviews with detailed literature search, methodology, and inclusion/exclusion criteria that were published in full text, in English, from the year 2000. Reviews were identified by searching the databases MEDLINE, EMBASE, and PsycINFO. Reviews with pooled data are prioritized for inclusion. Reviews reporting fewer than 50% of items on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA[1]) checklist have been excluded from the library. The evidence was graded guided by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group approach[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 four systematic reviews that met our inclusion criteria[3-6].

- Moderate to high quality evidence finds the incidence rate of schizophrenia is higher in migrants than in native-born populations.
- Moderate quality evidence indicates increased incidence of schizophrenia for both first- and second-generation migrant populations, particularly for migrants with black skin and those living in the UK, The Netherlands, and Scandinavian countries.

Margarete Ainsworth Building, Barker Street, Randwick NSW 2031. Phone: 02 9399 1000. Email: info@neura.edu.au

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Bourque F, van der Ven E, Malla A

A meta-analysis of the risk for psychotic disorders among first- and second-generation immigrants

Psychological Medicine 2010; 21: 1-14

View review abstract online

Comparison	**Incidence in first- and second-generation migrants vs. native born populations.**
Summary of evidence	**Moderate quality evidence (large samples, mostly direct, imprecise, inconsistent across and within subgroups) indicates increased incidence of schizophrenia for both first- and second-generation migrant populations, particularly for migrants with black skin and those living in the UK, The Netherlands, and Scandinavian countries.**

First-generation migrants

Significant increased incidence of schizophrenia in first-generation migrants:

19 population level studies, N = 5508, incidence rate ratio = 2.3, 95%CI = 2.0 to 2.7,

$Q_W = 1071$, $I^2 = 94.4\%$, $p < 0.01$

Subgroup analysis showed no differences in risk between male and female first-generation migrants:

Males; incidence rate ratio = 2.1, 95%CI = 1.7 to 2.6

$Q_W = 654.2$, $I^2 = 94.8\%$, $p < 0.01$

Females; incidence rate ratio = 2.4, 95%CI = 1.9 to 2.9

$Q_W = 398.8$, $I^2 = 91.5\%$, $p < 0.01$

$Q_B = 0.49$, NS

Subgroup analysis showed risk is highest for first-generation migrants where black skin is the majority in their country of origin:

Black; incidence rate ratio = 4.0, 95%CI = 3.4 to 4.6

$Q_W = 80.8$, $I^2 = 79\%$, $p < 0.01$

Other; incidence rate ratio = 2.0, 95%CI = 1.6 to 2.5

$Q_W = 97.8$, $I^2 = 84.7\%$, $p < 0.01$

White; incidence rate ratio = 1.8, 95%CI = 1.6 to 2.1

$Q_W = 175.4$, $I^2 = 89.7\%$, $p < 0.01$

Incidence in migrants

$Q_B = 57.2$, $p < 0.01$
Subgroup analysis showed risk is highest for first-generation migrants from black African and black Caribbean ethno-racial groups: White; incidence rate ratio = 1.8, 95%CI = 1.6 to 2.1 $Q_W = 175.4$, $I^2 = 89.7\%$, $p < 0.01$ Black Caribbean; incidence rate ratio = 3.9, 95%CI = 3.4 to 4.6 $Q_W = 42.6$, $I^2 = 74.2\%$, $p < 0.01$ Black African; incidence rate ratio = 4.3, 95%CI = 2.8 to 6.8 $Q_W = 38.1$, $I^2 = 86.9\%$, $p < 0.01$ Asian; incidence rate ratio = 1.7, 95%CI = 1.3 to 2.3 $Q_W = 32.2$, $I^2 = 81.4\%$, $p < 0.01$ Middle East; incidence rate ratio = 2.3, 95%CI = 1.4 to 4.0 $Q_W = 31.9$, $I^2 = 87.5\%$, $p < 0.01$ $Q_B = 61.8$, $p < 0.01$
Subgroup analysis showed risk is highest for first-generation migrants living in the UK, The Netherlands and Scandinavia: Israel; incidence rate ratio = 1.5, 95%CI = 1.1 to 2.1 $Q_W = 12.5$, $I^2 = 51.9\%$, NS (trend) The Netherlands; incidence rate ratio = 2.5, 95%CI = 2.0 to 3.2 $Q_W = 61.2$, $I^2 = 85.3\%$, $p < 0.01$ Scandinavia; incidence rate ratio = 2.3, 95%CI = 1.9 to 2.7 $Q_W = 185.0$, $I^2 = 92.4\%$, $p < 0.01$ UK; incidence rate ratio = 2.8, 95%CI = 2.2 to 3.5 $Q_W = 237.2$, $I^2 = 93\%$, $p < 0.01$ $Q_B = 9.5$, $p < 0.05$
Subgroup analysis showed no significant difference in risk based on study setting: Mixed urban/rural study setting; incidence rate ratio = 2.2, 95%CI = 1.9 to 2.6 $Q_W = 848.0$, $I^2 = 95.4\%$, $p < 0.01$ Urban study setting; incidence rate ratio = 2.7, 95%CI = 2.0 to 3.6 $Q_W = 179.1$, $I^2 = 88.8\%$, $p < 0.01$ $Q_B = 1.4$, NS

Margarete Ainsworth Building, Barker Street, Randwick NSW 2031. Phone: 02 9399 1000. Email: info@neura.edu.au

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Subgroup analysis showed no significant differences between studies with different sample acquisition methods: First admission; incidence rate ratio = 2.2, 95%CI = 1.9 to 2.6 Q_W = 961.2, I^2 = 95.5%, $p < 0.01$ First contact; incidence rate ratio = 2.9, 95%CI = 2.1 to 4.0 Q_W = 103.56, I^2 = 84.5%, $p < 0.01$ Q_B = 2.2, NS
Subgroup analysis showed no significant difference in risk based on diagnostic tool: DSM-IV; incidence rate ratio = 2.0, 95%CI = 1.5 to 2.5 Q_W = 20.4, I^2 = 65.7%, $p < 0.01$ ICD; incidence rate ratio = 2.2, 95%CI = 1.9 to 2.7 Q_W = 570.2, I^2 = 94.6%, $p < 0.01$ Non-standardised; incidence rate ratio = 2.7, 95%CI = 2.1 to 3.5 Q_W = 444.4, I^2 = 95.5%, $p < 0.01$ Q_B = 3.0, NS
Subgroup analysis showed no significant differences between high and average/low quality studies: High quality studies; incidence rate ratio = 2.2, 95%CI = 1.7 to 2.5 Q_W = 37.6, I^2 = 65.4%, $p < 0.01$ Average and low-quality studies; incidence rate ratio = 2.4, 95%CI = 2.1 to 2.8 Q_W = 1010.5, I^2 = 95.4%, $p < 0.01$ Q_B = 1.6, NS
Second-generation migrants
Significant increased incidence of schizophrenia for second-generation migrants: 10 population level studies, N = 4422 Incidence rate ratio = 2.1, 95%CI = 1.8 to 2.5 Q_W = 302, I^2 = 91.1%, 4.5, $p < 0.01$

Incidence in migrants

Subgroup analysis showed no differences in risk between male and female second-generation migrants:

Males; Incidence rate ratio = 2.5, 95%CI = 1.8 to 3.4

Q_W = 56.7, I^2 = 78.8%, $p < 0.01$

Females; Incidence rate ratio = 3.0, 95%CI = 2.1 to 4.2

Q_W = 33.2, I^2 = 63.9%, $p < 0.01$

Q_B = 0.60, NS

Subgroup analysis showed highest risk is for second-generation migrants where black skin is the majority in their country of origin:

Black; Incidence rate ratio = 5.4, 95%CI = 3.2 to 8.8

Q_W = 28.4, I^2 = 78.9%, $p < 0.01$

Other; Incidence rate ratio = 2.0, 95%CI = 1.0 to 4.0

Q_W = 15.3, I^2 = 73.8%, $p < 0.01$

White; Incidence rate ratio = 1.9, 95%CI = 1.2 to 3.0

Q_W = 23.5, I^2 = 87.2%, $p < 0.01$

Q_B = 10.6, $p < 0.01$

Subgroup analysis showed risk is highest for second-generation migrants from black African and black Caribbean ethno-racial groups:

White; incidence rate ratio = 2.3, 95%CI = 2.1 to 2.7

Q_W = 1.17, I^2 = 0%, $p < 0.05$

Black Caribbean; incidence rate ratio = 5.8, 95%CI unclear

Q_W = 26.3, I^2 = 77.2%, $p < 0.01$

Black African; incidence rate ratio = 3.7, 95%CI = 2.2 to 6.3

Q_W, I^2, p, NA – one effect size

Asian; incidence rate ratio = 1.3, 95%CI = 0.8 to 2.1

Q_W = 0.06, I^2 = 0%, p unclear

Middle East; incidence rate ratio = 2.3, 95%CI = 1.4 to 4.0

Q_W = 2.93, I^2 = 65.8%, $p < 0.01$

Q_B = 19.9, $p < 0.01$

Subgroup analysis showed risk is highest for second-generation migrants living in the UK and The Netherlands:

Israel; incidence rate ratio = 1.1, 95%CI = 0.9 to 1.3

Q_W = 12.8, I^2 = 68.8%, $p < 0.05$

Margarete Ainsworth Building, Barker Street, Randwick NSW 2031. Phone: 02 9399 1000. Email: info@neura.edu.au

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The Netherlands; incidence rate ratio = 3.0, 95%CI = 2.1 to 4.4

Q_W = 7.2, I^2 = 30.7%, NS

Scandinavia; incidence rate ratio = 1.8, 95%CI = 1.6 to 2.0

Q_W = 46.0, I^2 = 84.8%, $p < 0.01$

UK; incidence rate ratio = 3.7, 95%CI = 2.1 to 6.6

Q_W = 64.5, I^2 = 87.6%, $p < 0.01$

Q_B = 34.1, $p < 0.01$

Subgroup analysis showed no significant difference in risk based on study setting:

Mixed urban/rural study setting; incidence rate ratio = 1.7, 95%CI = 1.5 to 2.0

Q_W = 48.2, I^2 = 83.4%, $p < 0.01$

Urban study setting; incidence rate ratio = 2.6, 95%CI = 1.7 to 3.9

Q_W = 253.1, I^2 = 92.9%, $p < 0.01$

Q_B = 3.0, NS (trend)

Subgroup analysis showed risk is higher in second-generation samples from first contact studies:

First admission; incidence rate ratio = 1.6, 95%CI = 1.3 to 1.8

Q_W = 149.8, I^2 = 91.3%, $p < 0.01$

First contact; incidence rate ratio = 3.2, 95%CI = 2.1 to 4.7

Q_W = 67.6, I^2 = 80.8%, $p < 0.01$

Q_B = 10.6, $p < 0.01$

Subgroup analysis showed no significant difference in risk based on diagnostic tool:

DSM-IV; incidence rate ratio = 2.4, 95%CI = 1.4 to 4.1

Q_W = 24.9, I^2 = 79.9%, $p < 0.01$

ICD; incidence rate ratio = 1.9, 95%CI = 1.6 to 2.2

Q_W = 230.5, I^2 = 91.8%, $p < 0.01$

Non-standardised; incidence rate ratio = 3.7, 95%CI = 0.4 to 31.2

Q_W = 4.18, I^2 = 76.07%, $p < 0.01$

Q_B = 1.1, NS

Subgroup analysis showed no significant differences between high and average/low quality studies:

High quality studies; incidence rate ratio = 2.7, 95%CI = 1.9 to 3.7

Q_W = 32.2, I^2 = 65.8%, $p < 0.01$

Average and low-quality studies; incidence rate ratio = 1.8, 95%CI = 1.5 to 2.2

Incidence in migrants

$Q_W = 228.7$, $I^2 = 93.4\%$, $p < 0.01$ $Q_B = 3.8$, NS (trend)	
Consistency in results‡	Rates expected to vary across regions
Precision in results§	Unable to assess
Directness of results‖	Direct, apart from skin colour.

Castillejos MC, Martín-Pérez C, Moreno-Küstner B

A systematic review and meta-analysis of the incidence of psychotic disorders: the distribution of rates and the influence of gender, urbanicity, immigration and socio-economic level

Psychological Medicine 2018; 48: 2101–15

View review abstract online

Comparison	**Incidence of schizophrenia in migrants vs. native-born populations.**
Summary of evidence	**Moderate quality evidence (large sample, unable to assess consistency, imprecise, direct) suggests the incidence rate of schizophrenia or schizophreniform disorder is higher in migrants than in native-born populations.**
Diagnosis of schizophrenia or schizophreniform disorder	
A significant increased rate of schizophrenia or schizophreniform disorder in migrants; 4 population-based studies, IRR = 3.08, 95%CI 2.04 to 3.67, $p < 0.01$	
Consistency in results	Unable to assess – heterogeneity measure is not reported.
Precision in results	Imprecise
Directness of results	Direct

Jongsma HE, Turner C, Kirkbride JB, Jones PB

International incidence of psychotic disorders, 2002-17: a systematic

review and meta-analysis	
The Lancet Public Health 2019; 4: e229-e44 View review abstract online	
Comparison	**Incidence of schizophrenia in migrants vs. native-born populations.**
Summary of evidence	**Moderate to high quality evidence (large samples, inconsistent, precise, direct) suggests the incidence rate of schizophrenia is higher in migrants than in native-born populations.**
Diagnosis of schizophrenia	
A significant increased rate of schizophrenia or schizophreniform disorder in migrants; 6 studies (population and other designs), IRR = 1.41, 95%CI 1.15 to 1.75, $p < 0.05$, $I^2 = 88\%$	
Consistency in results	Inconsistent
Precision in results	Precise
Directness of results	Direct

McGrath J, Saha S, Welham J, El Saadi O, MacCauley C, Chant D

A systematic review of the incidence of schizophrenia: the distribution of rates and the influence of sex, urbanicity, migrant status and methodology

BMC Medicine 2004; 2: 13, doi:10.1186/1741-7015-2-13 View review abstract online	
Comparison	**Incidence of schizophrenia in migrants vs. native-born populations.**
Summary of evidence	**Moderate quality evidence (large samples, direct, unable to assess precision) suggests that the incidence of schizophrenia is higher in migrants compared to native-born individuals.**
Incidence of schizophrenia	

Incidence in migrants

24 observational studies in total (worldwide), population level data *Significantly increased incidence of schizophrenia for migrants compared to native-born populations:* Median rate ratio (10% and 90% quantiles) = 4.6 (1.0 to 12.8) Difference in harmonic means; $F_{1,13} = 51.8$, $p < 0.001$	
Consistency in results	Rates expected to vary across regions.
Precision in results	Unable to assess quantiles.
Directness of results	Direct measure of migration status

Explanation of acronyms

CI = confidence interval, IRR = incidence rate ratio, *p* = statistical probability of obtaining that result ($p < 0.05$ generally regarded as significant), Q_B = Q statistic (chi-square) for the test of differences in effect sizes between groups, Q_w = Q statistic (chi-square) for the test of heterogeneity in results across studies, vs. = versus

Margarete Ainsworth Building, Barker Street, Randwick NSW 2031. Phone: 02 9399 1000. Email: info@neura.edu.au

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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[7].

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† Different effect measures are reported by different reviews.

Reliability and validity refers to how accurate the instrument is. Sensitivity is the proportion of actual positives that are correctly identified - 100% sensitivity = predict all people who are at high risk as developing psychosis and specificity is the proportion of negatives that are correctly identified - 100% specificity = not predicting anyone as being at high risk 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. Standardized 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 moderate effect, and 0.8 and over represents a large effect[7].

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[8]. 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 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 trials (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 be considerable heterogeneity and over this is 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[9].

‖ 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 sized are of lower quality than those gained from head-to-head comparisons of A and B.

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