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# Increased rates of schizophrenia among immigrants: some methodological concerns raised by Danish findings

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## ABSTRACT

**Background.** Several studies during recent years have reported an increased occurrence of schizophrenia in selected immigrant groups. However, difficulties in establishing the population denominator for immigrant rates of mental disorder, selective referral for treatment, and other problems may have influenced such results. The current study aims at testing empirically the influence of some of these methodological problems.

**Methods.** Using nationwide case register data from Denmark, the diagnosis specific first-admission rates were compared between persons born in Denmark and other countries respectively. A case–control design was used to compare schizophrenia risk between different immigrant groups.

**Results.** Incidence rates of mental disorders among non-Danish residents calculated from admission data showed increased rates of schizophrenia (RR 1·7) and non-affective functional psychoses (RR 1·9). A case–control analysis utilizing non-psychotic admissions as control for schizophrenic admissions yielded essentially the same result, thus excluding selective referral as the sole explanation of the increased schizophrenia rate. However, this was almost exclusively due to increased rates in individuals born in countries neighbouring on Denmark.

**Conclusions.** While selective risk factors may be operating in various groups of immigrants, caution should be warranted in the interpretation of immigrant studies as large portions of transient visitors may obscure actual rates of mental disorders.

## INTRODUCTION

Reports of elevated rates of schizophrenia in the Afro-Caribbean population in the UK (e.g. Bebbington *et al*. 1981; McGovern & Cope, 1987; Harrison *et al*. 1988; Cochrane & Bal, 1989; Glover, 1989; Wessely *et al*. 1991; Thomas *et al*. 1993) represent some of the most intriguing findings in recent psychiatric epidemiological research. Selten & Sijben (1994) have extended these findings with data from the Dutch National Register showing increased rates of schizophrenia in Caribbean immigrants to The Netherlands. In the light of the presumed constancy of schizophrenia incidence across cultures (Sartorius *et al*. 1986), such reports remain puzzling. Although some increase in schizophrenia among immigrants in general might be expected due to differential demographic characteristics of immigrant populations or tendencies towards misdiagnosis (Cochrane & Bal, 1987), it is nevertheless difficult to explain the conspicuous increases found in certain immigrant groups when such factors are carefully controlled for. Findings of increased incidence of schizophrenia in both first- and second-generation Afro-Caribbean immigrants

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in the United Kingdom (Harrison *et al*. 1988; Wessely *et al*. 1991) have thus actualized important questions about predisposition towards schizophrenia in immigrant or ethnic groups.

The hypotheses that have been offered to explain increased rates of schizophrenia among immigrants from countries with incidence rates comparable to those in the host country have primarily focused on psychosocial factors such as stress (e.g. London, 1986; Westermeyer, 1988). However, while stress associated with resettlement might increase vulnerability to psychiatric illness in immigrants (Littlewood & Lipsedge, 1981; Creed, 1987), it is not readily understandable why rates of schizophrenia in particular should be resultingly higher than other forms of psychiatric disorder. Furthermore, evidence that stressful life events or adverse circumstances are significantly implicated in the aetiology of schizophrenia remains sparse (Chung *et al*. 1986; Hare, 1987). An alternative hypothesis is that differential selective mechanisms are in operation prior to migration. Thus, individuals at risk for schizophrenia may choose to emigrate as part of their incipient disturbance, as Ödegård suggested in his classic study of Norwegian immigrants to the USA (Ödegård 1932). Perhaps the most intriguing explanation for elevated rates of schizophrenia among certain immigrant or ethnic groups has been the suggestion of increased exposure to environmental risk factors of a more biological nature, such as obstetric complications or infectious agents (Harrison, 1990; Eagles, 1991). More recently, the notion that a specific vulnerability may exist for certain immigrant groups has been challenged by a study of first-contact incidence in a district psychiatric hospital in the UK where raised incidences of schizophrenia were found not specifically among Afro-Caribbeans but among all ethnic minorities (King *et al*. 1994).

While immigrant studies may help to elucidate the causes of schizophrenia, there are, nevertheless, methodological problems inherent in this type of research that need further clarification. Comparisons of rates between various population groups are crucially dependent upon the accuracy with which both cases and populations at-risk are determined. Apart from the much discussed problem of misdiagnosis (Littlewood & Lipsedge, 1981; Lewis *et al*. 1990; Sashidharan, 1993), there are additional biases associated with the use of hospital admissions as indices of incidence, as the underlying assumption that immigrants and native-born patients with schizophrenia have equal chances of being admitted to psychiatric hospitals may not hold. Differential selection may occur either due to differential patterns of help-seeking behaviour among ethnic/immigrant groups or, once contact has been established, selective referral for treatment or admission. In case–control studies (e.g. Wessely *et al*. 1991) patients with diagnoses other than schizophrenia are used in the estimation of the population distribution of the risk factor under study, i.e. ethnicity or immigrant status. However, if selective admission or diagnostic practices are operative, the use of non-psychotic or non-schizophrenic controls from the same treatment service may accentuate this type of bias described above, as any tendencies towards selective non-referral for disorders other than schizophrenia will result in seemingly elevated rates of schizophrenia in immigrants. While some studies have found that Afro-Caribbean patients may be more likely to be admitted under compulsory forms (Ineichen *et al*. 1984; Harrison *et al*. 1989), other studies have not shown a relationship between ethnicity and compulsory admission (Bebbington *et al*. 1994; Castle *et al*. 1994). It remains unclear whether rates of compulsory admission are elevated among immigrants with diagnoses of schizophrenia, and if so, whether this is due to selective admission practices or postponed treatment seeking by socially isolated immigrants.

Apart from the general problems associated with determining background population rates for mental disorders, there are more fundamental difficulties associated with establishing the correct population denominators for calculation of rates in immigrant groups. Generally, it is not known exactly how many immigrants live in a given area, as census data are most likely to underestimate the size of ethnic populations (Sashidaran, 1993). Almost all immigrant studies reliant upon census data are prone to possible errors in the estimation of population denominators for foreign-born residents due to such deficiencies. Even when place of birth is known, errors may arise due to assumptions of ethnicity based solely on birthplace. A problem that has

not been addressed in any study, to our knowledge, is the unknown number of illegal immigrants or transient visitors who seek treatment when psychotic, but, who nevertheless do not appear in population statistics. Thus, substantial numbers of transient foreign residents could lead to an artefactual finding of increased rates of mental disorders in immigrants.

The purpose of the current study was to examine rates of psychosis in first-generation immigrant groups in Denmark, utilizing information contained in the Danish Psychiatric Case Register. The Danish Psychiatric Case Register covering all psychiatric in-patient facilities in Denmark as well as other population registers in Denmark makes it possible to calculate reasonably accurate rates of psychiatric admissions among immigrants and to compare such rates with those of the general Danish resident population, i.e. people born in Denmark. We were interested in whether immigrants were at increased risk for all diagnostic categories of psychosis, or whether rates of schizophrenia in particular were elevated. These analyses were supplemented with a case–control study in simulation of the design chosen by Wessely *et al.* (1991). The case–control study served as a test of the possible bias that could arise from using non-psychotic controls selected from the same treatment facility, i.e. that increased rates of schizophrenia in immigrants could be due to selective non-referral for non-psychotic disorders.

## METHOD

The material consisted of all individuals who were recorded in the Danish Psychiatric Case Register as having been admitted for the first time in their lives for a psychiatric disorder during the period 1980–1992 inclusive. The Danish Psychiatric Case Register has been described in detail by Dupont (1983) and research applied has been discussed by Munk-Jørgensen *et al.* (1993). It covers all admissions to psychiatric in-patient facilities in Denmark. The immigrants referred to in this study include all persons born outside of Denmark, but residing in Denmark. Obviously some of these immigrants will be children of Danish citizens, but they will be a minority of this group.

The period 1980–1992 was chosen because it was the only period for which it was possible to obtain access to the age-specific number of individuals living in, but born outside of Denmark. Foreign- and Danish-born cases in the Psychiatric Case Register were identified on the basis of all those who had a non-missing value in the birthplace code in the Case Register (81% of the cases). Those cases for whom birthplace was not indicated were not included in the analyses. Diagnoses in the Register represent discharge diagnoses based on ICD-8 diagnostic criteria (WHO, 1974).

The calculation of the expected number of immigrant cases was based on the total population rates for each individual disorder (including only cases with known place of birth), the age-specific number of non-Danish inhabitants in Denmark, and an adjustment or correction factor of 1·47 which was the ratio between the number of inhabitants in Denmark born outside of Denmark (including Greenland and the Faroe Islands as part of Denmark) and the number of inhabitants in Denmark who were not Danish citizens. The adjustment was done by multiplying the expected number of cases by this ratio of 1·47. Ideally, of course, the calculation of the expected number of cases should have been based on the number of inhabitants born outside of Denmark, because this was the indicator of immigrant-status available in the Psychiatric Case Register. While such an adjustment is an approximation, it provides an operational way of adjusting the available population denominators of foreign citizens to represent more adequately the precise denominators needed in this study, i.e. individuals born outside Denmark. However, the population figures was only available for the years 1990 and 1991, and because of the increasing number of refugees coming to Denmark during recent years, the ratio of 1·47 probably overestimates the number of inhabitants in Denmark born in other countries. This, however, makes it likely that the relative risks in this study are underestimated, making it plausible that elevated risks are real but biased towards the null hypothesis, whereas relative risks smaller than 1 should be interpreted with more caution.

The relative risks shown in Table 1 were calculated separately for males and females respectively, and were adjusted for age using

indirect standardization, and the confidence intervals and *P*-values were calculated assuming the observed number to be Poisson distributed (Breslow & Day 1987).

Unfortunately, a large number of patients were classified as being born in countries other than Denmark, Greenland or the Faroe Islands with no other specification of country of birth. Because of this, it was not attempted to calculate incidence rates separately for different countries and compare these with the total Danish population as such rates would be biased towards a reduced occurrence among individuals born in any specific country other than Denmark. Assuming that this classification in the unspecific category of individuals born outside of Denmark would not differ between patients admitted with a diagnosis of schizophrenia (ICD-8 295) and non-psychotic diagnoses (ICD-8 300–315), it was decided to supplement this analysis with a case–control study where the cases consisted of all individuals admitted for the first time with a diagnosis of schizophrenia and the controls were seven individuals with non-psychotic diagnoses per case, randomly selected and matched for admission year. Thus, in addition to the relative risks obtained in the population study, odds ratios for schizophrenia for foreign-born inhabitants were calculated utilizing conditional logistic regression in the case–control study (Breslow & Day, 1980). Apart from providing an opportunity to compare relative risks in groups from various countries, this design simulates the design used by Wessely *et al.* (1991). In that study elevated rates of schizophrenia were reported in Afro-Caribbeans compared with non-psychotic controls. If in that study Afro-Caribbean immigrants were admitted at a selectively low rate for non-psychotic disorders, this would yield the artefactual result of an increased risk for schizophrenia. The present analysis enables a test of the selective admission hypothesis as the odds ratios for schizophrenia obtained by comparing all immigrant groups with Danish-born in the case–control study can be compared with the relative risk estimate obtained from the population-based study. Any major differences would indicate that different referral rates, for non-psychotic disorders and schizophrenia respectively, may have biased the estimates of relative risk for schizophrenia in immigrants, at least in the present study.

## RESULTS

The relative risks for the various psychiatric diagnostic categories for immigrants to Denmark are shown in Table 1. The results were analysed separately according to gender as first-generation immigrant populations may show an excess of males. The risks for first admission for schizophrenia, non-affective functional psychosis, all non-psychotic diagnoses, all diagnoses, and compulsory admissions were all significantly increased in both sexes. Manic-depressive psychosis occurred with a significantly reduced rate in both males and females born outside of Denmark whereas affective psychosis (i.e. manic-depressive psychosis plus reactive depression) occurred with a slightly increased risk in males while the risk in females did not differ from the general population, neither did the risk for affective psychosis in the total sample differ from the total population. As can be seen in Table 1, the risk increase was by far most marked in schizophrenia, the total group of non-affective functional psychoses, and in the category for compulsory admissions (albeit there will be considerable overlap between this category and psychoses, as compulsory admissions are only legal in Denmark if insanity, i.e. psychosis, is present), whereas the risk for affective psychosis, non-psychotic diagnoses, and all diagnoses combined only differed slightly from that of the general population.

The logistic regression analysis yielded similar results regarding risk for schizophrenia in the total group of foreign-born individuals (RR 1·34, $P = 0{\cdot}005$). These analyses were repeated for the following groups of countries: Scandinavia and European Union, Yugoslavia, Turkey, Pakistan and 'other countries'. Immigrants from Yugoslavia, Turkey and Pakistan were treated as separate groups as these constitute the larger group of immigrants during the 1960s and early 1970s who mainly emigrated to Denmark to take jobs primarily as unskilled workers, and they would thus constitute the more underprivileged groups of immigrants. When country of birth was included in the analysis, it was evident that the only significant excess was found in the group representing

Table 1. *Relative risk for ICD-8 psychiatric disorder among immigrants to Denmark, based on population rates*

| | Males | | | Females | | | Total | | |
|---|---|---|---|---|---|---|---|---|---|
| Diagnosis | *N* | RR | 95% CI | *N* | RR | 95% CI | *N* | RR | 95% CI |
| Schizophrenia | 102 | 1·71** | 1·40–2·08 | 41 | 1·68** | 1·20–2·28 | 143 | 1.70** | 1·44–2·01 |
| Non-affective functional psychosis | 419 | 2·10** | 1·91–2·32 | 306 | 1·70** | 1·51–1·90 | 725 | 1·91** | 1·77–2·06 |
| Manic-depressive psychosis | 103 | 0·80* | 0·65–0·96 | 159 | 0·74* | 0·63–0·86 | 262 | 0·76* | 0·67–0·85 |
| Affective psychosis | 260 | 1·16* | 1·02–1·31 | 333 | 0·95 NS | 0·85–1·06 | 593 | 1·03 NS | 0·95–1·12 |
| All diagnoses | 2294 | 1·18* | 1·13–1·23 | 2190 | 1·29** | 1·23–1·34 | 4484 | 1·23** | 1·19–1·27 |
| All non-psychotic diagnoses | 1615 | 1·06* | 1·01–1·11 | 1551 | 1·30* | 1·26–1·39 | 3166 | 1.18* | 1.13–1.21 |
| Compulsory admissions | 278 | 1·82** | 1·61–2·05 | 195 | 1·85** | 1·60–2·12 | 473 | 1·83** | 1·67–2·00 |

** $P < 0.005$;* $P < 0.02$; NS = not significant.

Table 2. *Relative risk for schizophrenia* v. *non-psychotic disorder among immigrants to Denmark: case–control study**

| Immigrant group | RR | 95% confidence interval | *P* |
|---|---|---|---|
| Total born outside Denmark | 1·34 | 1·09–1·64 | 0·005 |
| EU and Scandinavia | 1·48 | 1·11–1·98 | 0·008 |
| Yugoslavia | 0·92 | 0·21–4·03 | 0·912 |
| Turkey | 0·89 | 0·35–2·25 | 0·797 |
| Pakistan | 0·82 | 0·19–3·54 | 0·787 |
| 'Other' | 1·32 | 0·98–1·78 | 0·072 |

* Relative risks are adjusted for age and gender.

Scandinavian and European Union countries (see Table 2). No country group had a significant deficit of schizophrenia. The group representing 'other countries' did show a non-significant trend towards an excess risk for schizophrenia. The group of people born in the category 'other countries' can not be subspecified further, as this was a heterogeneous composite of all remaining countries of origin, including immigrants from e.g. the United States, Australia, as well as African and Asian countries. The proportion of Afro-Caribbean immigrants in this 'other' group is, however, estimated to be negligible.

## DISCUSSION

The present findings of increased rates of admission for schizophrenia and unspecified functional psychosis in immigrants to Denmark add to the growing body of results showing increased incidence of schizophrenia among immigrants to European countries (London, 1986; Cochrane & Bal, 1989; King *et al*. 1994; Selten & Sijben, 1994). Rates of compulsory admissions were also found to be increased, suggesting that psychiatric disorders in immigrants may progress to greater levels of behavioural disturbance before treatment is sought. Some specificity in the results may be indicated by the fact that foreign-born residents showed significantly decreased admission rates for manic-depressive psychosis and similar rates for the other diagnostic categories compared to the Danish population.

The study includes all psychiatric in-patient facilities available in Denmark. Therefore, the results can not be ascribed to the possible selection bias that could arise if the study only covered a region with, e.g. particularly poor social conditions, which might lead to an over-representation of immigrants with selectively low upward social mobility. Obviously in such a subgroup it would not be unreasonable to expect an increased proportion of individuals with severe mental disorders.

The potentially largest methodological problem in our study is the fact that place of birth was available only for 81% of the cases, and only these cases are used in the analyses. As the validity of our results is dependent upon the assumption that the distribution of place of birth was the same in the remaining 19% of cases in the Psychiatric Case Register, it may be worthwhile to explore the possible consequences if this assumption is not correct. To consider one extreme possibility, if all cases with unrecorded place of birth in reality had been born in Denmark, our relative risk estimates would be too high. However, if we increase our expected

numbers according to this assumption the risk for schizophrenia, non-affective psychoses and compulsory admissions respectively, would still be significantly increased, albeit this would not be the case for affective psychoses, non-psychotic disorders, or all admissions combined. The other extreme assumption, that all 19% of cases without information about place of birth had in fact been born outside Denmark would obviously increase the relative risk estimates very much, and because the proportion of people living in but born outside of Denmark is small, this assumption would actually require that a very large proportion of this population group had been admitted to a psychiatric hospital. Neither of the extreme possibilities considered above are realistic since the missing data probably are due to a more randomly distributed failure to report the data to the Psychiatric Case Register, and our cautious interpretation would be that at least the increased rates of schizophrenia, non-affective psychoses and compulsory admissions are real, whereas the other results, including the reduced rates of manic-depressive illness are more vulnerable to these methodological problems.

One possible limitation in the current design is that diagnoses were not based on prospective face-to-face interviews, as in Harrison *et al.* 1988. However, Munk-Jørgensen (1995) has shown in a sample of 53 patients identified with schizophrenia through the Danish Psychiatric Case Register that 90·6% (48 patients) fulfilled DSM-III-R criteria for schizophrenia, meaning that the vast majority of schizophrenia cases included will fulfil internationally accepted criteria for this disorder.

It was noteworthy that the direction of the relative risk from the case–control study was the same as in the study of incidence, although the excess risk observed was slightly smaller than in the incidence rate study. Thus, the current results do not support the notion that the case–control design such as the one utilized by Wessely *et al.* (1991) would lead to inflated risk for schizophrenia simply due to reduced admission rates for non-psychotic disorders. As the current results were based on first admission diagnoses, some reservations may be warranted due to possible subsequent changes in diagnoses upon re-admission.

While the case–control study yielded essentially the same results as the incidence study, increased rates of schizophrenia in non-Danish residents were almost exclusively due to increased rates in citizens from countries neighbouring on Denmark, as the group of patients from Scandinavian and European Union countries were mainly citizens of Norway, Sweden, and Germany. As it is unlikely that immigrants from these countries would experience acculturation to Denmark as more stressful than immigrants from Yugoslavia, Turkey, and Pakistan, such results are difficult to reconcile with the notion of migrational stress. The alternative that certain immigrants may travel during prodromal phases of their illness, or while actually ill, may bear some renewed consideration (Ödegård, 1932), particularly in light of the relative ease with which citizens from the surrounding countries may enter Denmark in contrast to e.g. immigrant groups from Yugoslavia, Turkey, or Pakistan. That a certain degree of pre-selection (both positive and negative) might occur among immigrant groups, depending upon geographical proximity of the receiving country and its actual immigration policy, may be gleaned from the correspondingly low rates of schizophrenia obtained in immigrants from Yugoslavia, Turkey and Pakistan. Immigration from Yugoslavia, Turkey and Pakistan to Denmark has been mainly restricted to foreign workers and their spouses. Thus, despite the fact that immigrants from these countries would typically have less socially advantaged backgrounds than other groups residing in Denmark, they may have been more 'positively' motivated from the outset. Our findings of lower rates of schizophrenia in immigrants from these countries would be consistent with Weyerer & Häfner's (1992) findings of lower prevalence of psychiatric disorders among Turkish immigrants in Mannheim.

While negative selection factors may have contributed to the increased rates of schizophrenia found in citizens from countries neighbouring to Denmark, our results suggest also the possible influence of a mechanism not yet fully explored in immigrant studies, the problem of transient visitors. A greater 'permeability' of the Danish border towards certain immigrant groups may increase visits of shorter duration or transiency. Any such tendency towards tran-

siency could obscure actual rates of mental disorder and pose problems for the ascertainment of exact population denominators. While the degree to which transiency may have been a factor of weight in our own study is entirely unknown, it is noteworthy that citizens from the nearby Nordic countries have very easy access to Denmark. Had information on duration of residency been available for all immigrants, this would have provided a better notion of the degree of accuracy of the current population denominators. In addition, such information would have helped to clarify whether the increased risk among immigrants primarily originated from illness among recently arrived immigrants (congruent with the prodromal hypothesis) or whether the increased risk was more generally distributed. In the absence of information on duration of residency, it is not possible to explicate at the present time the mechanism by which certain immigrant groups in Denmark seem to be at elevated risk, or why this risk seems specific for certain disorders, schizophrenia in particular.

Finally, it should be noted that while the composition of immigrant groups may vary from study to study, the general methodological problems will tend to be the same in any study of mental disorders in immigrants. In most, if not all, studies of psychiatric disorders among immigrants there is no explicit discussion of how transient visitors are handled in the analysis. The notation that patients without permanent residence are not admitted/treated or included in the study in addition to the inclusion of duration of residency in the particular area under investigation would seen to be of concern for future studies. While the proportion of transient visitors may vary from country to country, the changing ethnic profiles of many of the larger European cities suggest that it may be increasingly important, and difficult to establish correct population estimates in future studies of this type.

## CONCLUSION

This nationwide study replicates previous findings of increased first-admission rates for schizophrenia among immigrants. However, this was not due to increased rates among the more socially disadvantaged groups of immigrants, but more among individuals from countries neighbouring to Denmark. The possible importance of transient foreigners, or more generally duration of stay in the recipient country or region, for these findings should be addressed in future studies.

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