The role of cultural background in diagnosing psychotic disorders: Misclassification of psychiatric symptoms in Moroccan immigrants in the Netherlands
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He left my room to not come back to the clinic any more…

He with a cap on his head, with his big black eyes he stared at me: “I am afraid, I am falling apart, I feel my heart is coming to my throat, it is going to give up… I didn’t do anything right in my life…. Some thing is moving under my skin! I don’t know what, but it feels as armies of ants. Only darkness gives me some comfort to go outside, where nobody can look at me anymore as an alien. I am troubled. They don’t like me, actually - he whispered - they disgust me. Sleep doesn’t come to my eyes, nothing tastes the same as before. She stared at me!” I asked him if he heard voices. He became angry: “Look at me, lady - he whispered - I think you don’t understand at all how it does feel, to be far away from your mother as the eldest son when she is dying! Why do you ask me nonsense? You think that all of us are foolish or crazy, isn’t it?” And he shut the door (one of my first patients whom I could not include in this study).
Chapter 1

General Introduction
The focus of this thesis is on the impact of cultural sensitive assessment of psychiatric symptoms in order to diagnose psychotic disorders and in particular schizophrenia in Moroccans living in Morocco and Moroccan immigrants in Utrecht, The Netherlands. The overall theme is culture-based misdiagnosis as a potential bias in the frequently reported high rates of schizophrenia among non-Western immigrants in Europe. In this introductory chapter we give an overview of the population under study and of the main concepts on which our investigations are based. First the background of Moroccan immigration to the Netherlands and its mental health status will be described. Then some general background information is given about psychotic disorders and in particular schizophrenia and the background literature on the role of migration in the epidemiology of this disorder. Finally a general outline of the thesis will be provided.

1.1. Moroccan immigrants at risk

The ethnic diversity in the Netherlands population (16,665,799 inhabitants) consists of 79.4% native Dutch people and 20.6% ethnic minorities, including 9.2% Western and 11.4% non-Western immigrants (CBS, 2011). Of the non-Western immigrants, the Turks (20.1%), Moroccans (18.7%), Surinamese (18.2%), and Antilleans (7.4%) constitute the biggest groups. This thesis is about Moroccan immigrants: 355,883 inhabitants or 2.1% of the total population of the Netherlands.

The first Moroccan immigrants came to the Netherlands in the 1960s during industrial growth in Europe as unskilled “guest laborers”. Most of them were from the Rif region, almost all Moslems and mostly illiterate. The workers came alone to the Netherlands expecting to return to their home and their families after a few years. As a consequence, many of their children grew up in an extended family without a father in Morocco. Education level and income of Moroccan people like other main immigrant groups in the Netherlands are lower compared to that of the native population (Dagevos et al., 2003). According to the national survey records, second generation Moroccan immigrants also failed to climb higher on the socio-economic ladder (Dagevos et al., 2003). Of all immigrants, the highest rate of discrimination is reported by Moroccan immigrants (Hoogsteder et al., 2001). Psychiatric illnesses are still a taboo among a lot of Moroccan families and many prefer to go first to an indigenous healer as long as religious or traditional scriptures help.
Mental disorders among Moroccan immigrants

It is often assumed that migration can induce anxiety and tension leading to increased levels of mental health problems (Pawliuk et al., 1996; Berry, 1997; Martens, 1999). However, national epidemiological studies in Western countries that include non-Western immigrants are a relatively new phenomenon and are available only for the last decade. There is little doubt that migrants are frequently confronted with poverty, housing problems, unemployment and discrimination. However, reports regarding the impact of immigration stress on mental health and the presence of mental disorders among immigrants are far from consistent (McGrath et al., 2001; Bhugra, 2004; Weich et al., 2004; van Lindert et al., 2004; Vollebergh et al., 2005; Selten & Cantor-Graae, 2005; Swinnen & Selten, 2007; Veling et al., 2007; Williams et al., 2007; 2012). Although some studies indicate that migrants in the Netherlands experience worse general health (van Wersch et al., 1997; Weide & Foets, 1997), the second Dutch national general practice survey reported no substantial over-all mental health differences between ethnic minorities and natives (van Lindert et al., 2004). However, there are clear indications that (second/third generation) Moroccan children and adolescents in the Netherlands are at an increased risk to develop emotional and behavioural problems (Pels, 1991; 1998; Hammen & Rudolph, 1996; Helsen et al., 2000; Pels & De Haan, 2003) and relatively more Moroccan adolescents make use of youth assistance (Vollebergh, 2002). According to police records, Moroccan immigrants are overrepresented in the population of juvenile delinquents and they are relatively young at their first contact with the police (van Gemert, 1998). Also drug use disorders are reported to be increased among Moroccan immigrants (Selten et al., 2007). However Moroccan children do not appear to experience more anxious/behavioural health problems than their non-immigrant peers (Stevens et al., 2003) and levels of anxious/depressed, social and thought problems in immigrant children have not been found to be substantially different from native Dutch children (Vollebergh, 2005). Finally, teachers perceive higher levels of externalising problem behaviour with immigrant children (Stevens, 2003). However, until now there is no certainty about the difference in mental health problems between immigrants and native Dutch inhabitants. There are, however, serious concerns about the incidence and prevalence of some specific mental disorders in certain immigration groups.

For example, the risk of developing schizophrenia is reported to be substantially higher for immigrants to the Netherlands from Surinam, the Netherlands Antilles and particularly Morocco (Selten et al., 2001; Veling et al., 2006). In contrast there is no evidence of a higher risk of depression associated with migration among the same immigrant groups in
the Netherlands (Selten et al., 2003). The incidence of bipolar affective disorder among these groups of migrants in the Netherlands seems even to be lower than in the native Dutch population (Selten et al., 2003). With regard to the relatively high rates of schizophrenia among immigrants both biological and social stress hypotheses have been mentioned to explain this difference.

This thesis focuses on the possibility of misdiagnosis of psychosis in Moroccan immigrants as a potentially important (partial) explanation for the higher rates of psychosis and schizophrenia in this immigrant group in Utrecht, The Netherlands.

### 1.2. Schizophrenia

**Clinical definition**

Kraepelin (1899), in his revision of his textbook for a sixth edition, combined a group of mental disorders with different presentations that were distinguished on the basis of their poor prognosis, under the single heading of ‘dementia praecox’. Kraepelin emphasized the chronic aspect and a poor outcome of the disorder. However, in a follow-up of these patients he found that 12.5% of them recovered. For this group he introduced the term manic-depressive insanity, which was an episodic illness with a better prognosis. It was Bleuler (1908) who introduced the concept of schizophrenia and equated psychosis with schizophrenia, regardless of the presence of prominent mood symptoms for this group of disorders (Bleuler., 1911/1950). The main symptoms of this disease were the loosening of associations, disturbances of affectivity, ambivalence, and autism (the “4 A’s”). He was also the first to describe the symptoms as “positive” or “negative.” However, the splitting of psychological functions, resulting in a loss of unity of the personality, was the most important sign of the disease in Bleuler’s conception.

Schizophrenia is still considered to be one of the most disabling psychiatric disorders. This major mental disorder starts generally in late adolescence or early adulthood, the age of onset varies between men and women, where males tend to have a younger onset (Munk-Jorgensen, 1987). The peak incidence for males and females is between 15–24 years. The peak for young adults is more marked for males and females have a second peak in the years 55–64. Evidence suggests that males have a somewhat higher lifetime risk of developing schizophrenia then females (McGrath et al., 2004), although Saha et al., (2005) challenged
this widely held view and reported that they found no significant difference between males and females in their systematic review of prevalence data on schizophrenia across cultures.

The symptoms of schizophrenia can be divided in three dimensions: positive symptoms, negative symptoms, and symptoms representing disorganization of thought. Positive symptoms are outward expressions that usually involve distorted perceptions of reality, i.e. hallucinations and delusions, and bizarre behaviours. Negative symptoms, i.e. lack of emotion, apathy, anhedonia and alogia, refer to a reduction of normal function or distorted internal emotional states. Disorganization of thought includes cognitive impairments (i.e. trouble in attention, concentration, learning, and memory), psychomotor speed and executive function (Bilder et al., 1985; Mueser, 2004).

**Criticisms regarding the diagnosis**

Although the term schizophrenia is widely used across the globe there are also people with fundamental criticism regarding this concept (Blom, 2003). More specifically the reliability and validity of the diagnosis according to the classification of the American Psychiatric Association (APA), the “Diagnostic and Statistical Manual of Mental Disorders, fourth edition” (DSM-IV) (Pincus et al., 1998; Kendell et al., 2003; Baca-Garcia et al., 2007), has been seriously questioned. Although, the reliability of the DSM diagnosis has improved since the application of explicit inclusion and exclusion criteria and the use of structured clinical interviews (Segal et al., 1995; Lobbestael et al., 2010), the validity of the diagnosis is still questioned. Even in the case of a full assessment of all data over time (LEAD criterion) and the use of neuropsychological tests, neuroimaging indicators or other neurobiological markers, experts tend to talk about a “best estimate diagnosis” (Fenning et al., 1994; Basco et al., 2000). Recently a serious debate started again about the presence of a continuum of non-affective psychotic disorders and affective psychotic disorders (Phillips et al., 2007; Myin-Germeys and van Os, 2007). However there is not yet an agreement on an aetiology driven classification system.

Moreover, there is an ongoing debate regarding the cultural validity of the diagnosis of schizophrenia and the instruments that are being used to make the diagnosis. With regard to the latter, the issue of culture based misclassification remains an important point of discussion and disagreement. The view that cultural differences may influence the manifestations and definitions of various psychiatric disorders has been a matter of discussion for some decades, as is the need to maintain uniform methods and criteria in cross-cultural studies (Kleinman, 1997). Rogler (1996) notes that “the cultural distance between the diagnostician and the client
affects the degree of psychopathology inferred and affects the type of disorder diagnosed”. Similarly, Kleinman (1980, 1987) questioned the validity of applying Western diagnostic concepts to different ethnic groups in other than Western societies. He introduced the term “categorical fallacy” to describe the misidentification and misclassification which may result when culturally sanctioned idioms of expressing distress are interpreted as diagnosable pathological phenomena. Kleinman, as a member of the APA Taskforce on Culture - one of the working groups on DSM-IV - expressed his disappointment about this group and the result of their substantial labor over several years concerning the DSM-IV. Although for the first time, DSM-IV showed considerable interest on cross-cultural aspects of classification and diagnosis, the cultural formulation section - despite of the intention of its authors - still does not appear in the introduction but only in the ninth appendix, side-by-side with the Glossary of Culture-Bound Syndromes, in fact as a remote option (Kleinman, 1997). He further claims that the editors of DSM-IV tended to be in favor of more global statements in order to delete details of cultural differences in epidemiology, symptoms, course and treatment response. He claims that “Attention to culture without consideration of class, poverty, and professional bias is another example of Pyrrhic victory” (Kleinman, 1997). With this tradition in mind, we have chosen cultural differences in the classification and diagnosis of schizophrenia among immigrants as the overall theme of this thesis.

**Epidemiology**

Almost a century ago Kraepelin left his country as one of the first pioneers to study the clinical picture of psychiatric disorders, including dementia praecox, in various countries and among various peoples. He visited countries as remote as India, Java, Singapore, the United States and Mexico to explore his hypothesis that the increase of insanity during the 19th century was “a product of injuries to which the progress of civilization and its unpleasant accompaniments expose our mental health” (Kraepelin 1919). Although since the 1920s a growing number of studies have contributed to our knowledge of schizophrenia, these efforts to clarify the epidemiology and thus the etiology of schizophrenia were hindered by the limited comparability of research findings, because of the lack of a shared definition of the disorder (Cooper et al., 1964; Yolles, 1969; Babigian, 1975; Wilson, 1994). Since the late 1940s and early 1950s the robustness of epidemiological research findings has increased thanks to the introduction of explicit diagnostic criteria such as those of the sixth revision of the International Classification of Diseases, (ICD-6; WHO, 1948) and the first edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-I; APA, 1952). The next
step was the development of modern standardized epidemiological studies with more precise study designs, representative samples, and better techniques of data collection and data analysis. The next major step forward was the WHO Ten Country Study, a landmark study on the incidence of schizophrenia using a uniform methodology across 10 different countries (Jablensky, 1992). The reported incidence rates ranged from 7 to 14 new cases per 100,000 per year for ‘narrowly’ defined schizophrenia with at least a two-fold difference between the highest and lowest sites. Despite the different incidence rates, the authors concluded that there were no significant differences between the different sites. The incidence rate of broadly defined schizophrenia fluctuated even more between the countries. The highest incidence was 0.42 new cases per 1,000 persons per year in the rural area of Chandigarh, India and the lowest incidence was 0.16 new cases per 1,000 persons per year in Honolulu, USA. The question is why the results of the WHO Ten Country study have so often been misinterpreted as providing strong proof that the incidence of schizophrenia does not vary between countries (McGrath, 2004). Based on more recent studies, the year prevalence of schizophrenia in national populations is reported to range from 1.4 to 4.6 cases per 1,000 whereas the incidence ranges between 16 and 42 cases per 100,000 per year (Jablensky, 2000). Saha et al., (2005) in their systematic review of prevalence data on schizophrenia across cultures using data from 200 studies covering 46 nations, reported that the prevalence estimates from the “least developed” countries were significantly lower than those from the sites in “developed” countries.

In addition to the variation in incidence rates between countries by a factor of less than three, studies have shown that the variation between population subgroups within a single country can be much larger. Based on an analysis of the first admissions for schizophrenia in England and Wales between 1949–53 obtained from the General Register Office, for single men, the rate in social class V was 4.1 times higher than in social class I (Brooke, 1959). Sharpley et al., (2001) - in an overview of case–control studies using population denominators from the 1991 to 2001 UK census - estimated standardised incidence rates for schizophrenia in different ethnic groups to be approximately fourfold the risk in the native UK citizens. This was despite the use of widely varying standardised rate ratios to permit pooling of the data. The remarkable parallels between studies of lower social class and the immigrant studies, is eye-catching. In the UK, for example, incidence rate ratios of about 4 have been estimated both for black immigrant groups and for the lowest social class in the indigenous white population (Cooper, 2005).
Etiology

The cause of schizophrenia has not been uncovered as yet. Schizophrenia often persists throughout life and seriously affects the quality of life of the patients as well as their families. It probably comprises a group of disorders with heterogeneous etiologies and a wide range of clinical presentations, treatment response and courses of illness (Murray, 2003). The disorder schizophrenia is often considered as the poor outcome fraction of a truly ‘complex’ multidimensional psychotic syndrome (Van Os et al., 2010). Different long term follow-up studies, suggest a variety of signs, symptoms, conditions, and behaviours that are associated with different risks, but none with such strength or uniqueness as to be useful in the prediction of the disorder (Messias et al., 2007). Evidence from longitudinal studies conducted in the United Kingdom, Sweden, Finland, and New Zealand shows that individuals with schizophrenia differ from their peers even in early childhood in a variety of developmental markers (Messias et al., 2007) such as the age of attaining developmental milestones (Jones et al., 1994; Jones et al., 1997; Isohanni et al., 2001), levels of cognitive functioning (David et al., 1997; Gunnell et al., 2002), educational achievement (Jones et al., 1994; Isohanni 1998; Done et al., 1994; Cannon et al., 1999), and neuromotor, language, and cognitive development in the first decade of their lives (Cannon et al., 1999). The association of childhood developmental abnormalities and schizophrenia is supportive for the hypothesis that schizophrenia is a neurodevelopmental disorder and causes may be traced to a defect in early brain development (Murray & Lewis, 1987; Weinberger, 1995; Isohanni et al., 2004; Isohanni et al., 2005).

The neurodevelopmental model incurs that the disorder develops as the result of an interaction between genetic factors and environmental stressors early in life, which may lead to delicate alterations in the brain (Neugebauer, 1999; 2002; Hoek et al., 1998; Cannon 2003; Insel, 2010). The interaction between genes and environmental disruptions probably determines the onset and course of schizophrenia (Sullivan, 2003; Riley, 2005; Jaaro-Peled, 2010; Van Os et al., 2010). However, the responsible, most probably multiple (Kendler et al., 1996; Straub et al., 1998; 2002), genes are not identified yet (Riley, 2005). There is consistent evidence that different prenatal and perinatal stressors might act as risk factors (Susser et al., 1992; 1998; 2006; Mortensen et al., 1999; Brown et al., 2004; Sipos et al., 2004; Van Os et al., 2010). Therefore, proponents of the stress-diathesis model (Zubin & Spring, 1977; Susser 1996; Portin & Alanen, 1997) have been investigating a wide range of so-called “stressors”, including biological, environmental, psychological, and social factors in schizophrenia.
In a recent review, Van Os and his colleagues suggest that “Psychotic syndromes can be understood as disorders of adaptation to social context” (Van Os, 2010).

Family, twin, and adoption studies support the role of genetic influences in schizophrenia (Mc Gue & Gottesman, 1991; Portin & Alanen, 1997). While the general population lifetime prevalence is about 1%, relatives of schizophrenic probands have a higher risk. In this regard it is important to consider that first-degree relatives (e.g. siblings, dizygotic (DZ) twins) on average share about 50% of their genes and that the concordance for schizophrenia among first-degree relatives is only about 9%. The relatively high discordance among identical twins, who share 100% of their genes, clearly indicates that environmental factors are also likely to play an important role in this disruption (McGue & Gottesman, 1991; Labuda et al., 1993). Van Os et al., (2010), state that “Although heritability is often emphasized, onset is associated with environmental factors such as early life adversity, growing up in an urban environment, minority group position and cannabis use, suggesting that exposure may have an impact on the developing ‘social’ brain during sensitive periods. Therefore heritability, as an index of genetic influence, may be of limited explanatory power unless viewed in the context of interaction with social effects”.

Considering the role of social factors in the etiology of schizophrenia, one of the first important links that is known for more than half a century is that between social economic status (SES) and this disorder (Brooke, 1959). Two competing explanations for this consistently observed relationship - the social causation versus the social selection hypothesis - have been debated in literature for decades (Goldberg & Morrison, 1963; Fox, 1990). Goldberg & Morrison (1963), based on birth register data comparing the occupations of the patients with those of their fathers, found a large excess of low class cases among the patients, but not for the fathers. The important conclusion was that the affected people had not been socially disadvantaged from birth, but suffered from functional impairments that had handicapped them in early learning and working life. This study was an important milestone and brought the social causation hypotheses almost to an end. Even though the importance of selective social drift is hardly debated anymore, some recent findings have re-drawn attention to the social causation hypothesis. Cooper et al., (2005) summarized the evidence for this and divided the existing studies in three groups: first there are a number of studies which show that the risk to be diagnosed with schizophrenia is greater in modern urban societies and less in rural communities (Eaton et al., 2000). Being born or brought up in such an urban environment is in itself a risk factor for the condition (Harrison et al., 2001). Second, there are a number of studies showing that social adversity in childhood is associated with an increased risk of
developing schizophrenia (Hjern et al., 2004). Third, there are a number of studies showing a higher rate of psychotic illness among African–Caribbean and other black immigrants in the UK. This latter finding tends to be explained primarily by social factors rather than by genetic differences in vulnerability (Jarvis, 1998; Sharpley et al., 2001). In this regard is interesting to mention that Saha et al., (2005) in their review on the prevalence of schizophrenia reported a higher prevalence among migrants but not in urban compared to rural settings.

1.3. Race, ethnicity, culture and social adversity

Culture, ethnicity and social adversity are important concepts that need to be distinguished in immigrant studies on schizophrenia. Each of them can be a strong determinant and source of bias if not considered properly in health related outcomes. Whether observed racial/ethnic disparities in healthcare are due to race and ethnicity, race or ethnicity, socioeconomic position, a combination of all, or a yet unmeasured factor, is not clear so far (Egede, 2006). For example, race and ethnicity are different variables and should not be confused. The study of racial variations in health is driven by a genetic model that assumes that race is a valid biological category. However, the concept of race is shown to be a social construct rather than a biological reality, as it is shown that there is more genetic variation within races than between races (Cooper & David, 1986; Williams, 1994).

Ethnicity, a commonly used construction in studies of health disparities in the international studies among immigrants, refers to selected cultural and sometimes physical characteristics used to classify people into groups or categories considered to be significantly different from others. The concept of ethnicity is an attempt to further differentiate racial groups but like race, it carries its own historical, political, and social baggage (Oppenheimer, 2001). In spite of these limitations, ethnicity when combined with race provides more information than race alone as long as researchers define their measurement of the construct and justify its validity, reliability, and consistency (Oppenheimer, 2001). Although some ethnic groups involve only a loose group identity with little or no common cultural traditions, other ethnic groups, like newly arrived immigrants, are coherent subcultures with a shared language and a body of tradition (Egede, 2006).

Probably the most inclusive definition for culture, as most anthropologists would agree, is: “the thoughts, behaviours, languages, customs, the things we produce and the methods we use to produce them”. The ability of humans to create and transmit culture differentiates
us from the rest of the animal world (Jervis, 1998). The concept of culture as distinct from race/ethnicity has been proposed as a better explanation for differences in health behaviour and health outcomes (Pasick, 1994). Culture in the context of health behaviour has been defined as “unique shared values, beliefs, and practices that are directly associated with a health-related behaviour, indirectly associated with a behaviour, or influence acceptance and adoption of the health education message” (Pasick, 1994). Although culture seems to be a valid explanatory variable for racial and ethnic differences in health outcomes, researchers need to recognize that knowing someone’s ethnic identity or national origin does not reliably predict beliefs and attitudes (Hunt, 2005) and appropriate attention, methods and measures are needed to specify the cultural identity and cultural behaviour. This is why we tried in our study to be alert to this issue and to specify the patient’s behaviour according to his/her or the family’s explanation of that behaviour in the context of the cultural background of the patient.

The chronic stress related to social adversity, such as poverty, discrimination, racism, assimilation and acculturation, is currently the most popular and probably the most plausible explanation for the observed increased incidence of schizophrenia among migrants. The social defeat or social disadvantage hypothesis has been linked to most of immigrants who are black (Piep et al., 1991; Cantor-Graae & Selten, 2005), live alone (Burnett et al., 1999), are unemployed (Bhugra et al., 1997), belong to the lowest social class (Townsend, 1988) and are prone to racial discrimination (Karlsen, 2002; 2005; Veling et al., 2007). Acculturation is a concept that is often used to explain ethnic disparities in health outcomes. It is based on the assumption that culturally based attitudes and beliefs cause people to behave in certain ways, including health-related choices (Dressler, 1993). Acculturation measures assume that there is a “mainstream” culture and an “ethnic culture”. However, most studies on acculturation rarely include an explicit definition of culture or and often fail to describe what constitutes “mainstream” or “ethnic cultures.” (Hunt et al., 2004).

1.4. Background of our study

The incidence of Schizophrenia among migrants

One of the first credible studies about the effects of migration on psychiatric morbidity was “Migration and Insanity” (Ödegård, 1932). The study reported an increased incidence of schizophrenia of Norwegian immigrants compared to other residents of Minnesota (USA).
and these emigrated Norwegians were hospitalized with schizophrenia twice as often as Norwegians that never left their homeland. Based on his study, Ödegård formulated the theory of ‘selective migration’, stating that among migrants a relatively large percentage already had an increased risk of developing schizophrenia at the time they emigrated. He considered it to be unlikely that schizophrenia was caused by the stress of migration, since most of the migrant patients (75%) developed the illness after more than 5 years of living in Minnesota. It should be noted, however, that later analyses of the same study (Malzberg, 1955) demonstrated that stress associated with migration probably did play an important role in the development of mental disorders in these migrants, because the Norwegian immigrants became psychotic already during the first years after migration. It was Sashidharan (1993) who challenged Ödegård’s selective migration hypothesis based on the argument that there are important differences between different groups of migrants with some experiencing much more migration related stress than others, e.g. black Afro-Caribbean’s migrating to the United Kingdom versus white Norwegians migrating to the US.

Since the mid 1960’s different studies have repeatedly reported elevated rates of schizophrenia particularly among African-Caribbean’s in the UK. However it is important to mention that because of the crude methodology of the very first studies they should be interpreted with caution (Rwegella, 1977). The earliest first admission studies even lacked clear diagnostic criteria. In the 1980s a number of incidence studies were conducted particularly in the UK (Hitch and Clegg, 1980; Littlewood & Lipsedge, 1981; Dean et al., 1981; McGovern & Cope, 1987; Cochrane & Bal, 1989). These were all first admission studies using different methods of data collection ranging from case reports, case register information, and unstructured clinical diagnoses to diagnoses based standardized research instruments. These studies reported a ratio of schizophrenia among (dark) immigrants compared to (white) native citizens ranging from 1.1 to 6.2. Immigrants included in the studies were mostly first generation. In the 1990’s the methodology of the incidence studies improved mainly due to better sampling strategies and the use of structured assessment instrument for the diagnosis. However, immigrants from other Western countries were mostly excluded in these studies. The reference group in these studies were “whites” or the remainder of the general population (with or without Western immigrants). In addition, these studies often reported separate relative risks for first- and second-generation migrants. Some of these studies were based on first contact and not only on first admission rates. However, the reported rate of schizophrenia compared to the reference group remained remarkably high with a relative risk ranging from
During the last decade there is yet again great interest in the high rates of schizophrenia among immigrants, particularly in the UK (Bhugra et al., 2001, Kirkbride, 2006, Fearon et al., 2006), the Netherlands (Selten, 2001, Veling et al., 2006), Denmark (Cantor-Graae et al., 2003), Sweden (Zolkowska, 2001), and Australia (McGrath et al., 2001). These first contact incidence studies have even more sophisticated research designs with age standardization, clear inclusion and exclusion criteria, and the use of (semi-)structured interviews, some but not all also controlled for confounders such as socioeconomic status. The study of Selten et al., (2001) was one of the few that also controlled for neighbourhood levels of socioeconomic status although no confounding effect was found. However, one important shortcoming remains in all these studies: none of the (semi-)structured interviews that were used in these studies was validated for the different immigrant groups. Interestingly none of the authors mentioned this shortcoming as a possible source of bias in their studies. Strangely most of the authors mentioned the possibility of misdiagnosis due to the cultural background of patients but they remain in a status quo with regard to the methodology and none of them pays serious attention to cultural validation of the diagnostic instruments.

In addition to recent systematic reviews of the literature on the incidence of psychotic disorders among immigrants in general (Sharpley et al., 2001; Hutchinson, 2004, McGrath et al., 2004), two meta-analytic studies have been performed on the results of English-language publications in European countries (Cantor-Graae and Selten, 2005; Bourque et al., 2011). The first meta-analysis included 18 studies from 1977 to 2003 with very diverse methodologies, research criteria, recruitment strategies, ethnicity of immigrant groups, generations (sometimes first or second or the combination of both) and different diagnostic formulations (Cantor-Graae and Selten, 2005). The selection of studies was based on broad criteria in order to include as many studies as possible. According to this meta-analysis, the relative risk (RR) for first generation West-Africans in the UK was 26.1 (Rwegellera et al., 1977). The RR to develop schizophrenia for the first generation of Caribbean immigrants in the UK ranged from 0.6 (Thomas et al., 1993) to 8.9 (Harrison et al., 1988). Van Os et al., reported a relative risk of 4.2 for first and second generation Africans (1996). For Turkish first generation immigrants in the Netherlands an RR of 0.8 was reported, whereas the RRs for Moroccan and Surinamese immigrants were 4.5 and 3.2, respectively (Selten et al., 2001). Overall, the relative risk for second-generation migrants according to the results of the meta-analysis (based on seven comparisons) was 4.5 (95% CI=1.5-13.1), whereas for first
generation migrant the RR (with forty comparisons) was 2.7 (95% CI=2.3-3.2). Considering the persistence of an increased risk of schizophrenia and related disorders into the second generation, the authors suggest that post-migration factors such as perception of social inequality may play a more important role than pre-migration factors. The authors conclude that the increased risk for developing schizophrenia in migrants cannot solely be explained by selection. They also state that “the aspects of the environment that may contribute to this risk are still poorly understood, but perceptions of social inequality may be important.” They further suggest specific strategies to test the factors putatively involved in the migrant effect, e.g. ethnic groups across settings, differentiation between climate and socio-environmental factors, and urban versus rural upbringing.

A more recent meta-analysis (Bourque et al., 2011) included twenty-one studies from 1977 to 2008, including nine of 18 studies of the previous meta-analysis and a series more recently published studies from a variety of countries and less strongly dominated by studies from the UK, i.e. including additional studies from Israel, The Netherlands, Scandinavia, and UK. The most prominent risk factors in this study were ethno-racial status and host country (with ethno-racial categories: white, black Caribbean, black African, Asian and Middle East). This study reported no significant difference in relative risks between first and second generation migrants. Although there were generational differences in risk among some groups, this was not consistent across ethnic groups and countries. Almost all IRRs indicated a higher risk for psychotic disorders (including schizophrenia) in migrants with the exception of the Israel-based cohort study (Corcoran et al., 2008).

It is important to mention that there are also studies reporting negative findings concerning the relative risk of schizophrenia among migrants, which for some reason were not mentioned and not included in these meta-analytic studies. For example, in a study in the inner city of Mannheim (Germany) the age-adjusted incidence of treated psychiatric disorders among the German population exceeded that of Turkish immigrants (Weyerer, 1992). According to the authors, the most plausible explanations were segregation and differences in help seeking behaviour. According to the segregation hypothesis, the inner city of Mannheim was populated by a negative selection of vulnerable, lower class Germans that were no able to leave this part of the city (with a relatively high risk) and a positive selection of immigrants (with a relatively low risk). Another explanation for the relatively low use of psychiatric facilities by migrants was that the high proportion of immigrants in this area, mainly from Turkey and mostly workers were due to administrative factors, being recruited on the basis of good physical and mental health. Besides they may return to their country of origin for
care when they develop serious psychiatric disorders. Also in a review of the migrant studies by a Canadian Taskforce (1988) no increase of mental disorders among immigrants was found in comparison to native populations. Finally, an Australian case control study found that migrant status was associated with a significantly decreased odds of having a psychotic disorder (McGrath et al., 2001). As migration becomes increasingly accepted as a risk factor for schizophrenia and related disorders, it is remarkable that these negative studies with regard to the assumed increased incidence of psychosis among immigrants are not discussed in reviews or meta-analyses. As we mentioned before, the main concern with any migrant study remains the potential possibility of misdiagnosis (Sashidharan, 1993; Bhui & Tsangarides, 2008). All of the studies included in the meta-analyses used current diagnostic categories and procedures that were not culturally validated (Alarcón et al., 2002). The only attempt to deal with possible misdiagnosis based on the cultural background of patients in recent studies is a couple of studies that assigned a diagnosis based on clinical information that was blinded for ethnicity of the patient (Fearon et al., 2006; Selten et al., 2001). It looks like the authors of these studies were mainly concerned about racism as a possible source of misdiagnosis. However, this (blinding) approach ignores the crucial problem of the possible misinterpretation of stress indicators as psychotic symptoms and these studies may therefore still suffer from a serious number of culture-specific misdiagnoses resulting in inflated psychoses rates in migrants and inflated relative risks. Therefore, we do not agree with the conclusion that there is a “remarkable consistency of increased risk across a diversity of migrant populations and host society contexts” (Bourque et al., 2011). We feel that many if not most of the studies so far suffer from a serious flaw because the diagnosis was not based on a cultural sensitive diagnostic procedure and future studies should take this crucial aspect into serious consideration.

**Hypotheses to explain the high rates of schizophrenia in migrants**

In addition to the biological and/or psychosocial explanations that have been proposed to account for the repeatedly observed elevated rates of schizophrenia and other psychoses among immigrants, several authors have suggested that these findings could also be the result of methodological artefacts (Fernando, 1991), including differential pathways to care, diagnostic inaccuracies (language and cultural practices may hinder accurate diagnosis), confounding due to specific social inequalities, and problems in determining the numerator and denominator for the calculation of rates (McGrath, 2004). Here, we briefly review and evaluate these (alternative) explanations.
1.5. Explanations for increased incidence of schizophrenia in migrants

**Biological factors**

Several biological mechanisms have been proposed that may explain the increased rates of schizophrenia in migrant groups, such as differences in obstetric complications and infectious and inflammatory agents (Geddes, 1995). However, Hutchinson et al., (1997) examined a group of psychotic patients in London and reported that obstetric complications were almost twice as common among white patients in comparison to Afro-Caribbean patients with schizophrenia suggesting that differences in obstetric complications are not very likely to be the (main) cause of the high rates of schizophrenia in this migrant population. More studies are needed to fully exclude this possibility.

There are some preliminary data that older paternal age can contribute to the aetiology of schizophrenia (Malaspina et al., 2001; Byrne et al., 2003; Frans et al., 2011; Wu et al., 2012). However, there are currently no studies comparing the reproduction age of immigrants with native citizens looking at the relative risk of schizophrenia and, therefore, no conclusions can be drawn regarding this possible explanation.

There are some reports about maternal foliate deficiency during early pregnancy as a cause of schizophrenia (Geddes, 1995; McGrath et al., 2011). In addition, shorter inter-pregnancy intervals were investigated as a possible cause of foliate deficiency. The investigators reported an association between shorter birth intervals and schizophrenia in the offspring, albeit not linear (Krabbendam et al., 2005). In addition, prenatal vitamin D deficiency is associated with migrants living in cold climates and dark skin has been proposed as a risk factor for schizophrenia among second-generation migrants but not among first-generation migrants (McGrath, 1999, 2011). Moreover, the highest rates of vitamin D deficiency disorders in the UK have been in Asian immigrants that have lower rates of psychosis than black immigrants, making vitamin D deficiency an unlikely explanation for the high rates of schizophrenia in black immigrants.

In utero viral infections or inflammations have also been proposed to play a role in the aetiology of schizophrenia (Mednick et al., 1988; O’Callaghan et al., 1991; Brown et al., 2004; 2005). However, other studies did not find convincing evidence to support the prenatal exposure to the infection hypothesis (Glover, 1989; Selten et al., 1998, 2000). Eaton and Harrison (2000) suggested in this regard that the causal factor might not be exposure to some virus per se, but the response of the host to such an agent. However, no comparative data
are available for migrants and native citizens on this issue and, therefore, no conclusions are justified for this possible explanation for the increased rate of schizophrenia in migrants compared to native citizens.

Several authors propose increased substance use as a possible explanation for the higher rates of schizophrenia among immigrant, in particular cannabis (Zammit et al., 2002; Arseneault et al., 2004; Henquet et al., 2005). Although some studies have shown alcohol and drug abuse to be more common among ethnic minorities (Jayakody, 2006; Benschop 2011), this is not supported by other studies or population based data (Cantwel, 1999; Veen et al., 2002; Rodenburg, 2007).

In summary, none of these biological risk factors has strong empirical support. Moreover, none of these factors can explain the clearly different incidence rates of schizophrenia in different migrant groups or the relatively high rates of schizophrenia in second generation migrants.

**Genetics**

After the first reports about a higher incidence of schizophrenia among Afro-Caribbean immigrants in the UK, several authors have investigated this rate in some of the Caribbean islands, from which the immigrants originated. However, the incidence of schizophrenia in Jamaica (Hickling & Hodgers-Johnson, 1995), Trinidad (Bhugra et al., 1996), Barbados (Mahy et al., 1999) and Surinam (Hanoeman M, et al., 2002) was not higher than the range of world wide incidence rates of schizophrenia. In addition, Sugarman and Craufurd (1994) and Hutchinson et al., (1996) found similar risks for schizophrenia in the parents of Afro-Caribbean immigrants and native patients. Therefore, it seems unlikely that there is a race/ethnicity specific genetic vulnerability for these immigrants to develop schizophrenia.

**Sociodevelopmental factors**

More generally, across the life span, the chronic stress of poverty (Cohen, 1993; Saraceno & Barbui, 1997, Dohrenwend et al., 1992; Faris & Dunham 1939; Harrison et al., 2001) and some facets of a minority status like segregation (Mallett et al., 2002; Morgan et al., 2000 2007), discrimination and racism (Williams et al., 2003; Karlsen & Nazroo, 2002; Janssen et al., 2003; Veling et al., 2007), acculturation (Redfield et al., 1936; Halpern 1993; Fischer & Shaw, 1999; Harrison et al., 2001;Virta et al., 2004;) seem to increase the risk and to worsen the course of schizophrenia, although the direction and strength of these associations have not
yet been fully explored and findings are not always consistent (Jones et al., 1994; Harrison et al., 2001; Selten & Cantor Graae, 2004). According to Morgan and Hutchinson (2010), the higher prevalence of these indicators of higher social adversity in black Caribbean’s may partly explain the increased rates of schizophrenia. However, they note that this conclusion is rather speculative because the variables that were used are crude, no account was taken of explanatory factors and it was not possible to separate cause and effect. Hijern et al., (2004), in a national cohort study of 1.47 million adults and 1.16 million children and youth, found that social adversity contributes to the higher risk of schizophrenia and psychoses in two generations of immigrants of divers ethnicity. However, in a population-based study of first-episode psychotic disorders over three years in the UK, Kirkbride et al., (2008) reported that elevated rates of psychoses in black and minority ethnic groups could not be explained by socio-economic status. Moreover, the low incidence of schizophrenia among white working-class individuals with unemployment, inadequate housing and many other forms of deprivation is eye catching (Harrison, 1988; Leff, 1988; McGovern and Cope, 1991).

Finally, McGrath et al., (2001) reported that in Australia migrant status was associated with a significantly lower probability of having a psychotic disorder. For those born in Australia, neither migrant status of parents nor urban birth was associated with having a psychotic disorder. They conclude that environmental risk factors may operate in Europe but not in Australia.

However, there is little doubt that migrants are frequently confronted with poverty and social disadvantage. The stress diathesis model would simply state that increased stress will increase emotional distress and as a result psychiatric disorders will emerge and the increased rates of schizophrenia are just one specific consequence of the different stress factors related to migration (Bhugra, 2004; Myin-Germeys & Van Os, 2007). However, the low rate of schizophrenia in Turkish compared to Surinamese people in the Netherlands (Selten et al., 2001), who all experience racism and deprivation, is not consistent with this theory. Moreover, if the stress-diathesis model is true, one would expect primarily an increase of mood disorders, since for these disorders a relationship with major life events and daily hassles has been firmly established (Post, 1992). However, the reports regarding the prevalence of common mental disorders among immigrants are inconsistent (Bhugra, 2004; Weich et al., 2004; Vollebergh et al., 2005, Swinnen & Selten, 2007; Williams et al., 2007; McGrath et al., 2001, Menezes et al., 2011). Furthermore, the increased incidence of bipolar affective disorder among some migrant groups in the UK (Leff et al., 1976; Van Os et al., 1996b; Lloyd et al., 2005) has not been replicated among immigrant groups in the Netherlands (Selten et al., 2003). A meta-
analysis of the incidence rates of any mood disorders among different immigrant groups between 1966 to 2005 reported a mean relative risk of 1.38 (95% CI 1.17-1.62) which is not very convincing for a major increase (Swinnen & Selten, 2007). Considering the stress diathesis model, the authors fail to offer an explanation for this risk ratio compared with the strongly increased risk of schizophrenia (Selten et al., 2001; Veiling et al., 2006).

With regard to discrimination or factors associated with discrimination as part of a possible explanation, Veling et al., (2007; 2008) found an association between the incidence of schizophrenia and the perception of discrimination among ethnic groups. Further studies suggest that the incidence of schizophrenia among migrants and minority groups is highest in ethnically diverse areas where immigrants live among native inhabitants (Faris & Dunham, 1939; Boydell et al., 2001; Kirkbride et al., 2007). It has been suggested, that living in areas of high ethnic density (with little ethnic diversity) may have a protective effect against discrimination, isolation, and disadvantage (Kirkbride et al., 2007; Veling et al., 2008; Morgan & Hutchinson. 2010). Again this association is speculative and the ÆSOP study like other studies (Harrison et al., 1988) did not replicate the association between area of residence (with different degrees of population density) and high rates of schizophrenia in the black Caribbean population (Fearon et al., 2006; Kirkbrid, 2006). In a case-control study in Denmark the highest relative risk for schizophrenia and non-affective psychotic disorders is reported for the immigrants from other European Union countries and Scandinavia (Mortensen et al., 1997). The authors observed that schizophrenia was not increased primarily among socially disadvantaged immigrants but among individuals from countries neighbouring Denmark. They conclude that “it is unlikely that immigrants from these countries would experience acculturation to Denmark as more stressful to reconcile with the notion of migration stress.”

The resurgence of the interest in the potential role of socio-environmental factors in the aetiology of schizophrenia and other psychoses (Morgan et al., 2008), was at least partly a consequence of the findings of the reported higher risk of psychotic disorders in second generation compared to the first generation immigrants. It is thought that second generation are exposed to even more environmental stress than first generation migrants including racism and deprivation and as a result psychotic disorders like schizophrenia rates are even higher among second generation immigrants. However, the most recent meta-analysis on the risk for psychotic disorders among first- and second-generation immigrants found no significant risk difference between the generations (Bourque et al., 2011).
Here we like to emphasize that the central role of social factors and the sociodevelopmental pathways that have been proposed to account for the onset of schizophrenia in the last decade should not be considered as entirely distinct from the previously dominant neuro-developmental pathway (Morgan et al., 2010). This is exemplified by the higher incidence of autism in second generation Caribbean’s in the UK (Goodman & Richardson, 1995), the significantly higher risk of having a child with an autism-spectrum disorder for mothers born outside Europe with the highest risk observed for the Caribbean mothers compared with those born in the UK (Keen et al., 2010), the known overlap between schizophrenia and autism and the fact that the first symptoms of autism are present long before societal deprivation and discrimination may have exerted their influence.

It should be noted, however, that this complex set of findings explained by different models of specific facets of migrant life could also be the result of a culture based bias in the diagnosis based on a culture specific misinterpretation of symptoms. This is the overall theme of this thesis.

**Different pathways to care**

The pathways to care can vary considerably across ethnic/cultural groups and can lead to significant differences in apparent (treated) morbidity due to selection bias (Littlewood and Lipsedge, 1981; Sashidharan, 1993). Treatment seeking and referral can be influenced by sociodemographic, economic, and life style factors (e.g. drug use), beliefs and other cultural characteristics, that all can act different among diverse population groups. Without data on these characteristics it is difficult to really understand or discuss the reported high rates of treatment seeking patients with psychotic disorders among immigrants. One of the possible methodological problems in some of the incidence studies is the use of hospital admission statistics as indices of incidence. Although these records can provide reliable information in some instances, they can also be a source of serious bias. The admission rate could be influenced by factors such as different diagnostic or admission criteria for natives and ethnic minorities, differences in surveillance and referrals among different ethnic groups and different patterns of help-seeking behaviour (Littlewood and Lipsedge, 1981; Swinnen and Selten, 2007).

The higher compulsory admission rates and police involvement and the lower levels of general practitioner involvement for Afro-Caribbean patients are very important issues in this regard and have been observed already more than two decades (Rwegellera, 1980; Harrison et al., 1989; Pipe et al., 1991; Harrison et al., 1997; 1999; Bhui, 2003; Morgan et al., 2004;
According to the census 2006, the referral by the criminal justice system is one important factor among a wide range of factors that differs between black groups of immigrants in the UK and native patients, but it does not explain why second- and third-generation young black men are even more likely to be admitted to psychiatric hospitals (Bhui et al., 2003; The Count Me In Census 2006). Considering possible explanations for the higher risk of compulsory admission among immigrants from non-Western countries, it may be useful to distinguish between symptoms (e.g. hearing voices) and clinical presentation (e.g. aggression, as a response to hearing voices, or lack of motivation for treatment) (Morgan et al., 2004). It is suggested that differences in patient characteristics, such as clinical presentation and poor insight, and delay in help seeking are associated with the increased risk of compulsory admission. For example, delays in help seeking could occur due to different believes about mental illness and the quality of social networks.

In their study among 720 people referred to emergency psychiatric services in the Greater Rotterdam Area, Mulder et al., (2006) compared the risk of contact with psychiatric emergency services and of compulsory admission between immigrant groups and Dutch natives. They also looked for the unique contribution of ethnicity to compulsory admission. They conclude that “Non-Western immigrant groups were overrepresented in psychiatric emergency care and were admitted compulsorily more frequently, possibly owing to a different clinical presentation.” After controlling for symptom severity, danger, motivation for treatment and level of social functioning, non-Western origin was no longer associated with compulsory admission. They also mention another explanation for the higher rates of compulsory admission among immigrants: clinicians were mostly (90%) Dutch and could be ethnically biased. Evidence for such bias has also been reported by Lewis et al., (1990): “In our study, unfamiliarity with the way these immigrants present symptoms might have led to misinterpretation and to a greater perceived threat and more symptoms. Although danger to others and other clinical variables were measured using a structured assessment tool (SPI), this does not guarantee that these assessments were free from observation bias.”

In a recently published study, de Wit et al., (2010) reported a 2- to 3-fold higher incidence of acute compulsory admissions for any psychiatric disorder and for psychotic disorders among all migrant groups especially for second-generation from non-western countries in Amsterdam. The authors conclude “that the increased risk of acute compulsory admission in non-Western migrants can mainly be explained by the increased incidence of psychotic disorders in these groups.” Interestingly, their relative risk of acute compulsory admissions for psychotic disorders among Moroccan migrants was lower than expected on the basis
of incidence studies. In this regard factors like illness-related expression (the fact that non-Western groups were more often considered as a danger to others), access to care and quality of care are mentioned as possible relevant interacting factors in the observed increased incidence of psychosis among migrants.

Finally it is interesting to mention here that lower-class patients with schizophrenia were also more likely to be brought to treatment by the police or social agencies and to be compulsory admitted. We should not forget that both social class and immigrant issues have created a good deal of controversy in the epidemiology of schizophrenia (Cooper, 2005).

**Problems in determining the numerator and denominator**

Another important issue is the unknown real number of immigrants that live in a given area, are not registered but seek treatment when psychotic (Sashidharan, 1993). This can lead to an overestimation of the rate of treated mental disorders among immigrants (Mortensen et al., 1997). In addition, Harrison et al., (1997) discussed the possibility of under-enumeration of young men in the 1991 census. There is concern about the quality of the national census in the UK, in particular the possible underestimation of the number of young African-Caribbean men (Swinnen, 2007). Most of the immigrant studies did not discuss this issue explicitly (Mortensen, 1997). In order to resolve this problem, some studies from the Netherlands excluded subjects without legal residence from both the numerator and the denominator (Selten, 2001; Veling, 2006).

**Validity of diagnostic criteria and misdiagnosis**

The essence of the problem of misdiagnosis as a possible explanation for the reported high rates of psychosis among immigrants refers to the inability of (Western) psychiatrists to recognize culturally appropriate expressed emotional distress in response to difficult life circumstances in non-Western ethnic minority patients, the fact that they often miss the diagnosis of mood and brief reactive disorders and in stead make a diagnosis of psychotic disorder or even schizophrenia (McKenzie, 2008). Within the broad spectrum of psychoses some differences between ethnic groups in the presentation of symptoms and the way that distress is experienced are reported. In the United Kingdom a number of studies suggest that black patients compared with white patients tend to present more reality distortion and affective symptoms but are less likely or willing to present negative symptoms (Ndetei & Vadher, 1984; Hutchinson et al., 1999; Demjaha et al., 2006).
The lack of a cultural sensitive understanding of clinical presentations or symptoms has already more than a decade been considered as one of the most important shortcomings in epidemiological studies creating possible misclassification and overdiagnosis of psychotic disorder in ethnic minorities leading to scientifically unjustified high rates of schizophrenia in immigrant populations (Lewis-Fernandez 1996; Weisman 1997; Jenkins, 1998; 2003). Even though different authors underline the value of systematic attention to culture in order to improve the validity of clinical diagnosis, most incidence studies in the UK used rather standard methodology and made no serious effort to prevent cultural bias as a specific form of information bias. According to these authors, the use of structured interviews has minimized the possibility of misdiagnosis. Albeit the use of structured clinical interviews may help limit misdiagnosis in ethnic/racial groups, knowledge and attention to variations in symptom presentation is crucial and is generally not taken into account in these structured interviews (Strakowski, 1996). For example, structured interviews do not adequately address potential biases underlying ethnic differences in the recording of affective symptoms leading to an underestimation of the number of affective disorders in black psychiatric patients (Strakowski et al., 1997). This leads to the crucial question whether the reported higher rates of schizophrenia among some immigrants collected by culturally non-validated interviews and questionnaires can at least partly be the result of a methodological artefact (Fernando, 1991). Unfortunately, a systematic analysis of the validity of diagnostic tools is uncommon in transcultural epidemiology (Van Ommeren, 2003). For example the use of the CIDI is reported to be problematic due to the presence of construct, method and item bias in elderly migrants (Smit et al., 2005). However, in most studies, the authors did not question the validity of their (semi-)structured interviews in migrants. It is remarkable that most of them chose to be blind to the ethnicity of the subjects during diagnostic consensus meetings in order to prevent racial stereotyping in diagnosis. However, if the current categorical diagnoses and procedures for data collection are never validated for different cultures (Alarcón et al., 2002), the main question remains whether in cross-cultural studies “like is being compared with like” (Morgan et al., 2008).

Only a few studies have tried to assess the possible effect of ethnic/cultural issues as a possible reason for the reported high rates of schizophrenia in non-Western migrants. Hickling et al., (1999) compared the diagnoses of a group of black patients made by a British and a Jamaican psychiatrist. The two psychiatrists agreed in only 55% of cases, but the percentage of black patients diagnosed with schizophrenia was not different and thus there was no systematic bias. Different studies in US also have tried to compare research diagnoses with standard
clinical diagnoses. The findings of these studies suggest that misdiagnosis is at least one reason for race differences in the prevalence of schizophrenia in epidemiological studies (Mukherjee et al., 1983; Strakowski et al., 1997; Neighbors et al., 1999; Whaley 2001b). In a recent study, Eack and colleagues (2012) report that the interviewer’s perception of honesty of African-American participants are important contributors to disparities in diagnostic rates of schizophrenia. African-Americans were more than three times as likely as whites to be diagnosed with schizophrenia. However, after adjustment for perceived honesty, diagnostic disparities between African-Americans and whites were substantially reduced. Mediator analyses confirmed that interviewer-perceived honesty was the only consistent mediator of the relationship between race and schizophrenia diagnosis. (Shaun et al., 2012). Selten and Hoek (2008) mention the possibility of arbitrary diagnostic boundaries in certain populations, but they reject misclassification as a factor explaining “the schizophrenia epidemic among immigrants from developing countries to Western Europe” and dismiss attempts to study this issue as a “laudable motive to save the immigrants from the stigmatizing diagnosis of schizophrenia”.

In contrast to most studies on schizophrenia in migrants, the prevalence of depression has been reported to be low among some immigrant groups in the UK (Shaw et al., 1999; Bhugra 2003). In a recently published meta-analysis on mood disorders, no conclusions could be drawn about the risk of all mood disorders in migrants compared to natives (Swinnen & Selten, 2007). However, the mean relative risk of bipolar affective disorder for migrants compared to natives was increased (Swinnen & Selten, 2007; Van Os et al., 1996a, b). Van Os mentioned that this increase was particularly marked in individuals with schizomanic psychoses. More than a decade ago, McKenzie et al., (1999) already suggested that “the misdiagnosis lies in the fact that affective symptoms are missed or trumped by the symptoms of schizophrenia in the hierarchical minds of psychiatrists”. Population surveys have confirmed that psychotic-like experiences are prevalent in the community, and individuals with depression and anxiety are more likely to report these symptoms compared with individuals without mood and/or anxiety disorders. Interestingly, also the odds of endorsing any CIDI (Composite International Diagnostic Interview) hallucination or delusion item was increased in those with a major depressive or anxiety disorder (Varghese, 2011). Dissociative symptoms together with somatic symptoms in patients with depression and anxiety may create the impression of psychotic disorder (Kirmayer, 2001). Besides it is proposed that perceived discrimination predicts the development of psychotic or psychotic-like symptoms in healthy persons (Janssen et al., 2003) and this might be another source for the diagnosis
of psychosis among immigrants. According to Swinnen and Selten (2007) “It is possible that migrants with mood disorder are less likely to seek treatment compared with native-born people. It is conceivable, for example, that people from developing countries are less inclined to consider mood disorder as conditions that require medical treatment.” The findings of the meta-analysis of mood disorders and the findings of the meta-analysis of psychosis and schizophrenia among immigrants seem to indicate that affective symptoms are often missed and that affective disorders offer co-occur with psychotic or psychotic like symptoms and that this combination could result in an underestimation of mood/anxiety disorders and an overestimation of psychotic disorders in migrant populations. Although the authors did not mention the possibility of this shift of diagnosis between mood and psychotic disorders and misdiagnosis, they declare that they are surprised about the fact that the increased presence of stress associated with migration, poverty and low social-economic status was not associated with a considerable increase in mood disorders (Swinnen & Selten, 2007).

Course and outcome of psychosis in ethnic groups

The suggestion of a better prognosis of psychotic disorders in migrants (Littlewood and Lipsedge, 1981) is interesting since - besides a noted cross-culturally variability for the course of schizophrenia and a markedly superior prognosis for individuals from developing countries (Jablensky et al., 1992; Lom & Kleinman, 1988) - it could also point at some kind of culture based misclassification in which migrants run a risk to get an unjustified diagnosis of schizophrenia with an unexpected favourable prognosis. We will investigate this hypothesis in one of the studies in this thesis. McKenzie et al., (1995, 2001) reported that black Caribbean participants were less likely to have a chronic illness course and suggested the presence of a better course and outcome in psychosis for black Caribbean populations compared to other ethnic populations living in the UK. However, in a recent systematic review on this topic, Chroloton (2011) concluded that the number of studies is too small and that the quality of the studies is too low to ascertain whether the course and outcome of schizophrenia is better in migrants compared to native citizens: “The findings from studies are contradictory or inconclusive, which is not unexpected given the heterogeneity in the quality of the studies and in the methodological approaches taken. As such, drawing firm conclusions from the data reported in this review is not possible”.

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1.6. Outline and approach of this thesis

A substantial body of research has replicated the increased incidence of schizophrenia among different immigrant groups, particularly in the UK and the Netherlands. Although recent studies have increased diagnostic reliability and reduced information bias through the use of standardized diagnostic interviews, the importance of cultural aspects of the diagnostic process has been denied in almost all studies.

This thesis investigates the impact of a cultural sensitive assessment in treatment seeking Moroccans in Morocco and treatment seeking first and second generation Moroccan immigrants in the Netherlands. In the study among Moroccan immigrants in the Netherlands, treated incidence rates of psychosis and particularly schizophrenia are established for Moroccan immigrant and native Dutch patients comparing the results of incidence rates based on a standard semi-structured interview (CASH) and diagnoses obtained using the same standard semi-structured interview supplemented by cultural probes and decision rules (CASH-CS) in both native Dutch patients and Moroccan immigrants in Utrecht. The CASH-CS is an expanded version of the standard CASH with additional cultural relevant questions for almost all sections to clarify relevant items of the instrument and to help interpret answers of the patient. The assessment procedure with the CASH-CS also included the Retrospective Assessment of the Onset of Schizophrenia (IRAOS) (Häfner et al., 1992), an interview with a key informant and the patient to elicit additional background information on the history of the illness. A narrative history of the patients’ illnesses based on the CASH-CS and the CASH was discussed separately during two consensus meetings with the presence of the interviewers and one or more psychiatrists participating in each procedure to arrive at a consensus DSM-IV diagnosis.

In chapter 2 the main question is whether the CASH, a commonly used interview to diagnose psychosis and schizophrenia, is a valid instrument for the diagnosis of psychotic disorders among Moroccan patients in Casablanca, Morocco. In order to establish the differential validity of the CASH and the culturally sensitive CASH-CS, diagnoses based on these two assessment procedures are compared with diagnoses made by local Moroccan psychiatrists. The main question is whether addition of cultural probes and decision rules improves the agreement between the standardized diagnosis and the clinical diagnosis?

In chapter 3 we examine the incidence of schizophrenia among Moroccan immigrants in Utrecht, the Netherlands using the CASH and the CASH-CS. Specifically we try to answer the question whether the incidence rates of psychotic disorders including schizophrenia
among Moroccan immigrants to the Netherlands is higher than in native Dutch people and whether this difference remains significant when a cultural sensitive version of the assessment procedure (CASH-CS) is used.

In *chapter 4* we test the predictive validity of the diagnosis of different psychotic disorders according to the two different versions of diagnostic interview (CASH and CASH-CS) in Moroccan immigrant and native Dutch patients looking at diagnostic stability and at the course and outcome during a 30 months follow-up.

In *chapter 5* we examine whether Moroccan immigrants compared with native Dutch referred for the first time to a mental health service for a psychotic disorder have different symptom profiles according to the CASH and the CASH-CS. More specifically, we investigate whether the probability of a current depressive episode is different in Moroccan patients compared to native Dutch patients and whether this difference is dependent on the assessment procedure (CASH vs. CASH-CS).

Finally in *chapter 6* the most important findings are summarized and the implications for diagnosis, treatment and further research are discussed.
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