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Review article

Mood disorders in first- and second-generation immigrants: systematic review and meta-analysis

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Background
Although there are consistent reports of higher psychosis rates among immigrants, the information on mood disorders is limited.

Aims
To review and quantify the difference in incidence of mood disorders in first- and second-generation immigrant (FGI and SGI) groups *v.* non-immigrants.

Method
PubMed, EMBASE and PsycINFO were searched for articles from cohort studies reporting incidence of mood disorders among FGIs and SGIs.

Results
Eighteen studies met our inclusion criteria. The summary relative risk (RR) for FGIs was 1.25 (95% CI 1.11–1.41), based on 17 effect sizes and 6120 cases, and 1.16 (95% CI 0.96–1.40) for SGIs based on three effect sizes. Men seemed at higher risk (RR = 1.29, 95% CI 1.06–1.56).

Conclusions
Clinicians should view FGIs as a group at risk of mood disorders, especially men. Further research is needed to understand immigrants' risk, especially in SGI.

Declaration of interest
None.

With 3.2% of the world's population living outside their countries of birth,[1] the burden on health systems for understanding this population's risk of psychiatric disorder is pressing, along with its public health implications. Even for people who have not experienced forced migration due to refugee status, trafficking or traumatic events in their home countries, migration experiences encompass a number of adverse and stressful events, such as language barriers, cultural bereavement, marginalisation, isolation, discrimination and uncertainty regarding legal status.[2] Although there are consistent reports of a higher rate of psychosis among certain groups of immigrants,[3–5] there is little information on their risk of mood and anxiety disorders. Previous reviews on the subject did not find conclusive evidence for increased risk of mood disorders associated with migration.[6] However, they were limited in their sample size to examine the differential risk for first-generation immigrant (FGI) *v.* second-generation immigrant (SGI) groups – with the added problem of the term SGI being fraught with semantic difficulties – compared with native populations. Cross-sectional studies have found that whereas FGIs had a lower prevalence of mood and anxiety disorders compared with the native populations, this seemingly protective effect of immigration was somewhat attenuated in SGIs.[7] To our knowledge, no previous review has examined the differential risk for mood and anxiety disorders between FGIs and SGIs. The goal of this systematic review and meta-analysis was to synthesise the global evidence of the difference in incidence of mood and anxiety disorders in first- *v.* second-generation immigrant groups compared with native populations.

Method

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement for performing and reporting the present systematic review was followed.[8] Ethical approval was not required as our review used aggregate data from published studies. We searched for population-based incidence studies of FGIs and SGIs who had a diagnosis of a mood or anxiety disorder (measured by a validated tool or clinical diagnosis) or a record of hospital admission or first contact with mental health services for a mood or anxiety disorder.

Search strategy

The electronic databases PubMed, EMBASE and PsycINFO were searched through to 1 December 2014 without any country or language restriction. Searches were not limited by publication year. For PubMed a combination of MeSH terms and keywords were used as follows: (("Cohort Studies"[Mesh] OR cohort studies)) AND ((((((("Emigration and Immigration"[Mesh]) OR "Ethnic Groups"[Mesh])) OR ((((immigrant OR immigrants)) OR (alien OR aliens)) OR (foreigner OR foreigners)))) AND ((((((("Mood Disorders"[Mesh]) OR "Anxiety Disorders"[Mesh]) OR "Depression"[Mesh])) OR ((((((mood disorder) OR mood disorders) OR affective disorder) OR affective disorders)) OR depression)) OR (((((anxiety disorder) OR anxiety disorders) OR anxiety neuroses) OR neurotic anxiety states) OR neurotic anxiety states))). For EMBASE, EMTREE terms Migrant AND Anxiety Disorder OR Mood Disorder were used, using the terms also as free text in all fields, and exploding using narrower EMTREE terms as follows: 'anxiety disorder'/exp OR 'anxiety disorder' OR 'mood disorder'/exp OR 'mood disorder' AND ('migrant'/exp OR 'migrant'). For PsycINFO the following combination of index terms and keywords were used: (Human Migration) OR Index Terms: (Immigration) AND Any Field: (Affective Disorders) OR (Anxiety Disorders). Results were then narrowed by longitudinal, follow-up or prospective study design. The search was then limited by study type to cohort and longitudinal studies. Relevant reference lists were manually searched for any additional studies that could have been missed.

Eligibility criteria

Titles and abstracts of all citations identified were evaluated for appropriateness by the lead reviewer, applying predetermined criteria as per the study protocol (see online supplement DS1).

Potentially eligible articles were retrieved and the full text was reviewed. To be considered for inclusion the study had to report original data (i.e. not previously reported) and distinguish by FGI or SGI status. Studies that measured ethnicity as opposed to migrant status were excluded. Only population-based studies that reported age-adjusted incidence of either mood or anxiety disorder, or a combination of these conditions, were considered, in order to assess risk. All other study designs were excluded from this review in order to establish temporality and ensure migration preceded the mood disorder (which would not have been possible if designs such as cross-sectional studies were included). We included studies reporting risk estimates and their standard errors or confidence intervals for the association between immigrant status and incidence of mood/anxiety disorders, or enough information to calculate these. In this review, only adult populations were included to ensure comparability across diagnostic measurements. Other psychiatric diagnoses and mood/anxiety disorders secondary to other illnesses or conditions were excluded.

Uncertainty over inclusion at each stage of screening was discussed between authors. No study was excluded *a priori* for design weakness or quality. Unpublished studies were not considered. For different studies reporting overlapping data, the report with the longest follow-up period was selected.

Quality assessment

To assess the quality of the studies included in this review, the guidelines established in the Newcastle–Ottawa Scale for assessing quality of non-randomised observational studies in meta-analysis were followed.[9]

Data extraction

A template was developed for data extraction, which included study identity, first author, publication year, whether ICD or DSM was used, diagnosis, immigrant generation, refugee status, gender, region of origin, population, cases, incidence, risk estimate, 95% confidence intervals, confounders considered and quality score. Where available, information regarding risk estimates by gender was extracted, as was done for diagnosis type. Region of origin was classified into the following categories: sub-Saharan Africa, Asia (excluding west Asia), Europe, west Asia and north Africa, and the Americas. Where region of origin was not specified or was incompatible with these categories, estimates were recorded as 'not otherwise categorised'. Studies that did not report specifically whether or not they included refugees were classified as 'possibly including refugees', unless the region of origin made it reasonable to infer that immigrants were not refugees (e.g. immigrants to the UK from Commonwealth countries). For studies that did not provide a relative risk (RR), this was calculated using the number of cases, incidence and the population at risk when these were provided. The maximally adjusted results were used when several risk estimates with various adjustments were available.

Statistical analysis

We calculated the summary risk estimates and their confidence intervals using a two-step approach. We first used a fixed effects model within studies that did not provide a summary estimate, followed by a random effects model between studies, on the assumption that there were sources of heterogeneity between studies beyond random fluctuations.[10] Forest plots were generated for the association between immigrant generation and incidence of mood/anxiety disorders, along with results categorised according to gender, region of origin and diagnosis when available. To assess heterogeneity between studies, the I^2 and P values associated with Q statistics were used. Sensitivity analysis was conducted excluding studies on refugee populations, studies with quality scores lower than 7, studies where risk estimates were not provided and had to be calculated by us, and studies that did not follow ICD or DSM diagnostic criteria. A separate analysis on major depression was not possible owing to the small number of studies reporting this diagnosis separately. We therefore carried out a meta-analysis for any mood disorder (ICD-10 codes F30–F39) and another for bipolar affective disorder (ICD-10 codes F30–F31). All statistical analyses were performed using Stata version 14 and SAS version 9.3.

Results

A total of 1161 articles were identified through the electronic database search (online Fig. DS1). We found an additional 25 potentially relevant articles through manual search of the relevant reference lists. Therefore, a total of 1186 articles were included in the abstract screening phase. A total of 951 were excluded because they did not fulfil the inclusion criteria. The remaining 235 studies were assessed for eligibility, including all studies with no abstract. Twenty studies were included in the qualitative synthesis. Of these, one article could not be considered for data extraction because it did not provide risk estimates, nor the information needed to calculate these.[11] Two studies reported overlapping data,[12,13] and therefore a decision was made in favour of the study that covered the longest period.[13] Finally, 18 studies were included in the meta-analysis.[4,13–29] Six of these studies were from the UK,[18,21,23–25,29] four from Denmark,[4,15,17,22] three from Sweden,[13,14,16] and one each from Israel,[20] the USA,[28] Germany,[26] The Netherlands,[19] and Australia.[27] No population-based incidence study was found for anxiety disorders. Key features of the studies included in the meta-analysis can be found in online Table DS1. Most studies showed FGIs to be at higher risk of mood disorders;[13,14,17–20,23,24,28] one study showed a protective effect for FGIs,[4] and six studies did not find a significant relationship.[15,22,25–27,29] For SGIs two studies showed an increased risk,[4,16] and one did not find a significant association.[21]

All studies controlled for the potential confounding effect of age, either by adjustment, restriction or stratification. Although some studies did not report specific upper and lower age limits, most studies included participants aged 15–64 years. Four studies did not control for the effect of gender.[20,21,23,26] One study provided relevant data only for men.[18] All the other studies either adjusted for the effect of gender or reported separate estimates for men and women. A subset of studies also adjusted for other factors such as region of origin, employment, marital status, urbanisation, education, income and calendar year. Of the 18 studies included in the meta-analysis, 13 reported cases based on ICD or DSM diagnostic criteria, whereas the remaining 5 used either operational definitions,[23–25] the Present State Examination schedule based on ICD-8,[18] or did not mention how diagnostic criteria were defined.[27,28] With regard to quality (online Table DS2), five studies were given the highest possible score of 9;[4,13,14,19,22] six studies were given a score of 8,[15–17,25,27,29] and four were given a score of 7.[18,21,23,24] One study was given a score of 6,[28] and the remaining two were given a score of 5.[20,26] The risk estimates for nine of the included studies had to be derived from the information given (incidence, number of cases, population at risk).[18,20,21,23,25–29] All studies assessed information through medical records, using either registry data or case-finding in hospital catchment areas.

Meta-analysis

Results of the primary analysis can be found in online Table DS3. The result of the meta-analysis for FGIs is presented in Fig. 1. The summary RR was 1.25 (95% CI 1.11–1.41), based on 17 effect estimates and 6120 cases, whereas the summary RR for SGIs was 1.16 (95% CI 0.96–1.40), based on three effect estimates. The results of the meta-analysis for gender-specific estimates are presented in Figs 2 and 3 for men and women respectively. The RR for mood disorders for FGIs was 1.29 (95% CI 1.06–1.56) for men and 1.05 (95% CI 0.85–1.31) for women. A *Q*-test for heterogeneity between the RRs for FGI men *v.* women was not significant ($P = 0.17$). Six studies allowed separate analysis of the risk of bipolar affective disorder in FGIs, resulting in a summary RR = 1.09 (95% CI 0.89–1.34) (Fig. 4). A separate analysis was also carried out on FGIs excluding refugees for all mood disorders, and the summary RR was 1.22 (95% CI 1.07–1.39), based on 11 effect estimates (Fig. 5).

In regard to region of origin, although our estimates were based on a limited number of studies owing to the heterogeneity in reporting immigrant origin, an association was detected for the studies from the Americas (RR = 1.84, 95% CI 1.07–3.17). The results from the remaining regions were not statistically different and were limited by small numbers. Separate analysis compared studies that used DSM or ICD criteria in any of their versions with studies that used operational criteria defined by the authors: studies that used DSM or ICD criteria had a summary estimate of RR = 1.19 (95% CI 1.04–1.37) *v.* RR = 1.46 (95% CI 0.88–2.41), indicating no effect modification.

Two separate analyses investigated study quality. First, a meta-analysis was carried out for all mood disorders in FGIs, excluding studies with low weight. The resulting RR = 1.11 (95% CI 0.99–1.25) was obtained from summary estimates of 13 studies. The second analysis excluded studies that were given a score below 7 on the Newcastle–Ottawa Scale. A total of 14 effect sizes were taken to calculate the risk estimate for FGI for all mood disorders of RR = 1.28 (95% CI 1.11–1.48). Finally, a meta-analysis excluded studies whose risk estimates had to be derived because they were not provided in the original publication; the summary risk estimate for FGIs and for all mood disorders was RR = 1.17 (95% CI 1.00–1.36), based on seven effect estimates.

Publication bias

Both Egger's and Begg's tests were used to assess asymmetry due to possible publication bias, for the meta-analysis of mood disorders in FGIs.[30,31] We performed the Begg & Mazumdar adjusted rank correlation test for publication bias,[31] and the regression asymmetry test of Egger *et al* for publication bias,[30] along with its corresponding funnel plot. Neither the Begg ($z = 0.66$, $P = 0.51$) nor the Egger's (bias −3.58, $P = 0.38$) test provided evidence of publication bias (online Figs DS2, DS3).

Discussion

Our updated review and meta-analysis provides a systematic assessment of the risk of mood disorders among FGIs and SGIs. Being an FGI increased the risk of mood disorder by a quarter, a relationship that was found to be significant even after controlling for the possible confounding effects of refugee status,

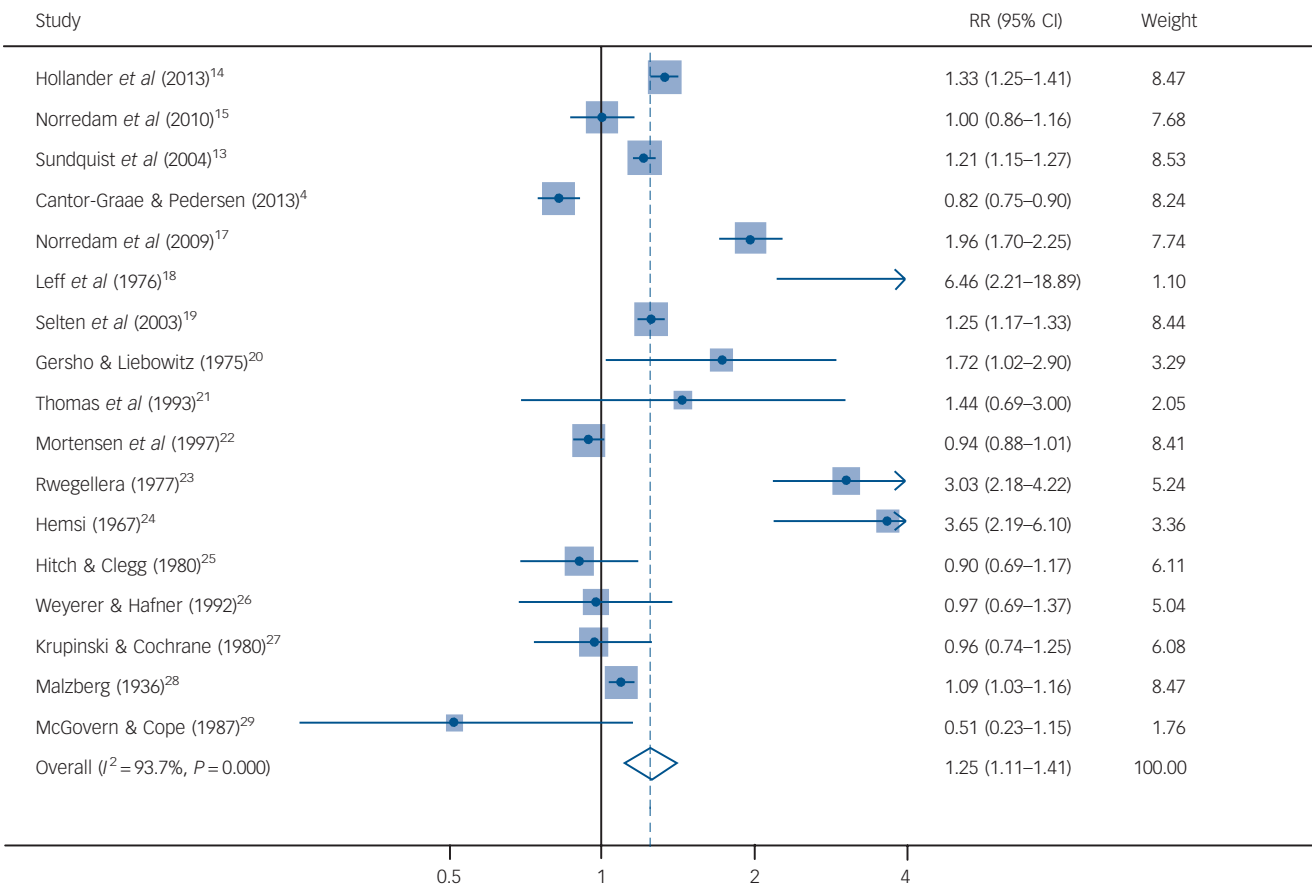

Fig. 1 Meta-analysis of mood disorders in first-generation immigrants. RR, relative risk.

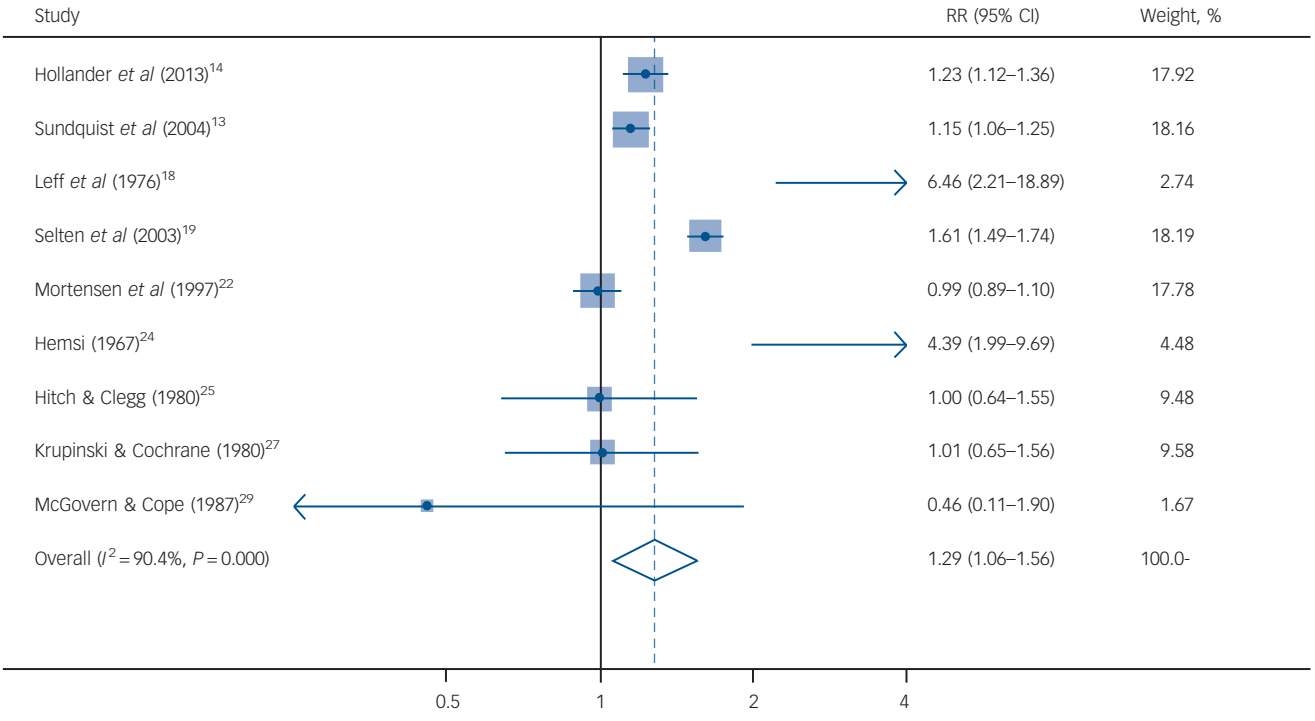

Fig. 2 First-generation immigrants: men. RR, relative risk.

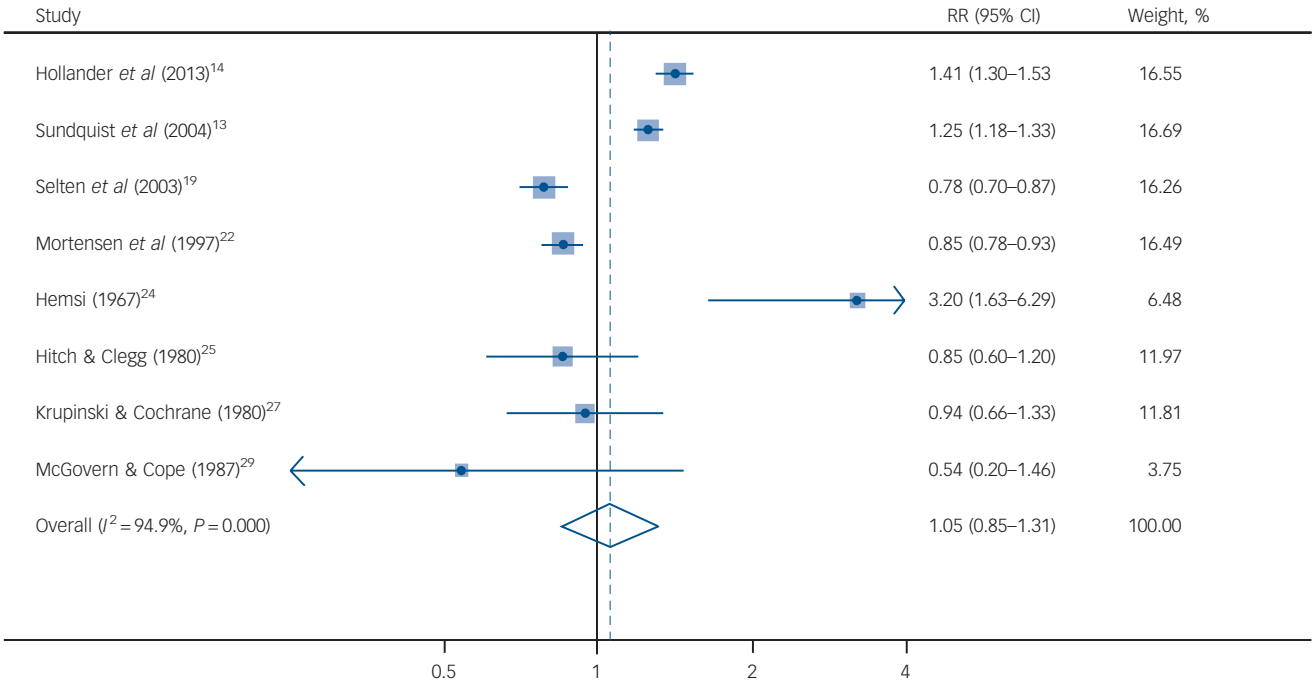

Fig. 3 First-generation immigrants: women. RR, relative risk.

study quality, age, gender and diagnosis. Second-generation immigrants did not seem to be at an increased risk of mood disorder, but this was based on three effect estimates only; furthermore, the summary risk estimates for FGI and SGI were not significantly different. Moreover, FGI men appeared to experience an increased risk of mood disorder in comparison with native-born individuals, whereas women did not seem to be at an increased risk. The excess risk found in men is consistent with the findings of the previous systematic review,[6] and should be interpreted with caution given the effect size. These results could be influenced by patterns in help-seeking behaviours; however, this is unlikely to account for all of the variance concerning different immigrant groups in different host countries. The excess risk found in men could be attributed to the experience of smaller support networks for primary migrant men, compared with those migrating for family reunification or accompanying spouses. Even

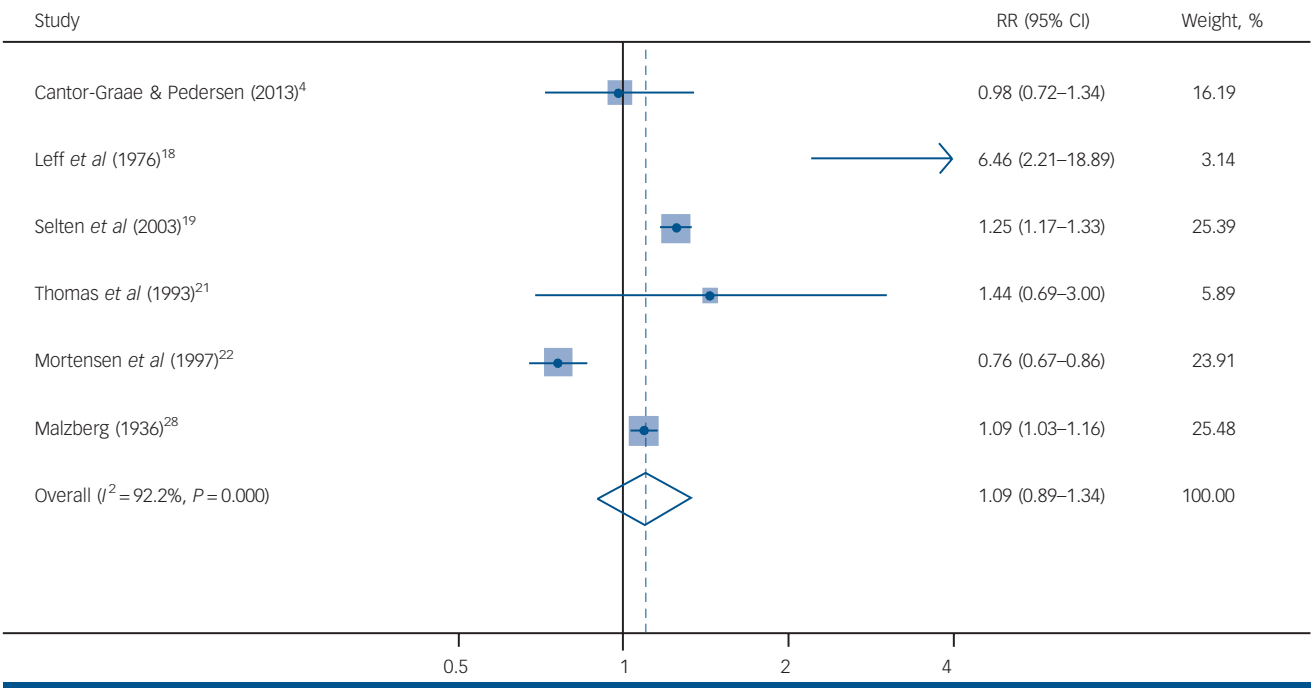

Fig. 4 Meta-analysis of bipolar affective disorder in first-generation immigrants. RR, relative risk.

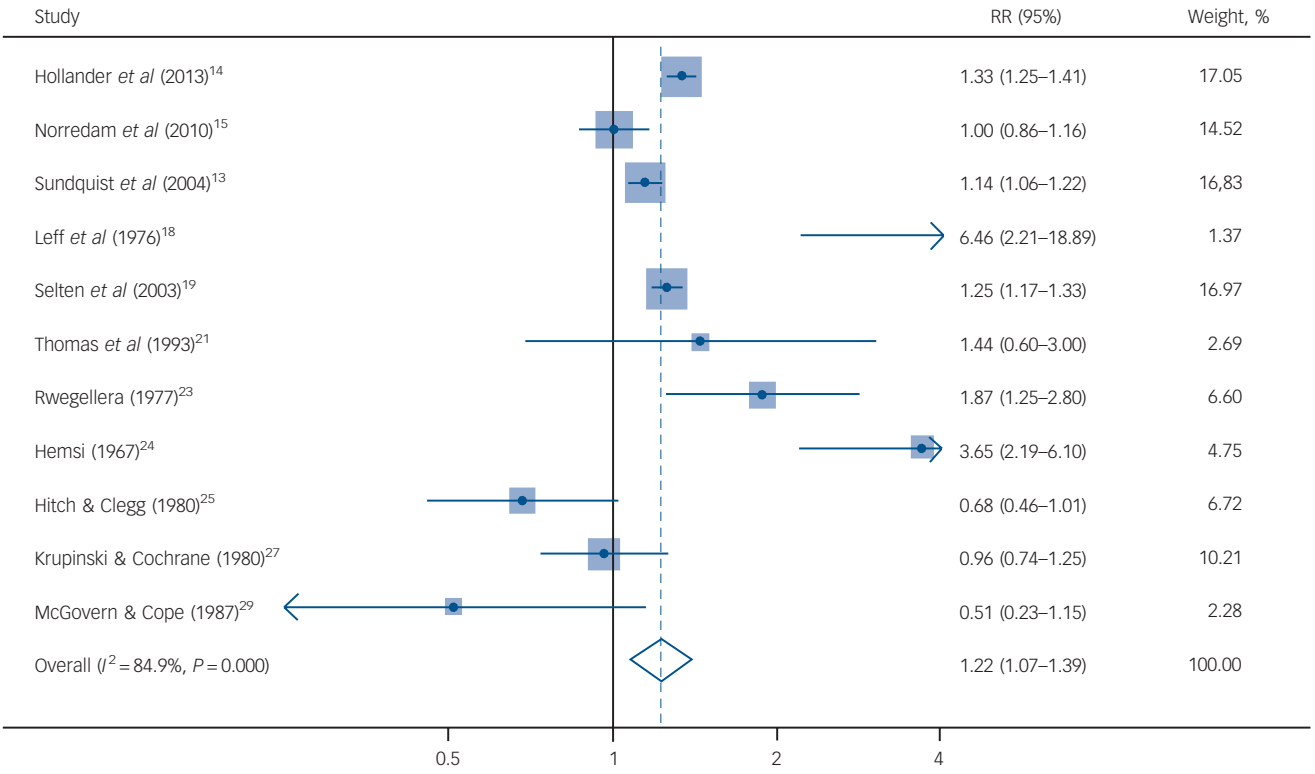

Fig. 5 Meta-analysis of all mood disorders in first-generation immigrants, excluding refugees. RR, relative risk.

if some men also migrate for these reasons, women appear to be more likely than men to migrate to join or accompany family members or because of marriage.[32–34] It was not possible, however, to test this hypothesis because no information was available regarding support networks for immigrants or whether they had emigrated alone or with their spouses or families, and the possible difference in risk between male and female FGIs warrants further investigation.

Although previous studies show higher rates among immigrants from the Caribbean, it should be noted that these studies are based on a limited number of cases, and that some were based on ethnicity as opposed to country of birth.[6,35]

Because of the heterogeneity in classifying region of origin across studies, it was difficult to explore in detail whether migration from different regions indeed carried differential risks. It is well established that refugees are at a higher risk of mood and anxiety disorders, with prevalence rates in refugees almost twice as high as those found among non-refugee migrants.[36] It is therefore important to distinguish between refugee and non-refugee immigrant populations, since otherwise the resulting summary estimates could overestimate risk among non-refugees. In our study, even after excluding studies of refugee populations, and studies that reported results comprising refugee and non-refugee migrants, our estimates for FGIs remained significant, supporting the hypothesis that non-refugee immigrants are nonetheless at an increased risk of mood disorders.

On the basis of a limited number of studies (six) we could not conclude that immigrants were at higher risk of bipolar affective disorder compared with non-immigrants. Although the previous systematic review had found a significantly higher risk of bipolar disorder among immigrants,[6] the heterogeneity found between studies could have been due to sampling error. Although in our study Q statistics indicated that the non-significance of the bipolar disorder summary estimate could not be due only to sampling error, it is noteworthy that of the six studies included in the calculation of this summary estimate at least one did not specify how the diagnosis had been made, and pre-dated the ICD and DSM classification systems.[28] However, it is difficult to draw conclusions based on the small number of studies available. We could not investigate the risk of major depressive disorder separately, since only a limited number of studies provided specific estimates for this diagnosis.

The literature on immigrant mental health has consistently found FGIs and SGIs to be at an increased risk of schizophrenia, but the research on mood disorders has been limited. A previous meta-analysis found no evidence to support the hypothesis of an increased risk of mood disorders in immigrants.[6] The differences in the results with our review could be accounted for by studies published recently, which have allowed us to compare FGIs and SGIs, as well as including individuals specifically identified as immigrants, as opposed to selecting individuals by ethnicity. Different explanations for the excess risk in immigrants have postulated both pre- and post-migration factors. Post-migratory stress is a contributing factor in the onset of depression,[37,38] along with experiences of discrimination and acculturation, with risk of depression increasing with length of stay.[39–42] Stress can come from the isolation, discrimination and perceived hostility found in communities where there is a negative context of reception, as opposed to communities offering positive contexts of reception with a larger opportunity structure, openness and acceptance.[43] Acculturation stress has been proposed to act on the hypothalamic–pituitary–adrenal axis, increasing the risk of depression.[39] Low socioeconomic status (SES), commonly associated with immigrant status, is also a well-established risk factor for hospital admissions for mental disorders.[44,45] It is, however, unlikely that SES on its own explains the difference in FGIs since increasingly more studies have adjusted for its possible confounding effect. The effects of social support networks on health have also been researched, with poor mental health being more likely to be associated with a lack of support,[46–52] whereas strong networks have protective effects on the risk of mood disorders.[46–48,50,53,54] Social support has been proposed as an explanation for the 'Latino paradox' in people of Hispanic origin in the USA, who appear to be in better health than non-immigrants. Strong support networks in these populations would serve to buffer the detrimental effect of discrimination and poverty.[55,56] This hypothesis may not hold equally across all immigrant groups and host countries, where social support networks may differ.

Strengths and limitations

One of the strengths of this study is the use of a written protocol, prepared in advance, to guide the method of review, data extraction and analysis. The use of the PRISMA guidelines is an approach that minimises bias.[8] Our search strategy maximised the possibility of identifying all relevant studies, and reference lists were also searched. We also considered publication bias in our analysis. Another strength was the inclusion of studies that measured migrant status, as opposed to relying on proxy indicators such as ethnic group, since individuals of a non-native ethnic group could have been in the country for many generations and therefore not have necessarily had experiences comparable with those of FGIs and SGIs. Along these lines, it seems that there could be a differential risk between FGIs and SGIs for mood disorders, like that observed in schizophrenia, although the evidence for differential risks between generations is mixed,[3,57] which warrants the need to study these populations separately. Although it was not always possible to control for the effect of various potential confounders owing to the heterogeneity in variable measurement in each study (e.g. region of origin), we attempted to tease apart the possible confounding effect of country of birth, gender, age, quality and diagnosis, among other variables. The fact that we included only population-based incidence studies allowed us to consider the cumulative risk for mood disorders in these populations, and capture the incidence of these disorders.

Selection is always a potential source of bias in studies on immigrant risk for various health outcomes, where the question is whether the sample population was in some way different from the non-migrant population in the country of origin, and whether this favoured immigration.[58] Recent studies, however, suggest this may not be the case.[59,60] The fact that data on SGIs and mood disorders are limited means that the conclusions drawn for this population should be interpreted with caution until more studies become available. Some of the earlier studies included in this meta-analysis were based on a small number of cases. However, we limited this possible bias by conducting sensitivity analysis excluding studies with low weight. Our main limitation was that the first stages of the systematic review were carried out by only one author; however, a detailed protocol was in place to guide this process, and any disagreement was discussed between authors.

Implications

Irrespective of the reasons for migration, the process of migrating in itself can be a highly stressful life event, which could lead to a higher risk of mood disorders. Immigrants can be vulnerable populations, with poorer access to the job market, education and employment. With 232 million international migrants in 2013,[1] there is a great need to prevent mental health disorders among this group, not only for the impact that mental disorders can have directly, but also indirectly through its moderating effect on a myriad of health conditions. Although a family history of mental illness and biological factors remain significant risk factors for mood disorders, the main clinical implication of our review is that FGIs – especially men – should be viewed as a group at risk of such disorders. Future research should attempt to study immigrant generations separately, since their stressors are different: whereas FGIs can experience migration and settling in a different country as stressful, SGIs can experience stress due to being bicultural. Greater homogeneity is also needed in respect to region of origin, to be able to understand whether different groups carry different risks. Lastly, although most research regarding the mental health of immigrants has focused on schizophrenia, greater attention should be paid to disorders that are more prevalent and overwhelmingly costly to individuals, their families and the community at large.

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EXTRA CONTENT ONLINE

psychiatry in literature

What *Lord of the Flies* teaches us about primitive defence mechanisms and societal discontent

Ruchi Bhalla and Christopher Kowalski

Published in 1954, William Golding's *Lord of the Flies* is one of the most celebrated pieces of literature of all time. Its depiction of a fragile community descending into violence and chaos seems all too relevant to modern-day society, where increased levels of societal division and civil unrest need to be understood in the context of economic recession, increasing acts of terrorism, fear-mongering, and the fostering of 'in' and 'out' group mentality by politicians and the media. Reviewing the novel's narrative from a psychoanalytic perspective offers an insight into a number of primitive defence mechanisms which may be important for conceptualising current issues in British society.

Faced with the growing realisation that their chances of survival are dwindling, a group of boys stranded on an island with no adults surviving soon reverts to more primitive modes of functioning. Without adult containment, the group disintegrates and regresses to the paranoid–schizoid position, held by Melanie Klein to be the earliest phase of psychic development. This position is dominated by persecutory anxieties and schizoid mechanisms, such as projection and the splitting of objects into either good or bad. At the same time, repressed id drives towards violence and death begin to surface, creating a dangerous mix of fear, anxiety, rage and lust for destruction.

As the fabric of their society appears to crumble around them, the boys become more and more preoccupied with the perceived dangers lurking on the island. Together, they create an external object – the 'beastie' – which they identify as a threatening, hostile entity. The 'beastie' can be viewed as both a projective identification of the boys' anxieties about fear of extinction and an evacuation of the urges for violence and destruction that this anxiety has created.

Dealing with primitive defences that arise from unconscious fear and anxiety is a common part of psychiatric practice. The paranoid–schizoid position, where fear and anxiety are unconsciously projected into external objects, manifests itself as suspicion of and aggression towards others. This may become worse at times of uncertainty. What we are now seeing is the enactment of these defences on a much wider sociological level. In times of uncertainty, it is not uncommon for groups to look for a collective enemy into which they can project and evacuate their anxieties as well as direct their growing feelings of anger and discontent. This is reflected, for instance, in the current discourse around migrants and refugees. We see a reinforcing and validating of an 'us' and 'them' mentality. In *Lord of the Flies*, the group disintegrates into two distinct factions with two opposing leaders. Such splitting can also be viewed as the enactment of primitive defences. Perpetuating this 'us' and 'them' narrative and stoking of the boys' fear of the 'beastie' helps one of their leaders to gain control over the group.

For psychiatric practice, this 'in' and 'out' group mentality is particularly dangerous, as it may begin to extend to other marginalised groups in society. Patients with mental health difficulties may, therefore, be at risk of vilification and further stigmatisation.

Where the schoolboys were eventually saved from impending destruction by a rescue party of adults, it is difficult to see how the enactment of these primitive defences will be ameliorated in British society when the current discourse in many quarters seems to be seeking to perpetuate it.

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Data supplement to Mindlis & Boffetta. Mood disorders in first- and second-generation immigrants: systematic review and meta-analysis. Br J Psychiatry doi: 10.1192/bjp.bp.116.181107

Protocol for systematic review

Title: Mood & Anxiety Disorders in first vs second generation immigrants:

systematic-review & meta-analysis

Authors: Mindlis, I, Boffetta, P.

Commenced November 15, 2014

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Protocol Template: Systematic Review

Review title: Background

I. Important characteristics

What are the important population and/or disease characteristics (diagnostic criteria, epidemiology, aetiology, prognosis)?

First and second generation immigrants with any mood or anxiety disorder.

II. Relevance

Does the review topic have important implications for health (individual and/or public), as well as health care, policy and research?

The review topic has important implications for immigrant mental health

III. Rationale

Does the evidence (including existing systematic reviews) fail to answer the review question, and why?

There are no previous systematic reviews on this topic that looks individually at first vs second generation immigrants. While there are consistent reports of a high psychosis rate among certain groups of migrants, there is little information on their risk for mood or anxiety disorders in regards to generation.

A previous meta-analysis on mood disorders and immigration found no conclusive evidence for a large increase in the risk of mood disorders associated with migration, but it did not look at FGIs vs SGIs.

IV. Justification

Is the need for the review justified in the light of the potential health implications and current limitations of the evidence base?

This systematic review would help overcome limitations of previous studies.

V. Specification

What are the PICO components of the review question / objective?

P: immigrants

I: N/A

C: 1st vs 2nd generation

O: mood or anxiety disorders

2. Methods

I. Search strategy

Which electronic databases will you search?

PubMed, Embase, PsycInfo

What are your key search terms?

Immigration

Anxiety disorders

Mood disorders

What other sources will you search?

References in relevant articles

II. Selection criteria

What are the inclusion / exclusion criteria?

Adults

Differentiate by 1st or 2nd generation

Published

Original data

Exclusion: All other psychiatric diagnoses or mood/anxiety disorders secondary other illnesses or conditions

Will you impose any additional limits, e.g. language, publication type, study design?

Languages included: English, Spanish, Portuguese

Peer reviewed

Population-based incidence study design

Age-adjusted

How will study selection be performed?

Uncertainty over inclusion at each stage of screening will be discussed between authors.

III. Quality assessment

What criteria will be used to assess methodological quality?

Newcastle-Ottawa Scale (NOS) will be followed to assess quality.

How will quality assessment be performed?
As outlined in the NOS guidelines.

IV. Data extraction

What are the key data to be extracted?
Relative risks for natives, first, and second generation immigrants, with confidence intervals.

How will data extraction be performed, and how will extracted data be presented?
Data extraction will be conducted using a standardized collection forms and presented in tables.

V. Data synthesis

How will data be combined (statistical or narrative), and why?
Both statistically and narratively (quantitative & qualitative analysis), the qualitative analysis will allow to report any studies that cannot be included in the quantitative analysis due to limitations in their data reporting.

What are the potential sources of effect heterogeneity and how will they be assessed?
Differences in diagnostic methods: separate analysis to be done for studies that did not follow DSM/ICD criteria.

Refugees will be analysed separately

Sex specific analysis to be done where possible

Region of origin analysis to be done separately where possible

Diagnoses to be broken up by major categories

3. Process

I. What resources are required to conduct the review, and are they available?

Relevant expertise: *Yes*

Computing facilities: *Yes*

Research databases: *PubMed, Embase, PsycInfo*

Bibliographic software: *RefWorks*

Statistical software: *SAS & Stata*

II. How will the findings of the review be disseminated?

Target audience: *Scientific community*

Publication type: *Peer reviewed Journal*

4. Timetable

	Completion date
Draft protocol for internal review	11/28/14
Protocol for external review	12/01/14
Pilot	12/06/2014
Searching and study selection	2/18/2015
Data extraction	3/31/2015
Quality assessment	4/15/2015
Draft report for peer review	6/15/2015
Submit for publication	8/01/2015

Fig. DS1

PRISMA Flow Diagram of literature search

Mood Disorders in first vs second generation immigrants: systematic-review & meta-analysis

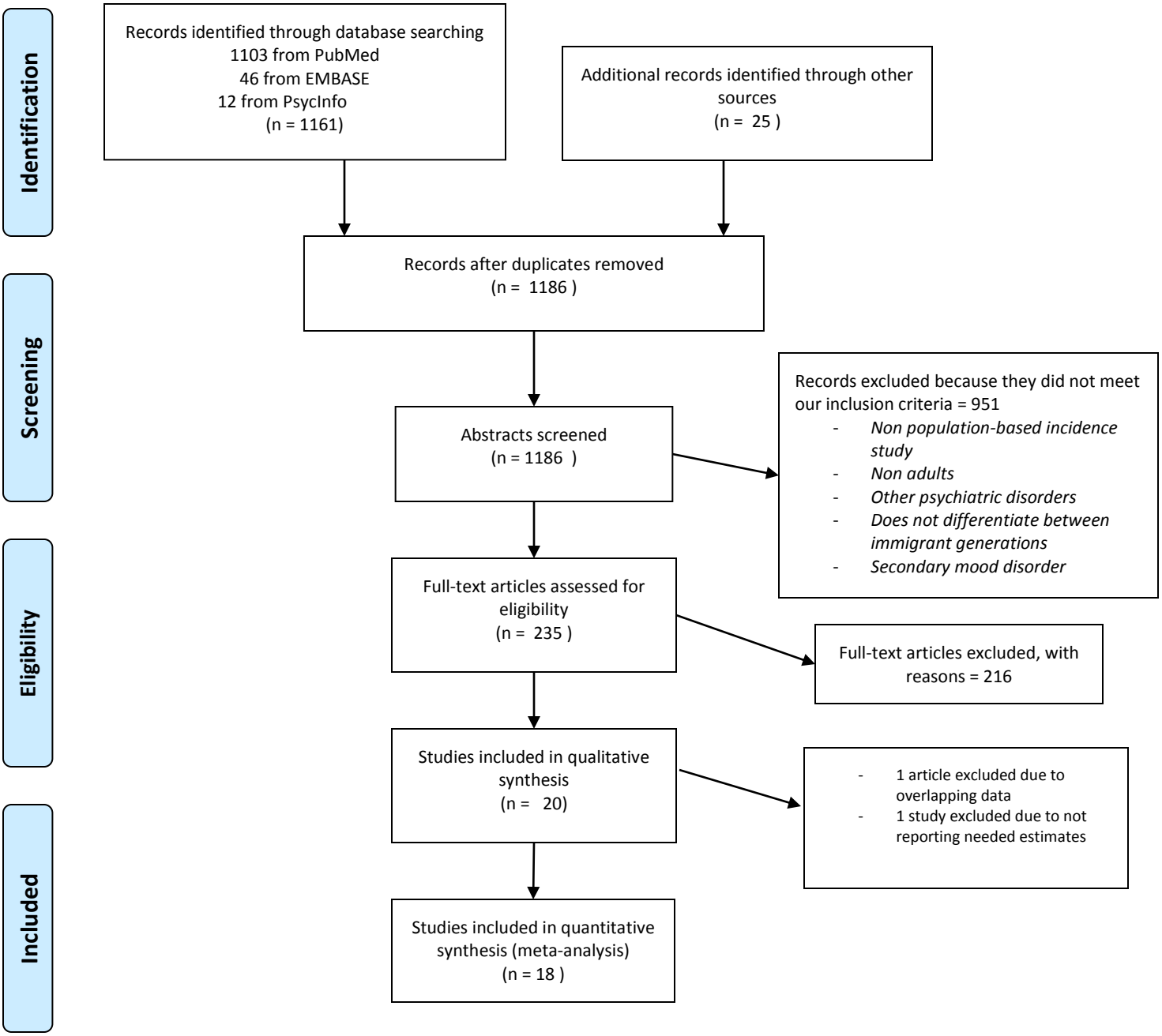

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Table DS1

Design of population based cohort studies on mood disorders in first and second generation immigrants

First author and year	Country	Exposure	Time period	Relative risk (95% CI)
Hollander 2013	Sweden	FGI	2000-2006	1.33 (1.25-1.41)
Norredam 2010	Denmark	FGI	1994-2003	1.00 (0.86-1.15)
Sundquist 2004	Sweden	FGI	1997-1999	1.21 (1.15-1.27)
Saraiva Leao 2005	Sweden	SGI	1995-1998	1.28 (1.18-1.39)
Cantor-Graae 2013	Denmark	FGI	1995-2010	0.82 (0.75-0.9)
		SGI		1.05 (1.02-1.09)
Norredam 2009	Denmark	FGI	1994-2003	1.96 (1.7-2.25)
Leff 1976	UK	FGI	1965-1974	6.46 (2.21-18.89)
Selten 2003	Netherlands	FGI	1990-1996	1.25 (1.17-1.33)
Gershon 1975	Israel	FGI	1969-1972	1.72 (1.02-2.9)
Thomas 1993	UK	SGI	1984-1987	1.41 (0.19-10.55)
Mortensen 1997	Denmark	FGI	1980-1992	0.94 (0.88-1.01)
Rwegellera 1977	UK	FGI	1965-1968	3.03 (2.18-4.22)
Hemsi 1967	UK	FGI	1961	3.65 (2.19-6.11)
Hitch 1980	UK	FGI	1968-1970	0.9 (0.69-1.17)
Weyerer 1992	Germany	FGI	1974-1980	0.97 (0.69-1.38)
Krupinski 1980	Australia	FGI	1970-1972	0.96 (0.74-1.26)
Malzberg 1936	USA	FGI	1928-1931	1.09 (1.03-1.16)
McGovern 1987	UK	FGI	1980-1983	0.51 (0.23-1.16)

Table DS2 Quality assessment Mood & Anxiety Disorders in first vs second generation immigrants: a systematic-review

Study ID	Author	Year	Selection				Selection score	Comparability	Comparability score	Outcome			Outcome score	Total score
			Representativeness of the exposed cohort	Selection of non exposed cohort	Ascertainment of exposure	Demonstration that outcome was not present at baseline		Comparability of cohorts on the basis of the design or analysis		Assessment of outcome	Was follow-up long enough for the outcome to occur	Adequacy of follow up of cohorts		
1	Hollander	2013	High	High	High	High	4	High	2	High	High	High	3	9
2	Norredam	2010	High	High	High	No	3	High	2	High	High	High	3	8
3	Sundquist	2004	High	High	High	High	4	High	2	High	High	High	3	9
4	Saraiva Leao	2005	High	High	High	No	3	High	2	High	High	High	3	8
5	Cantor-Graae	2013	High	High	High	High	4	High	2	High	High	High	3	9
6	Norredam	2009	High	High	High	No	3	High	2	High	High	High	3	8
7	Leff	1976	High	High	High	No	3	High	2	High	High	No	2	7
8	Selten	2003	High	High	High	High	4	High	2	High	High	High	3	9
9	Gershon	1975	High	High	High	No	3	No	0	High	High	No	2	5
10	Thomas	1993	High	High	High	High	4	Medium	1	High	High	No	2	7
11	Mortensen	1997	High	High	High	High	4	High	2	High	High	High	3	9
12	Rwegellera	1977	High	High	High	High	4	No	0	High	High	High	3	7
13	Hemsi	1967	High	High	High	High	4	Medium	1	High	High	No	2	7
14	Hitch	1980	High	High	High	High	4	High	2	High	High	No	2	8
15	Weyerer	1992	High	High	No	No	2	Medium	1	High	High	No	2	5
16	Krupinski	1965	High	High	High	High	4	High	2	High	High	High	3	9
17	Krupinski	1980	High	High	High	High	4	High	2	High	High	No	2	8
18	Malzberg	1936	High	High	No	High	3	High	2	No	High	No	1	6
19	McGovern	1987	High	High	High	High	4	High	2	High	High	No	2	8

Table DS3 Results of the meta-analysis

Analysis	Number of studies	RR	95 % CI	P value for heterogeneity	I ^2
FGI	17	1.25	1.11 - 1.41	<0.001	93.7%
SGI	3	1.16	0.96 - 1.4	<0.001	89.7%
FGI men	9	1.29	1.06 - 1.56	<0.001	90.4%
FGI women	8	1.05	0.85 - 1.31	<0.001	94.9%
FGI Bipolar disorder	6	1.09	0.89 - 1.34	<0.001	92.2%
FGI excluding refugees	11	1.22	1.07 - 1.39	<0.001	84.9%
FGI excluding low weight	13	1.11	0.99 - 1.25	<0.001	93.8%
FGI Subsaharan Africa	3	1.03	0.11 - 9.45	<0.001	96.3%
FGI Asia	3	0.68	0.28 - 1.64	0.019	74.9%
FGI Europe	3	1.29	0.72 - 2.31	<0.001	94.4%
FGI Americas	6	1.84	1.07 - 3.17	<0.001	85.5%
FGI using DSM or ICD criteria	12	1.19	1.04 - 1.37	<0.001	94.3%
FGI not following DSM or ICD criteria	5	1.46	0.88 - 2.41	<0.001	93.6%
FGI excluding quality score <7	14	1.28	1.11 - 1.48	<0.001	94.8%
FGI Derived by authors	7	1.17	1.00 - 1.36	<0.001	96.6%

Fig. DS2 Funnel plot with pseudo 95% confidence limits

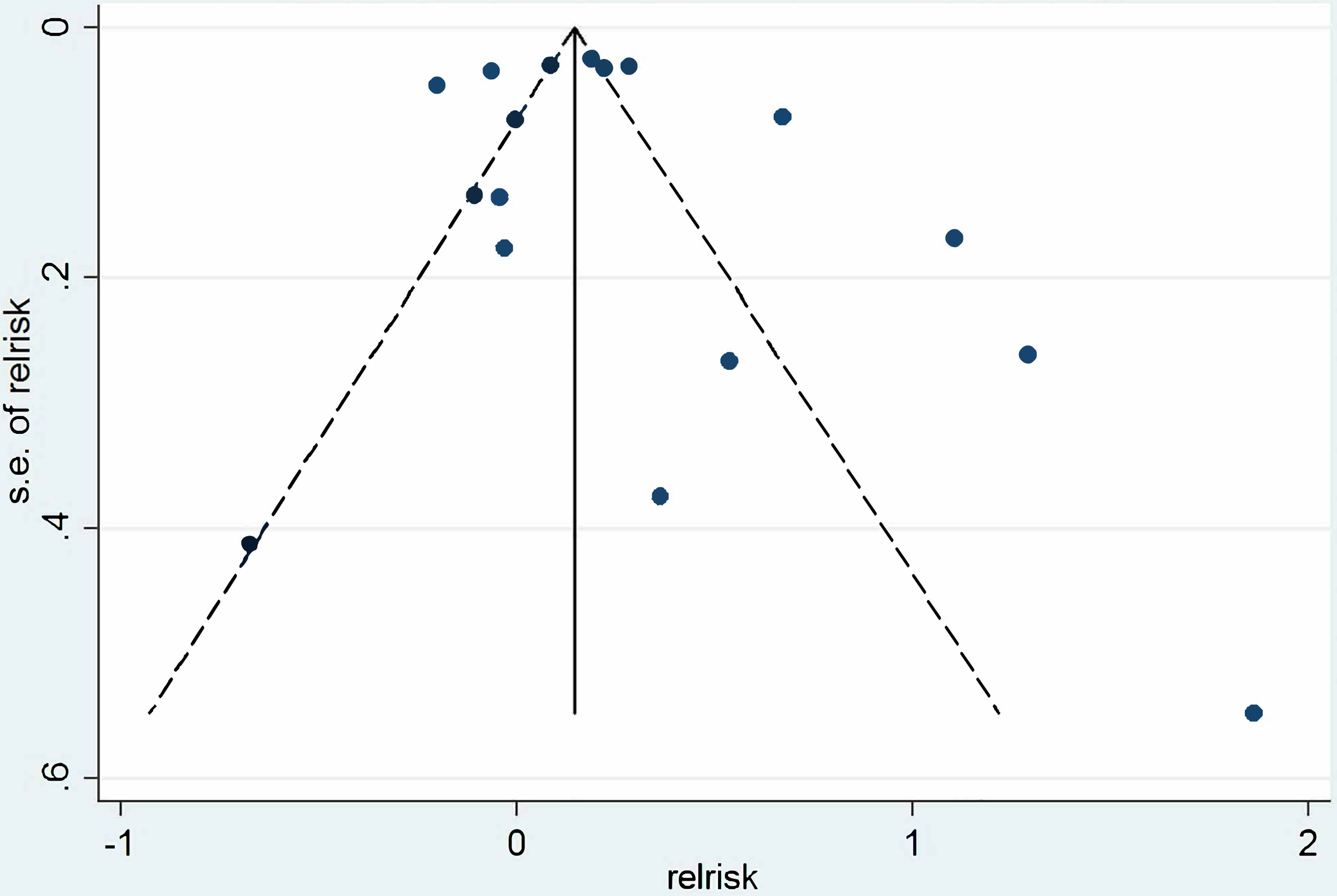
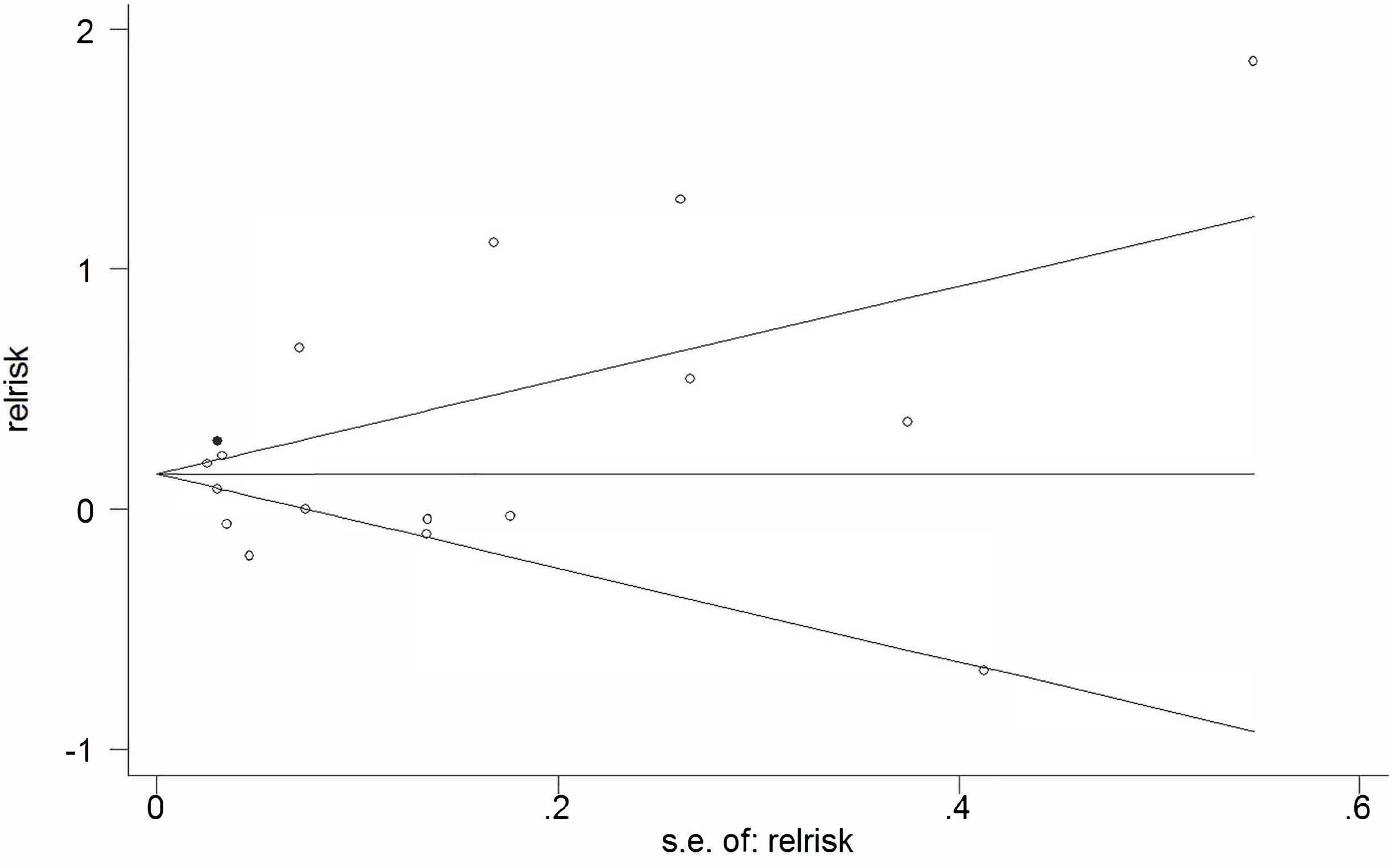


Fig. DS3 Begg's funnel plot with pseudo 95% confidence limits



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