The role of cultural background in diagnosing psychotic disorders

Misclassification of psychiatric symptoms in Moroccan immigrants in the Netherlands

Tekleh Zandi

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Het belang van culturele achtgrond bij de diagnose van psychotische stoornissen

Fouten bij het vaststellen van psychiatrische symptomen bij Marokkaanse immigranten in Nederland.

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Faculteit der Geneeskunde

Voor mijn moeder en vader

Contents:

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 mental 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 preaecox, 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 form 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 life time 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

1.9 to 10.0 (Castle et al., 1991; Selten et al., 1994; Van Os et al., 1996; Selten et al., 1997; Harrison 1997; Goater 1999).

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 caching (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;

2005; 2006). 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 colleges (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., 1996 a, 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”.

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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Chapter 2

The need for culture sensitive diagnostic procedures: a study among psychotic patients in Morocco.

Zandi T, Havenaar JM, Limburg-Okken AG, van Es H, Sidali S, Kadri N, van den Brink W, Kahn RS. Social Psychiatry and Psychiatric Epidemiology 2008, 43: 244-250.

Social Psychiatry and Psychiatric Epidemiology 2008, 43: 244-250.

Abstract

Objective

We examine the procedural validity of a standardized instrument for the diagnosis of psychotic disorders in Morocco.

Method

Twenty nine patients from Casablanca, Morocco, with a psychotic or mood disorder were examined using the Comprehensive Assessment of Symptoms and History (CASH) an adapted version using cultural formulation to make the instrument more culturally sensitive (CASH-CS). Chance corrected agreement was calculated between diagnoses based on these two versions of CASH and independent clinical diagnoses according to local psychiatrists.

Results

Agreement for traditional CASH versus clinical diagnosis and for CASH versus CASH-CS was low (kappa = -0.19; sd 0.16 and kappa = 0.21; sd 0.16 respectively). De CASH-CS, showed good agreement with clinical diagnosis (kappa = 0.79; sd 0.11).

Conclusion

Standardized instruments for the assessment of psychosis such as the CASH may be liable to cultural misinterpretations. This may be relevant to the interpretation of the high incidence rates of schizophrenia among immigrants.

Significant outcomes

Agreement between a culturally naïve version of a standardized diagnostic instrument for the assessment of psychosis and clinical diagnosis by Moroccan psychiatrists is poor. Adding additional probes and decision rules based on cultural formulation improves agreement with clinical diagnosis significantly.

Limitations

The study was conducted in a small sample. Both versions of CASH were administered by the same interviewer in a single interview session.

Key words: standardized diagnosis, schizophrenia, psychosis, cultural formulation, Morocco.

1. Introduction

The repeated findings of an increased incidence of schizophrenia and other psychotic disorders among immigrants have challenged the common belief that schizophrenia is a disorder with a roughly equal incidence across countries and ethnic groups (Saha et al., 2005). Especially, the higher incidence rates among Afro-Caribbean immigrants in the UK (Murray & Hutchinson, 1999; Sharpley et al., 2001; Bhugra & Cochrane, 2001) and immigrants from Morocco to the Netherlands (Selten et al., 2001) have raised the interest in the role of social and cultural factors in the aetiology of this disorder. As yet the underlying mechanisms to explain these findings have remained elusive. A number of authors have criticized the methodology of these studies and challenged the validity of the increased incidence of schizophrenia among immigrant populations. Several authors have demonstrated that the ethnicity, language preference and related cross-cultural factors may influence mental health service utilization (Stuart et al., 1996; Folsom et al., 2007). Differences in admission rates and diagnostic evaluations between ethnic groups may have led to an overestimation of the treated incidence among these immigrants (Mortensen et al., 1997; Mckenzie, 1999; Littlewood & Lipsedge, 1981; Sashidharan, 1993; Hickling et al., 1999; Haassen et al., 2000). Others have questioned the effectiveness of standardized diagnostic procedures for the comparison of psychopathological phenomena in cross-cultural psychiatry (Wing et al., 1974). A number of these studies has demonstrated that factors such as race, gender and ethnicity are associated with considerable diagnostic bias, even when standardized diagnostic criteria and assessment procedures are being used, particularly when patients and psychiatrists differ from each other on these variables (Neighbors et al., 2003; Reeves et al., 2003; Arnold et al., 2004). E.g., Littlewood and Lipsedge showed that West Indian patients were much more often diagnosed as schizophrenic by the medical staff, even in the absence of Schneider's First Rank Symptoms (Littlewood & Lipsedge, 1981a; Littlewood & Lipsedge,1981b). The fact that such biases occur even when standardized diagnostic criteria and assessment procedures are being used, has serious consequences for the validity cross-national studies and for incidence studies comparing the rates of psychiatric disorders between ethnic groups within a population. Since the original introduction of standardized diagnostic instruments for the assessment of schizophrenia a number of studies has demonstrated the reliability of such instruments in various countries and cultural settings (Karno et al., 1983; Pakaslahti, 1987; Vazquero -Barquero et al., 1998; Strakowski et al., 2003). However, most of these studies have used diagnostic raters from the same cultural background as the patients. Only a few studies have

examined the procedural validity of these instruments when applied by diagnostic raters with a cultural background different from the patients (Hickling et al., 1999; Haassen et al., 2000). Kleinman (1980) questioned the validity of applying diagnostic concepts to different ethnic groups in Western societies and has introduced the term "categorical phalacy" to describe the misclassification which may result when culturally sanctioned idioms of expressing distress are interpreted as diagnosable pathological phenomena (Kleinman, 1987).

Two areas of pathology are particularly relevant in this respect, i.e. hallucinations and dissociative symptoms. In some cultures hearing voices and seeing images or faces of relatives is quite common and not necessarily pathological. Hearing voices may actually be a key presenting symptom of emotional problems which sometimes is perceived to be related to supernatural events (Alsughayir 1996; Al-Issa, 2000). Hearing voices, especially if experienced as originating from inside the head, can be a normal experience of thought. The differentiation between traditional, non-pathological idioms of distress and religious experiences, and true positive symptoms of psychosis can be very crucial in diagnostic procedures (Zarrouk, 1975; Rack, 1982; Al-Jadiri, 1996).

The second area of possible misinterpretation is that of dissociative experiences. In Morocco, as in some other areas in Africa, the Middle East, and Asia, people can enter a state of trance or dissociation during religious ceremonies. Many people have either had such an experience themselves or have observed other people in such states. In these regions sensations of floating above or outside of the body are not necessarily a medical condition, but a religious phenomenon or a culturally appropriate idiom of distress (van Duijl et al., 2005). In such a state a person experiences that his or her mind and body is taken over by an external force such as a spirit. In many parts of the world witchcraft and possession are idioms of distress and are culturally sanctioned ways of accounting for misfortune and are socially accepted. A "possessed" person may perform actions that are totally out of character. They are sometimes misdiagnosed as schizophrenia and treated as such (Dein, 1997).

These two areas of possible false positive symptoms can be the source of misclassification in epidemiological studies. Therefore, the American Psychiatric Association recommends using a "cultural formulation" as an aid to assist the proper interpretation of symptoms against their cultural back ground)(APA, 1994). Unfortunately, very few studies have been conducted to assess the potential impact of a cultural formulation on diagnostic decisions. As yet, to our knowledge, no attempts have been made to incorporate cultural formulation into standardized diagnostic instruments.

In this paper we describe the results of a study using a standardized diagnostic instrument in a sample of treatment seeking psychiatric patients in Morocco with and without the application of additional probes and decision rules based on a cultural formulation. Diagnoses based on the original version of the CASH (CASH: Comprehensive Assessment of Symptoms and History) (Andreasen et al., 1992, and on the culture sensitive version of the CASH-CS (CASH-Cultural Supplement) specially developed for use among Moroccan patients were compared with each other and with independent clinical diagnoses made by local psychiatrists.

2. Material and methods

2.1. Subjects

Patients were recruited in a period of five weeks (April and May 2003) from the Ibn Rochd hospital in Casablanca (Morocco). This hospital is the main psychiatric facility of Morocco. It is affiliated with the University of Casablanca with 200 beds in a city with almost 4,000,000 inhabitants. During this period, we included newly referred patients who agreed to participate in our study, inpatients as well as outpatients (response rate 90%). The only inclusion criterion was to have a schizophrenia spectrum disorder or a mood spectrum condition. Exclusion criteria were the probable presence of organic cerebral disorders or disorders related to substance abuse. Because we were primarily interested in the validity of the instrument in cases of recent onset psychoses, all patients with a onset longer than two years ago were excluded. All subjects gave verbal informed consent, as may of them were analphabetic.

2.2. Instruments

The CASH is a semi-structured standardized diagnostic interview, specifically designed for making the diagnosis of schizophrenia spectrum disorders and affective spectrum condition according to different classification systems including DSM-IV. The CASH has been used primarily in studies on the neurobiology of schizophrenia and major affective disorders in clinical settings, and has more recently been used in a first contact incidence study of schizophrenia in the Hague, the Netherlands (Selten et al., 2001).

2.2.1. Adapting the CASH to Moroccan culture

For the purpose of a planned study to re-evaluate the high first contact incidence rates among Moroccan immigrants in the Netherlands, a modified version of the CASH was developed. The purpose of this modification was to arrive at a culturally sensitive, unbiased interpretation of psychotic symptoms, taking into account the cultural back-ground of these immigrants which can determine the content of illness and the way that it is expressed.

The adapted culture sensitive instrument, which we call CASH-Cultural Supplement (CASH-CS), was developed to differentiate between true positive symptoms of psychosis and other, culturally appropriate idioms of distress among Moroccan patients.

As a first step in the development of CASH-CS a number of focus group sessions were held in which each of the CASH-items was reviewed for comprehensibility and appropriateness of formulation for use among patients of Moroccan descent. The members of these groups were trained psychiatrists, psychologists and a translator, all with extensive experience in working with Moroccan patients. Some of them were themselves of Moroccan origin.

One focus of attention was how to differentiate between non-pathological idioms of distress, described in the introduction, and true positive symptoms of psychosis. As one participant pointed out, Moroccan parents often ask their children when they are ill whether they hear voices. This is based on the fear that sick children are particularly prone to become possessed by demons. Based on such expectations, some Moroccan adults still hear voices whenever they have a fever.

A second important area was the assessment of affective symptoms. The Moroccan language does not have a specific word for depression (Tijdink & van Es, 2003), so our patients may not immediately know the meaning of this word. A third area was that of dissociative phenomena which is also discussed in our introduction. For each of these areas we formulated ways to introduce the item, words that could be used to describe the item, and appropriate translations to make sure all items were easy to understand. In addition guidelines were formulated to make sure the patient would feel fully at ease to freely discuss his or her experiences, without breach of taboos of feeling shame.

Appendix 1 gives an overview of the general and specific instructions for conducting the adapted version of the instrument and items which were adapted in the CASH-CS on the basis of the procedure described above.

2.3. Procedure

During a period of five weeks the recruited patients in Casablanca, Morocco were interviewed by a Dutch resident psychiatrist (TZ) of Iranian descent and a Dutch translator of Moroccan descent who was an experienced social worker. The translator translated the questions from the interviewer into Arabic or Berber language and used the Dutch language to convey the patient's responses to TZ. Both interviewer and translator worked in a mental health institute in Utrecht, the Netherlands. Before starting the study in Morocco both the interviewer and the translator were extensively trained in the use of the CASH. Positive symptoms were scored on the basis of the CASH interview, and were rated before and after applying the additional cross-cultural probes and decision rules described above. As is standard procedure in using the CASH, diagnoses are only made after taking all available clinical records into account. However, for these patients only limited documentation of prior medical history was available. Whenever possible information was gathered about the history of the illness from the family of the patients, either directly or through local residents or employees of the hospital who had contacts with the family. The interviewers remained blind for clinical diagnosis. A case history based on the CASH, family information (if available) was compiled. For CASH-CS a cultural formulation of the positive symptoms was added where appropriate. Diagnoses based on CASH and CASH-CS were formulated during consensus meetings in the Netherlands in which four Dutch psychiatrists participated (JMH, AL, SS and HE). These raters, who were also blind to the clinical diagnosis of patients and their names, discussed and decided on the DSM-IV diagnostic classification (Diagnostic and Statistical Manual of Mental Disorders, 4th edition, 1994) on basis of CASH and CASH-CS information at two separate consensus meetings.

Clinical diagnoses were established routinely using un-structured clinical interviews and clinical observation by experienced Moroccan hospital psychiatrists who were blind to the data collected with the CASH and the CASH-CS. The Moroccan psychiatrists interviewed the patients in their native tong. They applied DSM IV as diagnostic criteria. These diagnoses were kept separately in a list.

2.4. Statistical analysis

In order to establish cross-cultural validity of the CASH and the CASH-CS, DSM-IV consensus diagnoses based on these instrument were compared with the independent clinical

diagnosis of the local psychiatrist using the overall percentage of agreement and a chance corrected measure of agreement: Cohen's Kappa for dichotomous data (Cohen, 1960).

3. Results

The sample consisted of 29 patients (16 men, 13 women, mean age 32 years) with a clinical diagnosis of a psychotic or affective disorder. Table 1 shows the socio-demographic characteristics of the patients: 56% males, 38% married, 31% employed. Fourteen patients had a clinical diagnosis of schizophrenia and 15 patients a mood disorder. One patient had no clinical diagnosis at intake, but later when we finished inclusion she was clinically diagnosed with a factitious disorder.

Rates of employment were rather low in both clinically psychotic and mood disorder patients (21% versus 40%), but previous occupational status was somewhat higher: 57% in clinically psychotic patients and 71% in clinically mood disorder patients.

Tables 2a, b, c provide an overview of diagnoses based on CASH, CASH-CS and clinical diagnoses and pair wise of chance corrected agreement between the different diagnostic approaches. A psychotic disorder was present in 73%, 41% and 48% of the patients according to the CASH, the CASH-CS and the local psychiatrist respectively. Table 2a shows that 11 out of 15 patients (73%) with a clinical diagnosis of mood disorder were diagnosed as psychotic, but according to table (2b) none of these were classified as such by the CASH-CS. The agreement between CASH-CS and the clinician's diagnosis of a mood disorder was perfect. This difference between the CASH and CASH-CS in their correspondence to the clinicians diagnosis was mainly attributable to the different interpretation of voices and trance states, which were rated as psychotic phenomena according to the CASH. In addition to over classification of positive symptoms we also observed considerable underestimation of the presence of mood disorders by the CASH in comparison to both the CASH-CS and the clinical rater. 4 out of 14 patients with a clinical diagnosis of psychosis (28%) were classified as having a mood disorder by the CASH, whereas this was the case in only 2 cases (14%) on the basis of the CASH-CS.

Also we found some indication that using the standard CASH interview some psychotic symptoms were missed. Interestingly, 50% of patients with a mood disorder according to CASH was clinically diagnosed as psychotic. For CASH-CS this was only 12%.

Chance corrected agreement between the different diagnostic approaches were Kappa=

-0.03 (sd 0.16) for clinical diagnosis versus CASH, Kappa =0.79 (sd 0.11) for clinical diagnosis versus CASH-CS, and Kappa = 0.18 (sd 0.14) for CASH versus CASH-CS.

Table 1: Sociodemographic characteristic of patients

	characteristic	psychosis	mood disorder
Number of patients	29	14	15
Male/ Female	56%	78%	33%
In-patient(%)	41%	50%	33%
Married	38%	14%	60%
occupation.	31%	21%	40%

Table 2: Agreement between the various diagnostic approaches

2a: Clinical diagnosis versus CASH

	Clinical Psychosis	Clinical Mood disorder	Total
CASH Psychosis	10	11	21
CASH Mood disorder	4	4	8
Total	14	15	29

Percentage agreement = 48%
Kappa = -0.19 (sd 0.16)

2b: Clinical diagnosis versus CASH-CS

	Clincal Psychosis	Clinical Mood disorder	Total
CASH-CS Psychosis	12	0	12
CASH-CS Mood disorder	2	15	17
Total	14	15	29

Percentage agreement = 93 %
Kappa = 0.79 (sd 0.11)

2c: CASH versus CASH-CS

	CASH Psychosis	CASH Mood disorder	Total
CASH-CS Psychosis	10	2	12
CASH-CS Mood disorder	11	6	17
Total	21	8	29

Percentage agreement = 55 %
Kappa = 0.15 (sd 1.32)

4. Discussion

The purpose of this study was to assess procedural validity of a standardized diagnostic instrument for the diagnosis of psychotic syndromes in Morocco and to examine the impact of adding cultural sensitive probes and decision rules to a standardised diagnostic interview. These were added to clarify the presence or absence of symptoms in the context of the local culture and language. To our knowledge, this is the first study to compare the procedural validity of a standardized diagnosis in cross-cultural research against a clinical diagnosis of a fully culturally informed local psychiatrist and to assess the impact of using the specific cultural formulation on standardized diagnosis. Hickling et al., (1999) re-evaluated Afro-Caribbean patients diagnosed with schizophrenia in the UK by a Jamaican psychiatrist using clinical assessment and the PSE CATEGO system. They found that the agreement about a diagnosis of schizophrenia between a Jamaican, British psychiatrist and the PSE CATEGO system was poor. Diagnostic disagreement was greatest when the British and Jamaican psychiatrist were compared with PSE CATEGO system, and particularly so among Afro- Caribbean and/or black patients. These authors conclude that the high reported rates of schizophrenia in African or African-Caribbean populations in UK cannot be explained on the basis of misdiagnosis by British psychiatrists. However, they state that the PSE CATEGO system may have overestimated the rates of schizophrenia in African-Caribbean and white populations. One of the study implications is that the PSE generates a diagnosis of schizophrenia among African-Caribbeans in the UK at a higher rate than clinical evaluations. This study suggest that the PSE-CATEGO is also liable to over-diagnose of psychotic disorders, despite the fact that this instrument is accompanied by glossary which aim to help to differentiate between psychotic symptoms and culturally specific beliefs of experiences.

In this study by interpreting the symptoms in the context of culture, we were able to arrive at diagnoses which showed far higher agreement with the independent clinical judgement of local psychiatrists, than the original standardized interview. The study shows the value of using additional contextual information along cultural formulation guidelines to achieve greater diagnostic agreement with culturally informed local psychiatrists. This finding suggest that excluding cues about the cultural background of the patient, as applied as a method to exclude cultural bias by some authors (Selten et al., 2001), may itself introduce a source of bias.

In the present study the observed differences in agreement are mainly attributable to different scores for positive symptoms and the hierarchy of affective symptoms. After comparing

the results it looks like additional information as discussed in appendix I by considering the cultural beliefs could appropriately guide the Netherlands psychiatrists to distinguish the typical idioms of distress among Moroccan patients from psychotic symptoms and to more correctly identify mood symptoms. We found also some indication that the CASH-CS interview may pick up some psychotic symptoms missed by the original. The better agreement of CASH-CS with clinical diagnosis may be due to the additional information collected as part of CASH-CS, which may overlap with the contextual information routinely collected by the clinician as part of his routine diagnostic evaluation.

The study has a number of limitations which should be taken into consideration. First, the number of patients is relatively small. Second, the CASH and CASH-CS were administered and scored by the same interviewer and during a single session. Therefore the comparison presented in this paper can not be regarded as a test of inter-rater reliability, but rather as a test of procedural validity accessing only the impact of adding additional cultural information. It is important to note that diagnosis were made independently by a panel of psychiatrists, thereby limiting any possible bias from the interviewer.

Despite these limitations, the high agreement between clinical diagnosis and CASH-CS, in contrast with the regular CASH interview, cannot be ignored. Even though there is no gold standard against which a diagnostic psychiatric interview can be adequately calibrated, the results of our study seem to implicate that the CASH-CS is less likely to lead to false positive diagnose of psychotic illness in a sample of Moroccan patients.

Future larger scale epidemiological studies should pay more attention to the interpretation of the emotional language of the patient in a specific cultural setting. This can be a crucial element in reaching a valid diagnosis in both clinical and research settings.

Whether the findings presented in this paper can be generalized to other standardized instruments remains to be further investigated.

5. Conclusion

On the basis of the findings presented in this paper it seems advisable to use an adapted version of a standardized diagnostic instrument similar to the CASH-CS in future epidemiological studies about psychotic illness, involving patients of diverse cultural background. Particularly our study seems to imply that the traditional CASH interview may be sensitive, but not very specific to positive symptoms of psychosis and may therefore give rise to false positive

diagnoses of psychosis and to an overestimation of psychotic illnesses in epidemiological studies among Moroccan patients.

The study also shows the potential benefits of using cultural formulation as an adjuvant to classification. The study shows that excluding cues about the cultural background of the patient, as applied as a method to exclude cultural bias by some authors (Selten et al., 2001), may itself constitute a source of bias. If more attention and informed interpretation of the emotional language of the patient can be a crucial element in reaching a valid diagnosis, more attention to cultural formulation of symptoms in the future epidemiological studies about the incidence of schizophrenia among various groups of immigrants.

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Appendix:

General instructions for a diagnostic interview for psychosis among Moroccans

- Take enough time. If necessary have contact with the family (siblings) to get more information about the patient.
- Make sure to establish a good rapport. Mostly you get reliable answers only if the patient trusts you. Repeat several times that all reported information is confidential.
- Before you start with each section, explain to the patient the purpose of that section. Make it clear that if you ask different questions this is because it is a part of the questionnaire and not because you expect him or her to have these symptoms.
- In Moroccan culture shame for forbidden acts (sin) and respect to elders sometimes inhibits people to give a direct answer. This should be taken into account with most of questions related to drugs or alcohol use, sex, physical and mental health.
- Ask all questions in concrete words (e.g. sad, tired, happy). Avoid abstract words as much as possible (e.g. depression, shame, guilt) and use plain concrete language to explain these conditions. Double-check whether the patient has understood your question correctly.
- Be alert that some people may try to obtain social facilities with a factitious medical or psychiatric diagnosis.

Instructions for specific symptoms among Moroccans

Depression:
Always check for affective symptoms carefully; patient may not report these spontaneously after an initial, straight-forward question. For some sub-groups of Moroccans depression is not accepted as a disease. The Berber language, which is one of the major languages in Morocco, does not have a proper word to directly and simply express depression. Only if one has serious somatic disabilities or severe symptoms one is not obliged to fulfil his social obligations. Hearing voices or noises can actually express a distressed situation and is not necessarily a manifestation of psychosis.

Mania:
During special days, like in the month of Ramadan and during Offer Ceremony, some Muslims can appear irritable or excited. Do not confuse this with mania or hypomania.

Suicide:

Suicide is forbidden in Islam. Muslims will not readily talk about it directly. An alternative question is whether one hopes or prays that God will take him of her sooner to Himself

Delusions:

Make it clear that you are talking about a situation which is out of the ordinary. Check through the translator if this is fully understood by the patient. Some young Moroccan immigrants feel they are

being observed because of recent international events. Consider if the experience of the patient may be understood in terms of a specific Moroccan tradition or religious belief. Some Muslims who have been in Mecca have had a religious experience, which may be mistaken for a delusion. Some people have similar experiences before falling asleep. Ask if somebody believes in evil eye, djunun (spirits) or magical powers, and whether his sickness is related to supernatural powers. On their own such traditional beliefs should not be considered as delusional. Always check with the family whether they consider it abnormal.

Hallucinations:

For some Moroccans hearing sounds or noises inside their head is the expression of their thoughts. The sound does not come from outside the head. Some people spontaneously report that they hear their own thoughts. If this is an isolated phenomenon, it is usually not a hallucination. Other people sometimes hear somebody call their name. This is not necessarily hallucination. Feelings of ants under the skin ('*nemel*'), as isolated sensations, should not be considered as tactile hallucinations. Feelings of being touched on the shoulder by somebody as an isolated sensation should not be considered as hallucinations. Ask if somebody received help from a religious or traditional healer for these symptoms. Ask if these sensations are happening because of a curse on the family. It is very important to distinguish these traditional or religious experiences from hallucinations. The family may help you if you have doubts.

Negative symptoms:

Compare the persons level of functioning with a previous period during which the persons considered himself healthy. In the case of Moroccan, it should be realised that among healthy immigrant youth the percentage of unemployment, and thus inactivity during most of the day, is rather common and occurs more frequently than in the native population.

Dissociation:
Dissociative experiences are relatively common and are mostly interpreted as being possessed by Djin. In this state of mind it is accepted to see figures and hear voices of people (e.g. a holy person) or animals. The feeling of being touched is very common in this situation. It is also quite common for people to enter into a state of trance during religious ceremonies. Many people had such an experiences themselves or have observed other people in such a state. In these states, sensations of floating above or outside of the body can occur. If short-lived and not limiting to a persons role functions these experiences are usually a religious phenomenon, rather than a medical condition. The family may help you if you have doubts.

Substance abuse:
Be alert that some Moroccans start the use of cannabis at a very young age.
In Islam alcohol is forbidden, but it does not mean that Muslim people do not drink. Take time and explain that the answer is important for a correct diagnosis.

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Chapter 3

First contact incidence of psychotic disorders among native Dutch and Moroccan immigrants in the Netherlands: influence of diagnostic bias.

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Abstract

Background

Several studies have reported increased incidence rates of psychotic disorders among immigrant groups. Surprisingly, the cross-cultural validity of the diagnostic instruments that were used was never tested.

Aims

To examine whether the incidence rates of psychotic disorders including schizophrenia among Moroccan immigrants to the Netherlands remain increased when a cultural sensitive diagnostic interview is used.

Method

We compared first contact incidence with a standard and a cultural sensitive version of a diagnostic interview.

Results

Age and gender adjusted relative risk for psychotic disorders and schizophrenia among Moroccans compared to native Dutch was 7.9 (95% CI 4.7- 13.5) and 7.8 (95% CI 4.0-15.2) respectively based on the standard diagnostic interview and 4.2 (95% CI 2.3- 7.9) and 1.5 (0.5-4.3) respectively based on the cultural sensitive version the diagnostic interview.

Conclusion

First contact incidence of schizophrenia among Moroccans was no longer significantly higher than among ethnic Dutch people when a cultural sensitive diagnostic procedure was applied.

Declaration of interest

None.

Key words: standardized diagnosis, schizophrenia, psychosis, misdiagnosis, ethnic minority.

1. Introduction

Epidemiological studies in the UK consistently reported increased incidence rates of schizophrenia among ethnic minority groups (Harrison et al., 1997; Wessely et al., 1991; Van os et al., 1996; Bhugra et al.; 2001). In the Netherlands, particularly high rates have been reported among Moroccans (Selten et al., 2001). Several authors have postulated that cross-cultural biases (Mckenzie, 1999; Littlewood & Lipsedge, 1981a; Sashidharan, 1993; Strakowski, 1996) may have influenced admission rates and diagnostic evaluations among immigrants and thus may have led to an overestimation of the incidence rates among ethnic minorities.

The aim of the current study was, therefore, to examine whether incidence rates of first contact schizophrenic disorders among Moroccan immigrants in the Netherlands remained increased when a cultural sensitive diagnostic interview was used. For this purpose we compared the risk of schizophrenia and other psychotic disorders among Moroccans and native Dutch, with a standardised diagnostic assessment and one based on a culturally sensitive adapted version of the same instrument based on the principles of cultural formulation.

2. Method

2.1. Study design

In order to reach maximum comparability to the afore mentioned study that reported higher first contact incidence rates of schizophrenia among Moroccans than among native Dutch people (Selten et al., 2001), we used similar methodology, but added a cultural sensitive assessments of complaints. The current study took place in the city of Utrecht, the Netherlands, which has a population of 262.888 inhabitants. Every patient aged 15-54 years who made contact with one of the mental health services in Utrecht with a suspected psychotic disorder for the first time between May 1st 2002 and April 30th 2004 was reported to a central office where these referrals were screened for eligibility. Patients with a history of psychosis or with a clear substance induced psychosis, and patients without psychotic symptoms or a non-psychotic disorders were excluded. In our study we included all native Dutch and all (first and second generation) Moroccan immigrants who had been registered as a legal citizen of Utrecht for at least 6 months prior to the study. All patients who met the inclusion criteria were approached through their treating physician to participate in the study.

Permission to perform the study was obtained from the institutional review board of the University Medical Center of the University of Utrecht.

2.2. Assessment

After informed consent was obtained, patients were interviewed with the standard Dutch version of the Comprehensive Assessment of Symptoms and History (CASH) (Andreasen et al., 1992). A second interview with a modified, cultural sensitive version of the CASH (CASH-CS) (Zandi et al., 2008) was administered to all Moroccan and an equal number of native Dutch patients. The two versions of the instrument were administered in random order.

2.2.1. Standard diagnostic interview

The CASH is a semi-structured diagnostic interview designed to provide a comprehensive description of phenomenology for patients suffering from the broad range of psychotic disorders, including mood disorders and substance abuse disorders. In addition, the medical file of each subject was screened for additional information and, if questions remained, the rater contacted the patients' physician. A consensus DSM-IV diagnosis (APA, 1994) was made based on this information. All interviewers were academic psychiatrists (or residents), trained to use this semi-structured interview. In case a patient refused to have contact with the team, anonymous diagnostic information was obtained from the treating physician.

2.2.2. The cross-cultural interview

The CASH-CS is a modified version of the standard CASH interview that was developed for the purpose of this study. The procedural cross-cultural validity of this interview was examined previously in Casablanca, Morocco (Zandi et al., 2008). The aim of developing this special version of the CASH was to arrive at a culturally sensitive interpretation of symptoms and making use of a cultural formulation. Three areas of pathology are particularly relevant in this respect, i.e. hallucinations, dissociative symptoms and affective symptoms (Vega et al., 2006; Arnold et al., 2004; Littlewood & Lipsedge 1981b; Karno et al., 1983). In brief, in Moroccan culture hearing voices, seeing things or dead persons, being influenced by an outside force or sensations of floating above or outside of the body can represent symptoms of emotional distress or can be part of a ('dissociative') possession state. In contrast to the standard CASH, we rated such symptoms as "low confidence or not significantly present" (score 2-5 on the CASH) if such culturally accepted experiences were mentioned by the

patient or a key informant. The third area of misinterpretation of symptoms is the presence or absence of depressive symptoms. There is no word for depression in Berber, the most commonly spoken language by Moroccan immigrants in the Netherlands, and admitting to such feelings is a taboo in this culture. In appendix 1 we present two cases in order to illustrate some of these differences.

As with the standard CASH, the medical files of the subjects were screened and if necessary the rater contacted the physician. The CASH-CS interviews were administered by the some of the authors (T.Z./ J.M.H./ H.E./A.G.L.O.) and a Moroccan psychiatrist who all were experienced cross-cultural psychiatrists (or residents) who were trained to use CASH and CASH-CS. The cultural sensitive interviews also included the Retrospective Assessment of the Onset of Schizophrenia (IRAOS) (Häfner et al., 1992), an interview with a key informant and the patient him/herself to elicit additional cultural background information, e.g. on the history of the illness and help-seeking . The CASH-CS and the narrative histories about the patients' illnesses based on these questionnaires were discussed to arrive at a second consensus DSM-IV diagnosis. Besides the first author and the research nurse all psychiatrists participating in this research were present during most of these meetings.

Whenever the interviewer judged that the Dutch language level of the Moroccan patient was insufficient, an interpreter was asked to translate the interview. In the case of the CASH-CS, always the same interpreter was used, who had also participated in training sessions for the interview.

2.3. Statistical analysis

Denominators in the study were based on data provided by the Central Institute of Statistics (CBS) in the Netherlands. The CBS defines a person as a first generation immigrant when he/she was born outside the Netherlands, has immigrated at any later age to the Netherlands and has legal residence in the Netherlands. As second generation immigrant is considered an individual born in the Netherlands with at least one parent born outside the Netherlands. The CBS defines a person as native Dutch if both parents are born in the Netherlands.

First contact rates were calculated for suspected psychosis (all cases which fulfilled inclusion criteria), psychotic disorders (those who received a DSM IV diagnosis of schizophrenia, schizophreniform disorder, schizoaffective disorder, delusion disorder, brief psychotic disorder, major depression or bipolar disorder with psychotic features and psychotic disorder not otherwise specified). Incidence rates are calculated by dividing the number of the new cases by the number of person-years. The risk was calculated for the first and second

generation Moroccan immigrants, aged 15 -54 in Utrecht. Gender and age-adjusted rate ratios (RRs) with 95% confidence intervals were calculated with Poisson regression as provided by the program Egret [Cytel Software, 1999] (MacMahon & Trichopoulous, 1996). We also calculated the risk for males and females separately.

3. Results

Within the 2- year study period, a total of 145 patients aged 15-54 were registered after having contacted the mental health services with a suspected psychosis (55% native Dutch) (Figure 1). After initial screening, 28 patients were excluded (71% native Dutch): 7 non-psychotic disorder (86% native Dutch), 1 died (native Dutch), 6 were not residents of Utrecht city (50% native Dutch), 5 were homeless (80% native Dutch) and 9 patients were registered despite a previous psychosis (67% native Dutch). After a second screening, another 15 patients were excluded (73% native Dutch): 4 patients with a substance-induced psychosis (all native Dutch) and 11 because of absence of psychotic symptoms (64% native Dutch). Finally 102 patients (65 males and 37 females) were eligible for the study: 48 native Dutch (52% male), 29 Moroccan (68% male) and 25 with other ethnicities. Willingness to participate in the study was somewhat higher among Moroccan patients (26/29 = 89%) than among native Dutch patients (37/48 = 77%), which in turn was higher than the response among other foreign origin patients (10/25 = 40%). However, after controlling for gender and age, these differences were not statistically significant.

All registered Moroccan patients with a suspected psychosis were born in Morocco, and all were considered first generation. (Figure 1)

Table 1 gives an overview of the population at risk and relative risks of all cases that where referred to the central reporting office with suspected signs of psychosis during the observation period.

Figure1. Flowchart of research from registration to two interviews in Utrecht, 1 April 2002 until 1 April 2004

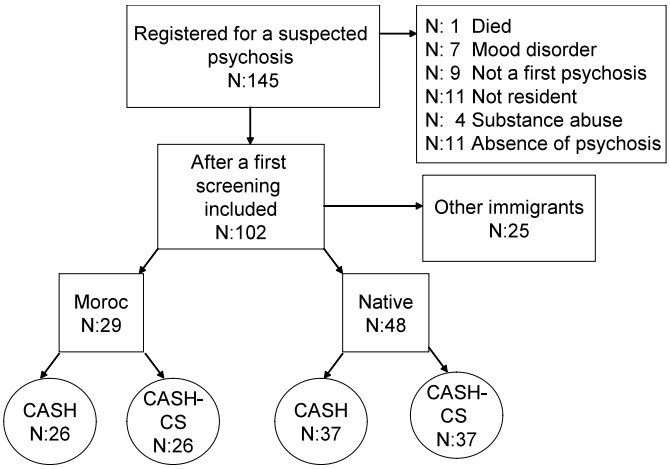

Table 1. Adjusted rate ratios for a suspected psychosis for Moroccan immigrants in Utrecht, 1 April 2002 to 1 April 2004.

Sample group N:77		person-years at risk,15-54 years	first contact cases suspected psychosis	Incidence[1] rate (95%CI) suspected psychosis	RR_{adj} (95% CI) suspected psychosis
Moroccan	all	24334	29	11.9 (8.0 - 17.1)	5.6 (3.5- 9.0) *
	male	12794	20	15.6 (9.5- 24.1)	6.5 (3.6- 11.8) **
	female	11540	9	7.8 (3.6 – 14.8)	4.4 (2.0- 9.6) **
native Dutch	all	236338	48	2.0 (1.5 - 2.7)	reference
	male	114930	25	2.2 (1.4 - 3.2)	reference
	female	121408	23	1.9 (1.2 - 2.8)	reference

Incidence rates are per 10.000
*Age-and sex-adjusted
**Age adjusted

3.1. Registration data

The overall first contact rate for a *suspected psychotic disorder* was 3.0 (95% CI 2.3- 3.7) per 10.000 population. This rate was significantly different for native Dutch and Moroccan immigrants: 2.0 (95% CI 1.5- 2.7) and 11.9 (95% CI 8.0-17.1) per 10.000 persons at risk respectively. The age and gender adjusted RR for Moroccans was 5.6 (95% CI 3.5- 9.0).

3.1.1. CASH data

Based on the diagnoses made with the standard CASH, the overall age and sex adjusted RR for *any psychotic disorder* was 7.9 (95% CI 4.7- 13.5) (Table 2). For males and females age-adjusted RRs were 9.7 (95% CI 5.0-19.2) and 5.4 (95% CI 2.2-13.5) respectively.
The age and sex adjusted rate ratio of *schizophrenic disorders*, was 7.8 (95% CI 4.0-15.2). RRs for males and females were 12.4 (95% CI 5.3- 29) and 3.1 (95% CI 0.8- 11.2) respectively.
All Moroccan and 84% of native Dutch participants with a possible psychotic disorder were diagnosed with one of the psychotic disorders; 65% of the Moroccan and 51% of the native Dutch participants with a possible psychotic disorder were diagnosed as having schizophrenia.

3.1.2. CASH-CS data

Based on the CASH-CS and the IRAOS, the overall age and gender adjusted RR of *any psychotic disorder* was 4.2 (95% CI 2.3-7.9). The RRs for males and females were 4.9 (95% CI 2.2- 10.5) and 3.0 (95% CI 1.0- 9.3) respectively.
The age and gender adjusted rate ratio of *schizophrenic disorders* was 1.5 (95% CI 0.5- 4.3). For males it was 2.4 (95% CI 0.8- 7.7) and for females the rate ration could not be calculated due the absence of schizophrenia among Moroccan females in our sample. The age and gender adjusted RR for Moroccan versus native Dutch patients with a suspected psychosis but no psychotic disorder on evaluation was 23 (95% CI 8.0- 68). Non-psychotic Moroccan patients (n=11) were diagnosed with a mood disorder without psychotic features (n=7), a factitious disorder (n=3) or a dissociative disorder (n=1). Non-psychotic native Dutch patients (n=5) were all diagnosed with a non-psychotic bipolar disorder.
Fifty-eight percent of Moroccan and 86% of Dutch native participants with a possible psychotic disorder were diagnosed to have one of the psychotic disorders, and 15% of the Moroccan patients and 59% of the native Dutch participant with a possible psychotic disorder received a diagnosis of schizophrenia according to the CASH-CS.

Table 2. Comparing the incidence, the age and sex-adjusted relative risk ratio and frequency of psychotic disorders and non-psychotic disorders according to CASH and CASH-CS

Patients* N=63		All psychotic disorders[1] cases(male/ female)	incidence[2] rate (95%CI)	RR_{adj} (95%CI)	Schizophrenic disorders[3] cases(male/ female)	incidence rate (95%CI)	RR_{adj} (95%CI)	Non- psychotic disorders[4] cases(male/ female)	incidence rate (95%CI)	RR_{adj} (95%CI)
CASH	total	35/22	2.2 (1.7-2.8)		23/13	1.4 (1.0-1.9)		3/3	0.2 (0.08- 0.5)	
	Moroccan	19/7	10.7 (7.0-15.7)	7.9 (4.7- 13.5)	14/3	7.0 (4.1-11.2)	7.8 (4.0-15.2)	0/0	0 (0-1.5)	not estimable
	Natives	16/15	1.3 (0.9-1.9)		9/10	0.8 (0.5-1.3)		3/3	0.3 (0.09- 0.6)	
CASH-CS	total	28/19	1.8 (1.4-2.4)		15/11	1.0 (0.7-1.5)		10/6	0.6 (0.4- 1.0)	
	Moroccan	11/4	6.2 (3.5-15.7)	4.2 (2.3- 7.9)	4/0	1.6 (0.4-4.2)	1.5 (0.5- 4.3)	8/3	4.5 (2.3-8.1)	23 (8.0- 68)
	Natives	17/15	1.4 (0.9-1.9)		11/11	0.9 (0.6-1.4)		2/3	0.2 (0.07- 0.5)	

*· study participants

[1]. Includes DSMIV categories schizophrenia, schizophreniform disorder, schizoaffective disorder, delusion disorder, brief psychotic disorder and psychotic disorder not otherwise specified and major depressive or bipolar disorder with psychotic features

[2]. Incidence rates are per 10000 and RRs are adjusted for age and sex

[3]. Includes DSMIV categories schizophrenia, schizophreniform disorder, schizoaffective disorder

[4]. Includes mood disorders without psychotic features, factitious disorders and dissociative disorders

4. Discussion

The aim of this study was to investigate whether first contact incidence of schizophrenia and other non-affective psychotic disorders among Moroccan immigrants would remain higher than among the native Dutch if a cultural sensitive instrument was used instead of a standard diagnostic interview. To our knowledge this is the first study to assess the impact of a systematic application of the principles of cultural formulation in the context of a standardized diagnostic interview.

In the current study, the overall observed risks of first contact with mental health services because of a suspected psychotic disorder of all psychotic disorders and of schizophrenia obtained by the standard CASH interview was higher among Moroccans compared with the ethnic Dutch and the relative risk was even higher than the one reported in the previous incidence study (Selten et al., 2001). The RR for psychotic disorders and schizophrenic disorders in this study were 4.8 (CI 95% 3.1- 7.5) and 5.0 (CI 95% 2.8- 8.9) respectively. However, in the current study the RR for broadly defined psychosis was substantially attenuated when a culturally sensitive diagnostic procedure was applied but remained statistically significant (7.9 → 4.2), while the RR for schizophrenia became non-significant (7.8 → 1.5).

Surprisingly during the observation period no second generation Moroccan immigrants contacted the central reporting office in Utrecht. This was independent of the type of interview used. We were therefore unable to replicate the extremely high relative risks 9.3 (95% CI 3.7-23.4) for second generation Moroccan immigrants, reported in The Hague. This failure can not be explained by the number for the second generation Moroccans in Utrecht: the number of person-years at risk for the study period for this group in Utrecht was 4206, which is almost twice as much as for the same period in The Hague with 2172 person-years at risk.

A limitation of the current study, or at least a deviation from the study we partly replicated (Selten et al., 2001), is that the background information obtained by key informants with the IRAOS was not available for the diagnosis based on the standard CASH and also, in contrast to the set-up of that study the diagnostic team which used the standard CASH was not blind to the ethnic background of the patients. In the Hague study (Selten et al., 2001), psychiatric residents interviewed patients using the (CASH) and screened the medical file. A research nurse interviewed key informants using the (IRAOS).A narrative history of the patient's illness omitting any clue to the patient's ethnicity was then used during a diagnostic meeting where two psychiatrists, who remained blind to ethnicity, made a consensus DSM-

IV diagnosis. This difference in availability of information, therefore, may explain why we found even higher RR's with the standard CASH than the Hague study (Selten et al., 2001). It appears therefore that the method used by them, which was also used in the AESOP incidence study (Fearon et al., 2006) takes away some of the ethnic bias at the level of diagnostic decision making. However, it does not preclude misinterpretation of culturally appropriate expressions of distress as signs of psychosis at the time of the interview when symptom ratings are assigned. This may, therefore, still lead to over-diagnosis of schizophrenia in ethnic minorities. However, one could argue that in our study clinicians who used the adapted version of the CASH may have been reluctant to diagnose schizophrenia among Moroccans (Zandi et al., 2008; Selten & Hoek, 2008). In the absence of a gold standard to ascertain which of the two diagnostic procedures renders the most "truthful' results, we have to rely on the results of a follow-up study investigating the possible differences between the two diagnostic procedures in terms of the stability of the diagnoses and the course and outcome of the disorders over an extended period of time (predictive validity). In a 30 months follow-up of the patients in this study, we showed that the prognosis for patients with a schizophrenia diagnosis according to the CASH was significantly better for Moroccan compared to native Dutch patients, whereas the outcome for non-schizophrenic patients according to the CASH was similar for Moroccan and native Dutch patients. In contrast, the prognosis for patients with schizophrenia according to the CASH-CS was very similar in Moroccan and native Dutch patients, whereas the outcome in non-schizophrenic patients according to the CASH-CS was significantly better in Moroccan compared to native Dutch patients (Zandi et al., submitted). These findings, indicate that the diagnoses according to the cultural sensitive CASH-CS had better predictive validity than those according to the standard CASH. We therefore feel that the absence of a significant difference between Moroccans and native Dutch patients in the treated incidence of schizophrenia according to a cultural sensitive diagnostic procedure is a valid observation and not the result of some reluctance of the interviewers to apply the diagnosis of schizophrenia to Moroccan patients.

According to the outcomes from the cultural sensitive version in this study differences in the incidence of first contact psychotic disorders between the ethnic groups became substantially smaller and the incidence of schizophrenia among Moroccans is no longer significantly higher than among ethnic Dutch people. Based on the CASH-CS 42% of the Moroccan patients with a suspected psychotic disorder were found not to be psychotic at al. For the native Dutch patients this occurred only in 14% of cases. These percentages were 0% and 16%, respectively based on CASH. The main differences between the outcomes based on the

two versions of the CASH resulted from high percentage of Moroccan patients who were re-classified from schizophrenia to non-psychotic disorders 29% or affective psychosis 47%. Relevant to this finding is the ongoing debate about the continuum of non-affective psychotic disorders to affective disorders (Bental, 2006; Myin-Germeys & van Os, 2007). Our study raises the question whether, if not schizophrenia, perhaps the incidence of affective psychosis is increased. For example, several studies have reported a higher prevalence rate of any psychiatric disorder among migrant populations in the Netherlands. (Wit de et al., 2008, Toet et al., 2003, van der Wurff et al., 2004). However, the current study does not warrant a final conclusion on this issue since it was at measuring the incidence of cases where psychotic symptoms are the main presenting feature. The study was not developed to find patients with a primary mood disorder. In fact, cases with a clear affective (non-psychotic) disorder were excluded from the study. The high numbers of affective psychosis and non- psychotic disorders among Moroccan patients detected by CASH-CS in this sample is probably a result of a failure to detect affective symptoms at the screening level. The main reason why we reclassified many patients as non-psychotic on the basis of the cultural sensitive version of the CASH was that with this instrument the presence of hallucinatory and delusion-like symptoms among immigrant patients is not automatically interpreted as perception disturbance or thought disorder indicative of psychosis. In our earlier study among Moroccan patients in Casablanca, Morocco (Zandi et al., 2008), hearing voices (mostly animals, a deceased parent, or a voice just calling his name), seeing a strange, dark man, or feeling insects (mostly ants) in the whole body were the most commonly reported symptoms in all patients, regardless of diagnosis. In that study, we showed that diagnoses based on the culturally sensitive version of the CASH displayed much better concordance with diagnoses made by local Moroccan psychiatrists than the standard version of CASH, with substantially lower numbers of schizophrenia cases according to CASH-CS and local clinicians.

The other source of difference between CASH and CASH-CS was the poor recognition of mood symptoms in the Moroccan population with the standard version of the instrument. In the current study we observed that most of Moroccan patients with putative acute psychotic symptoms had been suffering from mood symptoms for quite a while before asking professional help, usually in combination with one or more of these “psychosis-like” cultural expressions of distress.

5. Conclusion

Our study demonstrates the vital importance of knowledge about the cultural background of the patient and the use of the principles of cultural formulation for a valid evaluation of symptoms in ethnic and culturally different populations (Vega et al., 2006; Arnold et al., 2004; Littlewood & Lipsedge, 1981; Karno et al., 1983). In the current study a culture-sensitive approach resulted in a substantial attenuation of the relationship between migration status and as a consequence the elevated rate of schizophrenia became statistically non-significant. However, given the limited sample size, no final conclusion can be drawn about the presence or absence of a difference in incidence rates between native Dutch and Moroccan immigrant patient in the real world. On the other hand, we would like to emphasize that similar attenuations might have occurred in other studies that failed to (adequately) adjust for possible cultural bias in the diagnostic process

Misinterpretation of symptoms may have serious consequences such as over-prescription of antipsychotics, under-prescription of potentially beneficial antidepressants and a negative influence on the prognosis of this group. We therefore would like to encourage the use of cultural formulation as a central element in the assessment of the symptoms of psychotic and affective disorders among immigrants.

Vingette 1

A 29-year old Moroccan woman was referred by her GP because she was hearing voices, seeing people who did not exist and had the fear she was followed by strangers. She was living with her sister already for months because she was afraid to be alone. During the standard CASH interview she confirmed all these symptoms and the interviewer noted two symptoms in the depression section. The diagnosis based on the standard CASH was schizophrenia, paranoid type.

In the second interview with the CASH-CS almost all symptoms of the depression section were scored with rather high severity. She was hearing sounds of animals particularly around her monthly cycles. For the patient her periods were the sign she was not pregnant. About seeing unknown people she said: "I am not really seeing a person, but I can feel a spirit that is arranged by someone to watch or follow me, it takes my fertility away!" She referred to this spirit as a 'jinn', which in Moroccan and other Islamic cultures is an accepted phenomenon. She told us that she can not clearly say what she can see during these periods because it looks like she is not in her own body any more. She said the sounds which she sometimes hears are actually inside of her head. Apart from hearing conversing voices which would occasionally comment on her behaviour she had no other first rank symptoms of schizophrenia and no bizarre delusions. Sometimes if she feels sad, she falls down to the ground and starts shaking all over. Her family confirms this is a sign of possession by a jinn. Talking about jinn, she said that it gives her sense of peace that her non-fertility is not just caused by a physical problem. During the IRAOS interview the patient's sister said the patient has been trying to become pregnant for 8 years and the sadness of infertility was killing her. She was surprised that we asked so many times about hearing sounds and seeing pictures instead of asking about the deeper feelings of her sadness. Based on information obtained with the CASH-CS, and the cultural background information, we concluded that the pseudo hallucinations the patient was experiencing had a religious and mystical connotation and should not to be considered as pathological. The diagnosis was a severe depression without psychotic symptoms. A diagnosis of dissociative disorder not otherwise specified could also be considered since these experiences also fit the pattern of demon possession. However, such experiences are rather common in Moroccan culture and are quite familiar cultural expressions of distress during difficult periods of life.

Vignette 2

A 42 year old Moroccan man was referred with a high emergency request from his GP because of psychotic symptoms. According to the referral letter these symptoms started very acute. He started hearing voices, seeing people who did not exist and feeling followed by strangers acutely since the last 4 weeks. According to his wife he had been restless for quite a while. He had problems sleeping and had reversed his day-night rhythm for several moths. He became angry easily and they had relational problems because of his behavior. According to his sister this resulted from the stress after his younger brother was sentenced for 4 years in prison. In the CASH interview the patients answered 'yes' on practically every question, thus scoring positively on acoustic hallucinations (hearing voices, including some that commented on his behavior), visual hallucinations (seeing invisible men and animals) and delusions (feeling that he was being followed on the street, feeling he could read people's thoughts, receiving messages through radio and television and feeling people were plotting against him). Only two symptoms of the mood section were scored as present. The diagnosis, based on the standard CASH interview, was schizophrenia, paranoid type. During a cross-cultural interview with the CASH-CS hardly any of these psychotic symptoms remained. In contrast, it became clear that he had experienced practically all symptoms of major depression. He told the interviewer that when he is very sad he can hear an unclear voice of a dog or a cow. Sometimes he could hear his father saying "you did not make it". However, after further questioning it turned out that he was hearing his father "in his mind". He said that he was ashamed to admit that he had been addicted to gambling and alcohol for several years. As a result of this he had a debt of around 12.000 euro and was afraid to be followed on the street by his creditors. He said that whenever he feels depressed it feels as if a dark shadow of a man is sitting on his shoulders. Further probing with the aid of the translator revealed that he was not certain of the reality of these experiences; they were more his feelings. Hearing voices of animals is quite common among rural Moroccan people. Hearing his father saying punishing words is a culturally appropriate expression of being ashamed. In the CASH-CS we scored these symptoms not being certain enough to accept these symptoms as psychotic. According to the history of his illness obtained by CASH-CS the diagnosis was a severe depression without psychotic symptoms.

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Chapter 4

Predictive validity of a culturally informed diagnosis of schizophrenia: a 30 month follow-up study with first episode psychosis

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Abstract

Background

Previous research has shown discrepancies between a standard diagnostic interview for schizophrenia (CASH) and a culture sensitive version of this instrument (CASH-CS) in Moroccan patients. More specifically we showed that among Moroccan immigrants the CASH-CS resulted in fewer patients with a diagnosis schizophrenia compared with diagnoses based on the CASH, whereas for Native Dutch patients there was no difference between the CASH and the CASH-CS. The aim of the current study was to compare the predictive validity of a diagnosis of schizophrenia according to the CASH and CASH-CS.

Method

Thirty months after referral, 26 Moroccan and 26 native Dutch patients with a suspected first psychotic episode were compared with regard to 30-month diagnostic stability, symptom development, psychosocial functioning, medication use and hospitalization using baseline diagnoses based on the two versions of the CASH.

Results

Moroccan patients who were diagnosed with schizophrenia using the standard CASH at baseline had a significantly better 30-month prognosis than native Dutch patients with the same CASH diagnosis. Prognosis of schizophrenia according to the CASH-CS was similar for Moroccans and native Dutch patients. Diagnostic stability according to the CASH was high for native Dutch (92%), but low for Moroccan patients (27%), whereas diagnostic stability according to the CASH-CS was high for both groups (85% and 81%, respectively).

Conclusion

These data raise questions regarding the validity of the standard CASH in Moroccan immigrants in the Netherlands and support the validity of the CASH-CS. As a consequence, there are serious doubts about the validity of previous studies showing an increased incidence of schizophrenia in immigrants using standard diagnostic procedures.

Declaration of interest

None

Key words: Immigrant, psychosis, standardized diagnosis, schizophrenia, cultural formulation

1. Introduction

An increased incidence of schizophrenia among non-western immigrants has repeatedly been reported in different European countries. According to a recent meta-analysis, the mean weighted relative risk (RR) for these immigrants compared to the risk for natives was 3.3 (95% CI: 2.8–3.9) (Cantor-Graae & Selten, 2005). Several explanations have been suggested, including genetic differences, environmental influences related to migration and the living conditions of migrants and interactions between genetic and environmental factors (Boydel et al., 2001; Kirkbride et al., 2007; Veling et al., 2008). However, these explanations all assume that the higher incidence of schizophrenia in non-western migrants is a valid observation based on adequate assessments (Selten & Hoek, 2008). The possibility of an overestimation of the incidence in migrants due to cross-cultural bias in the assessment has been discussed from the very beginning of these studies (Mortensen et al., 1997; Mckenzie, 1999; Littlewoord & Lipsedge, 1981; Hickling et al., 1999). However, only rarely a cultural sensitive diagnostic procedure has been applied to prevent such overestimation, although some efforts were made to prevent cultural bias. For example, in the largest incidence study of psychosis in England (Fearon et al., 2006) and in the incidence study in the Netherlands (Selten et al., 2001), interviewers were blind to the ethnicity of the patients during the consensus procedure of formulating the diagnoses, which according to the authors prevented cultural bias in the interpretation of the recorded symptoms. However, this procedure does not prevent cultural bias in the assessment procedure itself or the misinterpretation of culturally appropriate expressions of distress as signs of psychosis. In order to really prevent this type of cultural bias, both the assessment itself and the interpretation of the data should be culturally informed.

Like in other European countries, high incidence rates of schizophrenia are reported among Moroccan immigrants in the Netherlands (Selten et al., 2001; Veling et al., 2006). However, in a previous study comparing the results from a standard semi-structured psychiatric interview and with the clinical diagnosis of psychosis in Moroccan patients in Casablanca, Morocco, we showed that misinterpretation of symptoms can be an important source of disagreement between a psychiatric diagnosis obtained with a standard semi-structured interview and the expert diagnoses of local Moroccan clinicians. Substantially fewer cases were diagnosed as schizophrenia by the local clinicians compared to the results of the standard semi-structured interview (Zandi et al., 2008). This study showed that traditional semi-structured interviews are sensitive, but not very specific with regard to the presence of positive symptoms of psychosis

and may therefore result in false positive diagnoses of psychosis and an overestimation of psychotic illnesses among Moroccan patients. Moreover, in a recent study in the Netherlands we showed that when a cultural sensitive diagnostic procedure is applied, the first contact incidence rate of schizophrenia in Moroccan immigrants is no longer significantly higher than in native Dutch inhabitants. Many Moroccan patients with a presumed diagnosis of schizophrenia received a diagnosis of depression with or without psychotic features instead (Zandi et al., 2010). These findings raise serious questions regarding the validity of the repeatedly reported higher incidence of schizophrenia in non-western immigrants compared to native Europeans. However, Selten and Hoek (2008) have questioned the neutrality and validity of the cultural sensitive diagnosis in our studies, arguing that two previous studies have shown that a standard diagnosis of schizophrenia is equally stable in non-western immigrants and native English and Dutch patients (Harrison et al., 1999; Veen et al., 2004). Unfortunately, these studies failed to compare long-term symptomatic and functional outcomes.

The aim of this study is to test the predictive validity of the culture sensitive diagnostic procedure that we applied in our previous study that showed no significantly different incidence of schizophrenia in Moroccan immigrants compared to the native Dutch population (Zandi et al., 2010). We hypothesize that the cultural informed diagnosis of schizophrenia shows better stability than the standard diagnosis of schizophrenia in Moroccan patients and that the cultural informed diagnosis is a better predictor of course and outcome than the standard diagnosis. More specifically, we will test whether the course of schizophrenia according to the culture sensitive assessment in Moroccan immigrants is more chronic than the course of the same diagnosis according to the standard assessment procedure, and that the course of the non-schizophrenic disorders among Moroccans according to the culturally informed diagnosis is not less chronic than those diagnosed according to the standard assessment procedure.

2. Methods

2.1 Subjects

Participants were recruited from the Utrecht First Contact Psychosis Incidence Study (Zandi et al., 2010). In brief, over a two year period from May 2002 to May 2004 all persons aged 15-54 years in Utrecht, the Netherlands, who came into contact with any of the mental health

services for suspected psychotic symptoms for the first time in their life, were assessed with a standard diagnostic interview and a culture sensitive version of this interview (Zandi et al., 2008). Patients with a possible substance induced psychosis were excluded from the cohort. All Moroccan patients with a suspected psychosis were born in Morocco and were thus considered first generation immigrants.

The follow-up study focuses on all 26 Moroccan and the same number of native Dutch subjects participating in the incidence study mentioned above (Zandi et al., 2010). Every native Dutch patient registered at baseline just after an included Moroccan patient was asked to participate in the follow up study. If this patient declined, the next native Dutch patient was asked.

2.2. Assessments

2.2.1. Baseline assessment:

All patients were examined using the standard Dutch version of the Comprehensive Assessment of Symptoms and History (CASH) (Andreasen et al., 1992), and based on this information a first consensus DSM-IV diagnosis was made by an interviewer and an academic psychiatrist. In another interview, the culture sensitive version of the CASH (CASH-CS) was administered (Zandi et al., 2008), supplemented with information obtained from the patient and a key informant by the Instrument for Retrospective Assessment of the Onset of Schizophrenia (IRAOS) (Häfner et al., 1992). All CASH-CS interviews were administered by clinicians that were experienced cross-cultural psychiatrists or residents. One of the psychiatrists was himself of Moroccan origin. The two versions of the instruments (CASH and CASH-CS) were administered in random order. A narrative history about the patients' illness based on these interviews was discussed and transformed into a second, culturally informed consensus DSM-IV diagnosis by a group of trained transcultural psychiatrists. During administration of the interview the interviewers were blind each other's diagnosis.

2.2.2. Follow-up assessment:

2.2.2.1. Symptoms and diagnosis

All Moroccan participants and an equal number of native Dutch patients were asked to be interviewed about two and a half years later (mean 30.5 months, SD 4.1) using the longitudinal follow-up version of the standard diagnostic interview, the CASH-UP (Ho et al., 1998), to assess the subjects' level of symptoms. To prevent considering patients in sustained

remission as having "no diagnosis", the follow-up diagnosis was based on the combination of a structured interview (CASH-UP) and the recorded clinical information during the total follow-up period. Thus, a change in diagnosis from baseline to follow-up cannot be attributed only to the (very recent) absence of psychotic symptoms during the follow-up assessment, but takes into account the entire illness episode.

Follow-up diagnoses according to the CASH-UP were compared to diagnoses according to the regular CASH and the CASH-CS at baseline. Four main diagnostic categories were assigned:

1) Schizophrenic disorders: a DSM-IV diagnosis of schizophrenia, schizophreniform disorder or schizoaffective disorder.
2) Other non-organic psychotic disorders such as delusional disorders, brief psychotic disorders, psychotic disorder not otherwise specified and substance induced psychotic disorders based on DSM-IV.
3) DSM-IV diagnosis of mood disorders with psychotic features including major depression or bipolar disorder.
4) DSM-IV diagnosis of mood disorders without psychotic features, factitious disorders and dissociative disorders.

Symptom ratings were based on data from all available sources of information, including the patient, key informants, patient registration database, medical records, and if questions remained, the patients' physicians. All interviews were conducted by T.Z. and a research assistant, who also conducted the baseline assessments. A narrative report about the patient's illness, primarily based on information from the medical files covering the 30-month interval and information obtained by CASH-UP (without including initial diagnosis) was discussed in diagnostic meetings to arrive at a follow-up consensus DSM-IV diagnosis. Apart from the first author, three experienced psychiatrists (J.M.H., A.G.L.O, H.E.) participated in these meetings.

2.2.2.2. Mental health care utilisation

During the follow-up assessment, the Life Chart Schedule (LCS) (Sartorius et al., 1996) was used to retrospectively measure whether a patient had used illicit drugs, had positive psychotic symptoms, was prescribed antipsychotic and/or antidepressant medication, had voluntary or involuntary psychiatric care or was admitted to a psychiatric hospital. The LCS has proven to be reliable for the assessment of the course of schizophrenia (Susser et al., 2000). We registered whether during the follow-up period the patient was mostly psychotic,

in complete remission (no psychiatric symptoms) or in partial remission (depressive or manic episode). This information was based on information from the medical file.

2.2.2.3. Quality of Life

Finally the following quality of life indicators were measured using the PSYCH-UP (Andreasen, 1989): occupational impairment, income source, impairment in household duties, enjoyment of recreational activities, relationship with family and friends and overall psychosocial functioning. These indicators are reported in different studies as important measures for quality of life among schizophrenic patients (Ho et al., 1998).

2.3. Statistical analysis

Stability of the diagnosis between baseline and follow-up was evaluated for two different versions of the baseline interview (CASH vs. CASH-CS) and for two ethnic groups (native Dutch vs. Moroccan immigrants). Changes from the baseline diagnostic category to another diagnostic category were regarded as diagnostic instability. Changes within a diagnostic category (e.g. from schizophreniform disorder to schizophrenia or schizoaffective disorder) were not considered as diagnostic instability. Diagnostic stability was expressed in terms of chance corrected agreement using quadratic weighted Kappa's (K_{sqw}: Fleiss-Cohen) (Schuster, 2004).

In addition to the differences in diagnostic stability, we looked at differences in clinical outcomes as derived from the CASH-UP, the patient files, and the PSYCH-UP. The outcome parameters 'occupational impairment', 'impairment in performance of household duties', 'relationship impairment with family and friends', 'enjoyment of recreational activities' and 'overall psychosocial functioning' were rated on a 5-point scale (excellent, good, satisfactory, poor, very poor) and then dichotomized using a cut-off score of 3 or higher into non-impaired and impaired. The outcome parameters 'current drug use', 'positive symptoms', 'using antidepressants', 'involuntary treatment', 'remission', 'medical file closure' and 'clinical care last thirty months' already were dichotomous. Financial independence was analysed relative to the scores at baseline. The outcome on this variable was therefore analysed as worse, equal or better than the baseline score. Remission was analysed as 'no remission', 'partial remission' or 'full remission'.

Differences in dichotomous variables were tested using chi-squared tests or Fisher's exact tests where appropriate. The only continuous variable, the total number of weeks of clinical care during the last 30 months, was analysed using independent sample T-tests.

All analyses were performed using SAS version 9.1 (SAS Institute Inc, Cary, NC). The level of significance was set to 5%.

3. Results

For all 52 patients (26 Moroccan and 26 native Dutch) we obtained enough information to make a diagnosis at 30 months follow-up. Four native Dutch patients did not agree to have contact with the research team at the time of the follow-up assessment in spite of their earlier informed consent. However, they did allow us to use their medical file and/or to interview a key informant. In addition, four patients (two Moroccans and two native Dutch) could not be traced by the research team, but there was sufficient information in their medical files to make a follow-up diagnosis. For one of these two Moroccan patients we did not have sufficient file or informant information to establish the main outcome variables. The two Moroccan patients were diagnosed as having no schizophrenia at baseline using the CASH-CS, but with schizophrenia using the CASH. At follow-up both were diagnosed according to CASH-UP as having no schizophrenia.

Baseline clinical characteristics for the 26 Moroccan participants and the 26 native Dutch participants are presented in Table 1. The group of Moroccan patients had a higher percentage of males, were more likely to be married, were less frequently employed before the onset of illness, had a lower level of education, and a lower income.

Table 1. Baseline characteristics of patients

	Moroccan patients	Native Dutch patients	
	N (%) or Mean (± SD)	N (%) or Mean (± SD)	p
Total patients	26	26	
Gender, male (%)	18 (69%)	13 (50%)	0.158
Age	33 (± 8)	32 (± 9)	0.594
Married	16 (62%)	8 (31%)	0.026
Employed before onset of illness	8 (31%)	15 (58%)	0.051
Highest education followed			
No information	3 (12%)	0 (0%)	0.024
Primary school	2 (8%)	0 (0%)	
Secondary school	15 (58%)	12 (46%)	
Higher education	6 (23%)	14 (54%)	
Income			
No information	5 (19%)	1 (4%)	0.126
No income	1 (4%)	0 (0%)	
Below minimum wage	16 (62%)	15 (58%)	
Below average wage	3 (12%)	5 (19%)	
Above average wage	1 (4%)	5 (19%)	
SD: Standard deviation			

The agreement between the follow-up diagnoses according to the CASH-UP interview and the baseline diagnoses according to the regular CASH and the CASH-CS interview are presented in Table 2.

Table 2. Baseline diagnoses according to regular CASH and CASH-CS (rows) compared to CASH-UP (columns) diagnoses at 30 month follow-up separately for Moroccan and Native Dutch patients Patients that did not change diagnostic category are marked in grey.

		Moroccans CASH-UP					Dutch CASH- UP				
		Dx.1	Dx.2	Dx.3	Dx.4	Total	Dx.1	Dx.2	Dx.3	Dx.4	Total
CASH	Dx.1	3	3	3	8	17	16	0	0	0	16
	Dx.2	0	2	0	1	3	1	4	1	0	6
	Dx.3	0	0	2	4	6	0	0	4	0	4
	Dx.4	0	0	0	0	0	0	0	0	0	0
	Total	3	5	5	13	26	17	4	5	0	26
		Squared Weighted kappa: 0.110 (-0.042 – 0.261)					Squared Weighted kappa: 0.935 (0.846 – 1.000)				
CASH-CS	Dx.1	3	1	0	0	4	15	0	0	0	15
	Dx.2	0	3	1	0	4	1	4	2	0	7
	Dx.3	0	1	4	2	7	1	0	3	0	4
	Dx.4	0	0	0	11	11	0	0	0	0	0
	Total	3	5	5	13	26	17	4	5	0	26
	p	Squared Weighted kappa: 0.918 (0.844 – 0.992)					Squared Weighted kappa: 0.773 (0.518 – 1.000)				

Dx.1: Schizophrenic disorder
Dx.2: Other non-organic psychotic disorder
Dx.3: Mood disorders with psychotic features
Dx.4: Mood disorders without psychotic features
Weighted kappa's calculated using quadratic (Fleiss-Cohen) weights

Diagnostic stability according to the regular CASH was high for native Dutch patients (overall agreement = 92%: K_{sqw} = 0.94), whereas it was low for Moroccan immigrants (overall agreement = 27%; K_{sqw} = 0.11). In contrast, diagnostic stability according to the CASH-CS was high for both native Dutch (overall agreement = 85%; K_{sqw} = 0.77) and Moroccan patients (overall agreement = 81%; K_{sqw} = 0.92). At a more detailed level, it was shown that 8 of the 17 (47%) Moroccan patients with a baseline CASH diagnosis of schizophrenia were diagnosed with a non-psychotic affective disorder at 30 months follow-up using the CASH-UP interview and an additional 3 patients with CASH diagnosis of schizophrenia at baseline (18%) were diagnosed with a psychotic affective disorder at follow-up, indicating that almost two-thirds (11/17) of the Moroccan patients with a CASH diagnosis of schizophrenia lost this diagnosis at follow-up. In contrast none of the 4 Moroccan patients with a CASH-CS diagnosis of schizophrenia had a follow-up diagnosis of psychotic affective disorder or non-

psychotic disorder. Moreover, none of the native Dutch patients with a CASH (n=16) or a CASH-CS (n=15) diagnosis of schizophrenia at baseline lost this diagnosis at follow-up. The outcomes of the Moroccan and Dutch participants that were diagnosed with schizophrenia according to the regular CASH or the CASH-CS questionnaire are presented in Table 3.

Table 3. Thirty month follow-up measures of Moroccan and Dutch participants with a baseline diagnosis of schizophrenia, using the regular CASH and CASH-CS, compared. P-values calculated using chi-squares, Fisher's exact or T-tests where appropriate.

			CASH			CASH-CS		
		Score	Moroccan (n=16)*	Dutch (n=16)	p	Moroccan (n=4)	Dutch (n=15)	p
CASH-UP	Occupational impairment	≤ 2	4	3	1.000	0	3	1.000
		≥ 3	12	13		4	12	
	Financial independence	Worse	4	7	0.218	2	6	1.000
		Equal	13	9		2	9	
		Better	0	0		0	0	
	Impairment in performance of household duties	≤ 2	9	5	0.154	3	10	1.000
		≥ 3	7	11		1	5	
	Relationship impairment family and friends	≤ 2	11	3	**0.004**	0	5	0.530
		≥ 3	5	13		4	10	
	Enjoyment of recreational activities	≤ 2	8	4	0.144	1	3	1.000
		≥ 3	8	12		3	12	
	Overall psychosocial functioning	≤ 2	9	3	**0.029**	1	4	1.000
		≥ 3	7	13		3	11	
	Current drug user	No	11	12	1.000	2	12	0.272
		Yes	5	4		2	3	
	Positive symptoms[¢]	No	11	3	**0.002**	1	3	1.000
		Yes	4	13		2	12	
	Using antidepressants	No	13	14	0.656	4	13	1.000
		Yes	4	2		0	2	
	Using antipsychotics	No	10	2	**0.004**	1	2	0.530
		Yes	6	14		3	13	
	Involuntary treatment	No	15	9	**0.037**	3	9	1.000
		Yes	1	7		1	6	
	In remission	No	5	15	**<0.001**	3	14	0.386
		Partial	2	1		0	1	
		Full	9	0		1	0	
	Medical file closed	No	11	15	0.172	3	14	0.386
		Yes	5	1		1	1	
	Clinical care last 30 months	No	12	10	0.446	2	10	0.603
		Yes	4	6		2	5	
	Weeks of clinical care last 30 months[Ø]	Mean ± sd	19.0 ± 24.8	24.8 ± 20.4	0.694	35.5 ± 27.6	26.0 ± 22.5	0.651

*: One Moroccan participant who was diagnosed with schizophrenia using the regular CASH was lost to follow-up before the outcome could be determined and is therefore not presented in this table.

[¢]: In one additional Moroccan participant the positive symptoms were not assessed.

sd: Standard deviation

[Ø]: In participants who received clinical care

Compared to native Dutch patients with a standard CASH diagnosis of schizophrenia, Moroccan patients with schizophrenia according to this instrument were less impaired in terms of household duties and overall psychosocial functioning, had less positive symptoms, used antipsychotics less frequently, were treated involuntary less often during the 30 months of follow-up, and were regarded to be in remission more often than Dutch patients. In contrast, there were no significant differences in outcome between Moroccan and native Dutch patients that were diagnosed with schizophrenia according to the CASH-CS.

The outcomes of Moroccan and Dutch participants that were not diagnosed with schizophrenia using either the regular CASH or the CASH-CS are presented in Table 4.

Table 4. Thirty month follow-up measures of Moroccan and Dutch participants with no diagnosis of schizophrenia, using the regular CASH and CASH-CS, compared. P-values calculated using chi-squared, Fisher's exact or T-tests where appropriate.

			CASH			CASH-CS		
		Score	Moroccan (n=9)	Dutch (n=10)	P	Moroccan (n=21)*	Dutch (n=11)	p
CASH-UP	Occupational impairment	≤ 2 ≥ 3	5 4	0 10	**0.011**	9 12	0 11	**0.013**
	Financial independence	Worse Equal Better	0 8 1	1 9 0	1.000	2 18 1	2 9 0	0.739
	Impairment in performance of household duties	≤ 2 ≥ 3	8 1	5 5	0.141	17 4	5 6	0.056
	Relationship impairment family and friends	≤ 2 ≥ 3	9 0	5 5	**0.033**	19 2	5 6	**0.010**
	Enjoyment of recreational activities	≤ 2 ≥ 3	7 2	4 6	0.170	14 7	4 7	0.142
	Overall psychosocial functioning	≤ 2 ≥ 3	7 2	4 6	0.170	16 5	4 7	0.053
	Current drug user	No Yes	7 2	7 3	1.000	16 5	7 4	0.681
	Positive symptoms	No Yes	6 3	5 5	0.650	16 5	5 6	0.123
	Using antidepressants	No Yes	4 5	6 4	0.656	13 9	7 4	1.000
	Using antipsychotics	No Yes	9 0	3 7	**0.003**	18 3	3 8	**0.002**
	Involuntary treatment	No Yes	9 0	9 1	1.000	21 0	9 2	0.111
	In remission	No Partial Full	1 3 5	5 0 5	0.061	3 5 13	6 0 5	**0.035**
	Medical file closed	No Yes	6 3	8 2	0.629	14 7	9 2	0.441
	Clinical care last 30 months	No Yes	9 0	8 2	0.474	19 2	8 3	0.310
	Weeks of clinical care last 30 months ø	Mean ± sd	- -	12.0 ± 2.8	-	2.5 ± 0.7	14.3 ± 4.5	**0.040**

*: One Moroccan participant who was diagnosed as not having schizophrenia using the CASH-CS was lost to follow-up before the outcome could be determined and is therefore not presented in this table.
sd: Standard deviation
ø: In participants who received clinical care

Compared to native Dutch patients not diagnosed with schizophrenia at baseline according to the CASH, Moroccan patients who were not diagnosed with schizophrenia at baseline with

the regular CASH showed less occupational impairment, less impairment in relations with family and friends, and used antipsychotic medication less frequently. Similar differences were observed when the CASH-CS was used instead of the regular CASH at baseline.

4. Discussion

To the best of our knowledge this is the first follow-up study assessing the impact of a systematic application of the principles of a cultural sensitive diagnosis compared to a standard diagnostic procedure in patients with a possible first episode psychosis.

Moroccan patients who were diagnosed with schizophrenia using the standard CASH at baseline had a significantly better 30-month prognosis than native Dutch patients with the same diagnosis, whereas the 30-month prognosis for patients with a CASH-CS diagnosis of schizophrenia was very similar for native Dutch and Moroccan patients. This finding underlines the limited validity of the standard CASH diagnosis in Moroccan patients and supports the validity of the CASH-CS diagnosis in both ethnic groups. This conclusion is corroborated by the comparison of the 30-months prognosis of Moroccan and native Dutch patients with a non-schizophrenic disorder at baseline: Moroccan patients showed a somewhat better prognosis than native Dutch patients according to both CASH and CASH-CS. This is remarkable because the Moroccan CASH-CS group with a non-schizophrenic disorder included many patients classified as having schizophrenia according to the standard CASH at baseline. Finally, it should be noticed that at baseline native Dutch patients had a more favourable prognostic profile in terms of occupational function and demographics than Moroccan patients, and yet Moroccan patients appeared to have a better prognosis.

In addition, there were serious differences between the two diagnostic procedures in terms of diagnostic stability. The diagnosis of a schizophrenic disorder at baseline among Native Dutch patients over 30 months according to both the CASH and the CASH-CS was highly stable. In contrast, the stability of diagnoses according to the baseline CASH was very low in Moroccan immigrants, whereas with the CASH-CS it was similar to that among native Dutch patients. The main reason for this difference in stability was that according to the CASH, 65% of the Moroccan patients had a diagnosis of schizophrenia at baseline and none of them was classified with a non-psychotic disorder, whereas according to the CASH-CS at baseline, only 15% of the Moroccan patients was classified as schizophrenic and 42% were diagnosed with a less severe, non-psychotic disorder.

The study has both strengths and limitations. The major strengths of the current study are the use of a representative first episode sample, the use of a broad diagnostic procedure, and the use of a prospective design to test the prognostic impact of a systematic application of a cultural formulation in the context of a standardized diagnostic interview. In contrast to traditional immigrant studies (Harrison et al., 1997; Selten et al., 2001; Fearon et al., 2006; Veling et al., 2006), we considered information about the cultural context of the presented symptoms of the participants as vital for the accurate formulation of DSM-IV diagnoses. (Littlewood and Lipsedge, 1981; Karno et al., 1983; Arnold et al., 2004;Vega et al., 2006; Zandi et al., 2010). Another strength of the current study is the use of the same interviewers and at baseline and follow-up thus minimizing inter-rater variability. However, this situation can also be viewed as a limitation since follow-up interviewers were not always completely blind to the results of the baseline assessment. It should be noted, however, that the other three psychiatrists involved in the diagnostic meetings were completely blind to the initial diagnosis.

A possible limitation of the current study might be the lack of a cultural sensitive version of CASH-UP. However, the focus of this study was assessing the impact of a cultural sensitive diagnosis compared to a standard diagnostic procedure at baseline with regard to the clinical course of the disorder over a longer period (30 months). It should also be noted that many of the outcome variables were quite objective and not dependent on the subjective judgment of the interviewers/raters, e.g. file information such as the use of antipsychotic medication, mental health care utilization, involuntary treatment, occupational impairment, and financial independence. We therefore believe that the follow-up assessment was less prone to cultural influences then the diagnostic procedure at baseline.

Another possible limitation of the study is that at baseline no collateral information was obtained from key informant with the IRAOS in combination with the standard CASH, whereas this additional information was available in combination with the CASH-CS. This difference in availability of information may explain why our relative risks with the standard CASH were somewhat higher than those in the Hague study where the interviewers collected information from the patient with the standard CASH in combination with information from key informants with the IRAOS. (Selten et al., 2001; Veling et al., 2006) However, the presence of collateral information does not preclude misinterpretation of cultural specific expressions of distress as signs of psychosis and false positive diagnoses of schizophrenia in ethnic minorities.(Zandi et al., 2008; Zandi et al., 2010)

Furthermore, the naturalistic nature of the study with no fixed medication or psychosocial treatment protocol can be considered as a limitation of the study. On the other hand, information on medication and hospitalization could now be used as indicators of the course related the ethnic differences. The small sample size of the study like other immigrant studies can be considered as another limitation of this study. A final limitation is that fact that we did not register specific information about duration of untreated psychosis (DUP) for the patients and that possible differences could not be taken into account as a possible predictor for course and outcome.

Our finding of a relatively low diagnostic stability of schizophrenia using the standard CASH in Moroccans is consistent with the study by Veen et al., (2004) reporting diagnostic shifts from or to schizophrenia after 30 months in 32% of the Moroccan and 60% of the Turkish immigrants in the Netherlands, as compared to shifts in only 17 % among native Dutch patients. Our findings regarding the low diagnostic stability in Moroccans using the standard CASH are also in contrast with the reported relative high stability of a diagnosis of schizophrenia in different studies in non-ethnic populations (Rufino et al., 2005; Schimmelmann et al., 2005: Enrique et al., 2007). However, using the adapted version of the CASH we found a diagnostic stability of 85% for native Dutch and of 81% for Moroccan immigrants, percentages that are consistent with older studies reported diagnostic stability of 83% among ethnic minorities (Harrison et al., 1999; Amin et al., 1999; Goater et al., 1999).

5. Conclusion

The findings of the current study show that a cultural specific diagnosis has superior stability and predictive validity compared to a standard, not culturally informed diagnosis. Therefore, studies comparing the incidence of schizophrenia or psychosis in native inhabitants with immigrant populations should always apply a culturally sensitive diagnostic procedure. Until now, most such studies have failed to pay adequate attention to this issue (Wessely et al., 1991; van Os et al., 1996; Harrison et al., 1997; Bhugra & Chochrane, 2001) or only took into account the cultural interpretation of symptoms without paying attention to the cultural specific presentation of stress experiences (Veen et al., 2004; Veiling et al., 2006). It remains, therefore, uncertain whether the repeatedly reported differences in the treated incidence of schizophrenia between native and immigrant populations is a true finding or (at least partially) the result of cultural diagnostic bias. In our previous study, the difference in the incidence of

treated first episode schizophrenia between native Dutch and Moroccan immigrant patients was greatly reduced and became non-significant after the regular CASH diagnoses were replaced by cultural specific CASH-CS diagnoses (Zandi et al., 2010). Based on these finding and the data regarding the predictive validity of cultural specific diagnoses compared to standard diagnostic procedures, it seems that the significance of many of the previous studies that did not adequately use culturally informed assessment procedures should be questioned. We like to emphasize that our culturally adapted version of the CASH is specific to Moroccan immigrants (in the Netherlands) with their specific believes and habits and that studies with different ethnic groups should use specially adapted instruments and procedures according to their specific cultural background (and their country of immigration). Future studies on the role of ethnic differences should always apply a culturally informed diagnostic approach and preferably a prospective design to arrive at valid conclusions leading to well-informed intervention strategies. In order to obtain more accurate outcome information also follow-up instruments such as the CASH-UP and the PSYCH-UP should also be adapted to the cultural background of immigrants.

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Chapter 5

Effect of a cultural sensitive assessment on symptom profiles in native Dutch and Moroccan patients with a first psychosis referral: an exploration

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Abstract

Previous studies have reported higher incidence rates of psychosis in Moroccan immigrants compared to native people in the Netherlands. However, these differences were substantially attenuated and no longer significantly different when cultural differences in symptom presentation were taken into account. In order to better understand the effect of different diagnostic procedures, we examine whether and how the use of a culture sensitive diagnostic interview compared to a standard semi-structured interview affects symptom profiles in Moroccan immigrant patients compared to native Dutch patients. A total of 26 Dutch and 26 Moroccan patients referred with a possible first psychosis were interviewed twice: once with the standard version and once with a culture-sensitive version of the Comprehensive Assessment of Symptoms and History questionnaire (CASH and CASH-CS, respectively). In native Dutch patients, symptoms profiles were very similar for CASH and CASH-CS. In contrast, in Moroccan immigrant patients, symptom profiles for CASH and CASH-CS were very different with more depression symptoms (+23%; p=0.071), more mania symptoms (+30%; p=0.027), less delusions (-31%; p=0.020), and less hallucinations (-23%; p=0.087) using the CASH-CS compared to the CASH. These results suggest that the previously reported over-diagnosis of schizophrenia in Moroccan immigrants with a first psychosis referral is the result of a tendency to underscore mood symptoms and to overscore positive psychotic symptoms in these patients when a standard diagnostic procedure is used. This can be corrected - at least partly - by the use of a culturally sensitive instrument such as the CASH- CS.

Key words: Immigrant, psychosis, standardized diagnosis, schizophrenia, cultural sensitive

1. Introduction

Several studies have shown that non-Western immigrants to Western societies have a higher incidence of treated psychotic disorders and particularly schizophrenia than the native population of these countries (Cantor-Graae & Selten, 2005). For example, in the United Kingdom, African-Caribbeans were shown to have an increased incidence of schizophrenia compared to the native UK citizens (Wessely et al., 1991; van Os et al., 1996; Harrison et al., 1997; Fearon et al., 2006). Similarly, Moroccan immigrants in the Netherlands were reported to have a higher treated incidence of schizophrenia compared to the Dutch native population (Selten et al., 2001; Veling et al., 2006). In a recent study we confirmed the higher incidence of psychosis in Moroccan immigrants compared to the native Dutch population using the same methodology as Selten et al. (2001) and Veling et al. (2006), but the difference in the incidence of first contact schizophrenia between the ethnic groups was substantially attenuated and became statistically non-significant when a culturally sensitive diagnostic procedure was applied (Zandi et al., 2010). The differences resulted mainly from the high percentage of Moroccan patients that was re-classified from schizophrenia to affective disorders using the cultural sensitive diagnostic procedure. The basis for this reclassification was twofold: (1) a failure to recognize the presence of depressive symptoms, and (2) a reclassification of psychotic symptoms as non-pathological indicators of distress or religious experience. These findings were in accordance with the literature reporting low recognition rates of depressive symptoms (Haasen et al., 2000) and over-identification of psychotic symptoms in patients from minority backgrounds (Zarrouk, 1975; Rack, 1982; Kleinman, 1985; Alsughayir, 1996; Al Jadiri, 1996; Dein, 1997; Al Issa, 2000; Kirmayer, 2001; Arnold et al., 2004; Van Duijl et al., 2005; Vega et al., 2006; Bebbington 2007; Gara et al., 2012; Ademola et al., 2012).

Thus in 2010 we presented the results of an incidence study of schizophrenia among Moroccan immigrants (Zandi et al., 2010) and the importance of a culturally sensitive diagnostic procedure (CASH-CS) compared to the standard diagnostic procedure (CASH). To ascertain the validity of the culturally sensitive diagnostic procedure, we examined the predictive validity of the CASH-CS compared to the standard CASH in terms of the stability of the diagnoses over time (Zandi et al., 2011). In the current study, we further explore the differences between the two diagnostic procedures at the symptomatic and dimensional level. We hypothesize that the application of the culture sensitive version of the CASH (CASH-CS) results in a significant reduction in psychotic symptoms and a significant increase in affective symptoms in Moroccan immigrant patients referred with a first episode of a possible

psychosis, whereas the differences between the two instruments will be negligible in native Dutch patients.

2. Methods

2.1. Sample

In this report we considered the same subjects included in our previously published follow-up study (Zandi et al., 2011). Briefly, we conducted a first contact incidence study (Zandi et al., 2010) in which (over a period of two years) every native Dutch and every Moroccan immigrant patient aged 15-54 years who contacted one of the mental health services in Utrecht with a suspected psychotic disorder for the first time was examined by the research team. Patients with a substance-induced psychosis were excluded. Twenty-six of the 28 Moroccan patients from in the incidence study (Zandi et al., 2010) also participated in the study about the impact of a culturally sensitive diagnostic procedure on diagnostic outcome (Zandi et al., 2011). In the current study, the same number (26) of native Dutch patients were recruited from the 37 native Dutch patients in the incidence study. The first registered native Dutch patient after a Moroccan patient was asked to participate. If that person refused, the next native Dutch patient was asked to participate. All Moroccan patients were first generation.
Permission to perform the study was obtained from the institutional review board of the University Medical Center of the University of Utrecht. All patients were informed orally and in writing and all patients provided written informed consent.

2.2. Assessment

All included patients were interviewed twice in random order: once with the standard Dutch version of the Comprehensive Assessment of Symptoms and History (CASH; Andreasen et al., 1992) and once with a cultural-sensitive version of the CASH; the CASH-CS (Zandi et al., 2008). The CASH raters were blind for the ratings of the CASH-CS and vice versa.
The CASH is a semi-structured interview to establish DSM-IV diagnoses such as schizophrenia, schizoaffective disorder and other psychotic disorders. It includes a comprehensive description of the phenomenology of patients suffering from positive or negative symptoms and from manic and depressive symptoms. Mood symptoms were rated dichotomously as present (1) or absent (0), and the diagnosis of mania or depression is established according to DSM-IV

criteria. Positive psychotic symptoms (delusions and hallucinations) and negative psychotic symptoms (affective flattening, alogia, avolition, anhedonia, and intentional impairment behaviour and thought disorders), are rated on a 5-point scale: subsequently scores 0 (absent) to 2 (mild) were rated as 'absent' and scores 3 (present) to 5 (severe) as 'present'.

A diagnosis of schizophrenia, schizoaffective disorder or other psychotic disorder is made according to DSM-IV criteria based on the presence of these symptoms. The CASH-CS is an expanded version of the standard CASH with additional cultural relevant questions for almost all sections to clarify some relevant items of the instrument and to help interpret answers of the patient, specifically developed for the purpose of the Dutch incidence study (Zandi et al., 2010). The aim of the development of this special version of the CASH was to arrive at a culturally sensitive assessment of psychiatric symptoms using a cultural formulation. To be more specific the following domains of pathology are particularly relevant when conducting a culturally sensitive psychiatric interview: positive psychotic symptoms (delusions and hallucinations) and affective symptoms (Vega et al., 2006; Arnold et al., 2004; Zandi et al., 2008). In the Moroccan culture, hearing voices (mostly animals), seeing dead persons, and being influenced by "the evil eye" or religious forces can be symptoms of emotional distress, which is sometimes associated with a state of dissociation.

In contrast to the standard CASH, we rated such symptoms only after we were certain that these symptoms were present outside the culturally accepted context and or beyond culturally accepted experiences mentioned by the patient or a key informant. In order to make this judgement, open questions were added to obtain more information on when and what they are really hearing, feeling or seeing. Special attention was given to the explain of our questions to the patients and to better understand the patient's answers. Another area of misinterpretation of symptoms is the presence or absence depressive symptoms. In fact, there is no word for concept depression in Berber, the most commonly spoken language by Moroccan immigrants in the Netherlands, and admitting to such feelings is a taboo in this culture. For depression symptoms we did not simply asked whether patients were depressed or not. In stead, we tried by additional questions to clarify what it means to be depressed: Are you happy? Can you enjoy your daily life? Is this different from some time ago? What is different? We tried again to explain our questions and asked patients to explain their answers. A case vignette is presented in order to illustrate some of the differences between the CASH and the CASH-CS (see Box 1). The concurrent cross-cultural validity of the CASH-CS was shown in a study we performed in Casablanca, Morocco (Zandi et al., 2008) and the predictive validity was established in a study in Utrecht, the Netherlands (Zandi et al., 2011).

In addition, the specific background and cultural information about the patient's illness was elicited from a key informant using the Retrospective Assessment of the Onset of Schizophrenia (IRAOS; Häfner et al., 1992) and made available to the CASH-CS raters for both the native Dutch and the Moroccan migrant patients. All CASH-CS interviewer were required to have ample experience in cross-culturally psychiatry. It is important to note that the CASH-CS contains the same items as CASH supplemented with culturally relevant questions and clarifications. The decision whether or not a symptom was present was based only on the answers of the patient, and not on the interpretation by the interviewer. This is similar to the procedure in the standard CASH. In a second, final step in the diagnostic procedure, the meaning and significance of a rated symptom was evaluated during a consensus meeting taking into account the context of culturally relevant experiences, the illness history of the individual patient and data obtained with the IRAOS. During these consensus meetings, the interviewer and one or more psychiatrists were present.
It is important to mention that the CASH was rated by academic psychiatrists. For these psychiatrist experience in cross-cultural psychiatry was not required. The CASH-CS was rated by the psychiatrists working in an social psychiatric service in the city of Utrecht who had experience in cross-cultural psychiatry and were specifically trained to administer and the interpret the results of the CASH-CS.

2.3. Statistical analysis

The primary outcome of the study was the difference in the prevalence of symptoms of depression, mania, delusions and hallucinations between the regular CASH and the CASH-CS for native Dutch and Moroccan immigrant patients. The difference in the average age between Moroccan and Dutch participants was assessed with student's T-test with a two-sided alpha of 0.05. The significance of the differences in the proportion of patients with at least one symptom present in a certain domain between the CASH and CASH-CS for each ethnic group was tested using chi-squared tests or Fisher exact tests where appropriate with a two-sided test at $p < 0.05$ and without Bonferroni correction, because stricter tests of significance would introduce an unacceptable high risk of type II errors (false negative findings). With the selected level of significance clinically relevant differences of 20% or more can be identified as significant whereas smaller differences will be regarded to be not significant. The magnitude of the effects using the different instruments (CASH vs. CASH-CS) was presented as Cohen's h by using an arcsin transformation of the probabilities with the following interpretation: h=0.2: small effect, h=0.5: medium effect, h=0.8: large effect

(Cohen, 1988). All analyses were performed using SAS, version 9.2 (SAS Institute Inc, Cary, NC).

3. Results

3.1. Clinical characteristics

Table 1 shows the clinical characteristics of the 26 Moroccan participants and the 26 native Dutch participants included in this study from a sample of 77 participants include in our incidence study (29 Moroccan and 48 Dutch patients). Moroccan immigrant patients were more likely to be male and married. All native Dutch and Moroccan immigrant patients were diagnosed with a psychotic disorder according to the standard CASH. However, according to the CASH-CS, only 15 (58%) of the Moroccan and all 26 (100%) of the native Dutch patients were diagnosed with a psychotic disorder. Similarly, according to the CASH 58% of the native Dutch and 65% of the Moroccan immigrant patients were diagnosed with schizophrenia, whereas according to the CASH-CS 58% of the native Dutch and only 15% of the Moroccan immigrant patients were diagnosed with schizophrenia.

Table 2 presents the prevalence of symptoms on the domains of depression, mania, delusions, hallucinations, behaviour disorder and thought disorder according to the CASH and the

Table 1. Characteristics of patients

		Moroccan patients	Native Dutch patients	
		N or mean	N or mean	p-value for difference
Total patients (N/%)		26	26	-
Male gender		20	13	0.044*
Age (years)		33	31	0.356
Married		16	8	0.026*
CASH	Schizophrenia	17	15	0.631
	Schizoaffective	3	6	
	Other Psychotic	6	5	
	Not Psychotic	0	0	
CASH-CS	Schizophrenia	4	15	0.003*
	Schizoaffective	4	7	
	Other Psychotic	7	4	
	Not Psychotic	11	0	

SD: Standard deviation; P-values calculated with Chi-squared tests, T-tests and Fisher's Exact Tests were appropriate. * Indicate significant differences between groups at a significance level of 5%

Table 2. Number and percentages of participants that score positive on depression, mania and psychosis items (at an item cut-off of 1+ for affective and mania symptoms and 3+ for psychosis symptoms). For both the CASH and the CASH-CS, separately for native Dutch and Moroccan participants significantly different percentages of positive answers within groups are marked in grey and starred. P-values were calculated with chi-squared or Fisher exact tests where appropriate and Cohen's h indicators of effect size were added for all comparisons.

Item	Group	CASH N=26	CASH-CS N=26	p-value for difference	effect size: Cohen's h#
Depression	Native Dutch	16 / 62%	11 / 42%	0.165	-0.40
	Moroccan	15 / 58%	21 / 81%	0.071**	0.51
Mania	Native Dutch	2 / 8%	2 / 8%	0.999	0
	Moroccan	9 / 35%	17 / 65%	0.027*	0.61
Delusions	Native Dutch	3 / 12%	5 / 19%	0.703	0.19
	Moroccan	13 / 50%	5 /19%	0.020*	-0.67
Hallucinations	Native Dutch	4 / 15%	5 / 19%	0.999	0.11
	Moroccan	13 / 50%	7 / 27%	0.087**	-0.48
Behavioral disorders	Native Dutch	2 / 8%	1 / 4%	0.999	-0.17
	Moroccan	3 / 12%	3 / 12%	0.999	0
Thought disorders	Native Dutch	1 / 4%	1 / 4%	0.999	0
	Moroccan	2 / 8%	0 / 0%	0.490	-0.57

* Indicates significant differences between groups at a significance level < 5%

** Indicates significant differences between groups at a significance level < 10%

Negative: prevalence CASH > prevalence CASH-CS; Positive: prevalence CASH < prevalence CASH-CS

Effect Size Magnitude: h= 0.20 small; h=0.50 medium; h= 0.80 large

CASH-CS. The global score for depression and mania disorders in the standard CASH are -1 (dubious), 0 (absent) and +1 (present). The overall scores for hallucinations and delusions in the standard CASH are 0 (absent), +1 (dubious), +2 (mild) and +3-5 (severe). Therefore we chose a cut-off of +1 for depression and mania and a cut-off of +3 for hallucinations and delusions. This categorizing is the same in the CASH-CS. This categorizing is also identical to the one used in The Hague study. In native Dutch patients, symptoms profiles were very similar for CASH and CASH-CS. In contrast, in Moroccan immigrant patients, symptom profiles for CASH and CASH-CS were very different with a higher prevalence of patients with at least one symptom in the domain of depression (+23%; p=0.071; h=0.51) and mania (+30%; p=0.027; h=0.61) and with a lower prevalence of patients with at least one symptom in the domain of delusions (-31%; p=0.020; h=0.67) and hallucinations (-23%; p=0.087; h=0.48) using the CASH-CS. These differences occurred because Moroccan patients had

fewer persecutory delusions, visual and auditory hallucinations and reported more depressed mood, sleep disturbance, insomnia, psychomotor retardation and train of thoughts on the CASH-CS than the regular CASH.

4. Discussion

In the current study we provide an in-depth exploration of the observed attenuation of the difference in the incidence in first psychosis between Moroccan immigrant referrals and native Dutch referrals to a mental health centre for a suspected psychosis when a standard diagnostic procedure is replaced by a culture sensitive diagnostic procedure. It was hypothesized that a cultural sensitive assessment would result in a reduction in psychotic symptoms and an increase of affective symptoms in Moroccan patients, as compared to native Dutch patients. Both hypotheses were confirmed: Moroccan patients indeed showed a significant and substantial increase in the prevalence of depressive (23%) and manic (30%) symptoms and a significant and substantial decrease in the prevalence of delusions (31%) and hallucinations (23%) with the CASH-CS compared to the CASH, whereas no significant differences in the prevalence of any of the symptom domains were found in the native Dutch patients. These findings indicate that changes in symptom ratings can at least partly explain the attenuation of the difference in incident psychosis between Moroccan immigrants and the native Dutch population (Zandi et al., 2011). The different interpretations of the recorded symptoms during the consensus meetings based on additional culturally relevant information, however, also needs to be considered to fully explain the diagnostic changes. Together, these findings seriously question the validity of the frequently reported higher rates of schizophrenia among some immigrants in studies based on culturally non-validated interviews and questionnaires (Zandi et al., 2010).

The view that cultural differences may influence the manifestations and definitions of various psychiatric disorders has been brought up by several authors (Kleinman, 1987; 1997; 2004; Kirmayer, 2001; Neighbors et al., 2003; Jarvis, 2008). For example, McKenzie suggested (1999) 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”. Moreover, McKenzie et al. (2008) argued that the failure of (Western) psychiatrists to recognize culturally appropriate expressed emotional distress, mood problems and brief reactive disorders and to differentiate these from psychotic disorders might be a possible explanation

for the reported high rates of psychosis among non-Western (immigrant) patients. Also some other authors have mentioned this as an important source of misclassification in immigrant studies (Haassen et al., 2000; Arnold et al., 2004; Vega et al., 2006).

Interestingly, in contrast to most studies on schizophrenia among migrants, the prevalence of depression is generally reported not to be increased among immigrant groups in the UK (Shaw et al., 1999; Bhugra, 2003). In a recently published meta-analysis on mood disorders in migrants, Swinnen and Selten (2007) found no conclusive evidence for a large increase in the risk of mood disorders associated with migration. The authors expressed their surprise 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. However, another study by Selten et al. (2012) did show an increased risk of receiving specialized treatment for mood disorders among Moroccans and other immigrants in the Netherlands. Unfortunately, the authors failed to take into account the treatment of mood disorders by private or primary care practitioners, a treatment setting that is likely to be preferentially used by native Dutch patients (Ten Have et al., 2004).

Importantly, the current study suggests that mood disorder symptoms may be missed or misinterpreted as 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.

The main limitation of the current study is the relatively small sample size. In order to prevent type II errors we decided to use a rather lenient significance level and not to correct for multiple testing. Despite these measures, it cannot be excluded that some meaningful differences were missed. At the same time, some of the findings may turn out to be false positive. Larger replication studies are needed to allow for a better balance between type I and type II errors. A further criticism can be that clinicians who were involved in the adapted version of the CASH may have been reluctant to diagnose schizophrenia among Moroccans (Zandi et al., 2008; Selten and Hoek, 2008). However, the results of our follow-up study clearly support the validity of the culturally sensitive diagnoses in our study (Zandi et al., 2011).

Another limitation of the current study is the absence of second generation Moroccan immigrant patients. During the inclusion period of two years, no second generation Moroccan immigrants (one or two parents born in Morocco but patient born in the Netherlands) contacted the central reporting office in Utrecht for a possible psychosis. We were therefore unable to replicate the high relative risks for second generation Moroccan immigrants, reported in

The Hague. Due to this situation, we can also not compare the results of two interviews for this group. However some of the included (first generation immigrant) patients were young, raised in The Netherlands and were fluent in Dutch. Based on the results of the current study, we found that traditional instruments like the CASH interview are not very specific to positive symptoms of psychosis among young first generation immigrant Moroccan patients, suggesting that such an assessment procedure may also cause false positive diagnoses of psychosis among second generation Moroccan patients. However because of the lack of information this is merely a speculation.

A final limitation of the current study may be that the background information obtained by key informants with the IRAOS was not available for the diagnosis based on the standard CASH.

The information obtained with the IRAOS from the family of the patient was instrumental for a contextual understanding of the presented symptoms. This difference in availability of information may partly explain the difference in relative risks according to the two procedures (Zandi et al., 2010). However, in The Hague incidence study on schizophrenia in migrants (Selten et al., 2001; Veiling et al., 2006) the IRAOS information was available at the time of the diagnostic decisions and they reported incidence rates among Moroccan immigrants similar to the ones we found with the standard CASH without including IRAOS information (Zandi et al., 2010). Together these findings suggest that additional background and cultural relevant information obtained by IRAOS is essential to make a valid diagnosis, but that this information can only be adequately used in combination with symptomatic information based on a culturally sensitive diagnostic interview such as the CASH-CS. In other words, information obtained by the IRAOS can not prevent misinterpretation of a cultural expression of distress as a sign of psychosis if symptom assessment is based on a non-culturally sensitive diagnostic instrument such as the CASH (Zandi et al., 2011). The ability of the diagnostician to determine whether the reported symptoms are truly pathological or culture-bound expressions of a non-psychotic nature is therefore of crucial importance (Selten et al., 2012). This conclusion was recently corroborated in a qualitative study among 23 migrants referred for psychiatric evaluation in a clinic in Stockholm (Scarpinati & Bäärnhielm, 2012). The study shows the need to contextualize symptoms for an in-depth comprehension of patients' phenomenology and concludes that a section on migration and acculturation should be added to the cultural formulation in the next edition of DSM.

5. Conclusion

The previously reported attenuation of the difference in the incidence of psychotic disorders and schizophrenia between Moroccan and native Dutch patients seems to result from a combination of a culturally sensitive assessment of psychiatric symptoms using a culturally sensitive diagnostic interview, a structured assessment of a patient's personal illness history with special attention for the cultural context, and a diagnostic consensus procedure needed for the interpretation and integration of all information (Zandi et al., 2010). These findings underscore the findings of other authors (Adeponle et al., 2012) and the importance of knowledge about the cultural background of the patients and the use of the principles of cultural formulation for a valid evaluation of symptoms in ethnic and culturally different populations.

Although we should be cautious not to over-interpret our findings, the observed attenuation of the difference in the incidence of schizophrenia/psychosis between native Dutch and Moroccan immigrants may have at least some relevance for previous reported differences in incidence between natives and immigrants in other countries (e.g. UK, Scandinavia, Canada) and the high rates of schizophrenia/psychosis among immigrants in these countries could at least partly be explained by issues related to misdiagnosis (Zandi et al., 2010). This, however, does not mean that we do not recognize that differences in social adversities between natives and immigrants are important and may result in real differences in the incidence of mental disorders between these groups, including differences in the incidence of schizophrenia/psychosis. We are convinced that future studies on the role of ethnic differences should apply strategies with a culturally informed diagnostic approach and should aim to use all possible sources of information to arrive at a valid diagnosis leading to well-informed interventions. Finally, we like to emphasize that this is not just an epidemiological debate, but that misdiagnosis of mental disorders in immigrants may lead to inadequate and possibly harmful treatments and thus to unnecessary human suffering.

Box 1; case vignette

A 35-year old Moroccan man was arrested by the police after continuous shouting and breaking the window of his friends' house. His friend told the psychiatrist at the police office that the patient thought that his friend was a bull, bit him and then wanted to jump from the window. That same night he was admitted involuntarily to a closed ward of a psychiatric hospital. According to his family he had been restless and had reversed his day-night pattern already for quite some time. According to his sister this was due to the stress he experienced after the 9-11 terrorist attack in New York.

During the interview with the CASH, only two symptoms of the mood section were scored: insomnia and concentration disturbances. According to the CASH he had high scores on visual and acoustic hallucinations and delusions of being followed on the street by unknown people. Based on the CASH, he was diagnosed with a psychotic disorder NOS with schizophrenia as a probable diagnosis. In the interview with the CASH-CS almost all symptoms of the depression section were scored with rather high severity. It became evident that he suffered from these symptoms for years without talking about it to anyone. On the question if he wanted to commit suicide, he did not give a clear answer. It is important to mention that suicide in Islamic religion and traditions is strictly forbidden. By the CASH-CS we recorded both visual and acoustic hallucinations as present, but with low severity. Delusions were scored as uncertain. In the history of his illness we noted that he repeatedly stated that he was afraid of everything and everybody. He could not explain what he has was afraid of exactly, but it was clear that he felt anxiety and fear. During the CASH-CS interview he said he heard two men talking and further stated that he heard sounds of animals inside his head, especially when he woke up in the morning to pray. At that hour of the day he was most afraid of his father because he felt he was not a good Muslim and not a good son for his father. Asked about hearing these two men talking he laughed and said it was "as if " he was hearing voices talking about his behavior, not in reality. He told us that he came to the Netherlands when he was sixteen. He was unable finish any form of education and said that he was ashamed to admit he had been addicted to gambling for a number of years. He had a € 12,000 gambling debt. He told us that he was very tired and confused that night and went to visit his friend because he could not bear the tension any more. Talking about his fear of being followed on the street, he declared that after 9-11 he developed some sympathy for a group of young Muslim activist in Europe. Two of these men had been arrested two months before and he was afraid to be followed by the police.

Based on information obtained with the CASH-CS and the IRAOS, we concluded that the patient was experiencing pseudo-hallucinations, which were metaphoric and should not to be considered as pathological. Based on the CASH-CS the diagnosis was severe depression without psychotic symptoms.

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Chapter 6

General Discussion

The focus of this thesis is on the impact of cultural sensitive assessment of psychiatric symptoms to assess psychotic disorders and in particular schizophrenia in two generations of 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 Moroccan immigrants in The Netherlands.

6.1. Main findings

In **chapter 2**, we examined the procedural validity of a standardized instrument for the diagnosis of psychotic disorders in Morocco. For this purpose twenty nine patients from Casablanca, Morocco, with a psychotic or mood disorder were examined using the Comprehensive Assessment of Symptoms and History (CASH) and an adapted version using cultural formulations to make the instrument more culturally sensitive (CASH-CS). Chance corrected agreement was calculated between diagnoses based on these two versions of CASH and independent clinical diagnoses according to local psychiatrists. Interestingly, agreements for the standard CASH versus clinical diagnosis and for the standard CASH versus the CASH-CS were low but agreement between CASH-CS and clinical diagnosis was good. Particularly our study showed that the traditional CASH interview seems to be sensitive but not to be very specific for the assessment of positive symptoms of psychosis and may therefore give rise to false positive diagnoses of psychosis and to an overestimation of psychotic illnesses in epidemiological studies among Moroccan patients. We therefore concluded that standard instruments for the assessment of psychosis such as the CASH may be liable to cultural misinterpretations. These findings are relevant considering the various attempts to interpret the high incidence rates of schizophrenia among immigrants. The study shows that excluding cues about the cultural background of the patient, as applied as a method to exclude cultural bias by some authors (Selten et al., 2001; Fearon et al., 2006), may itself constitute a source of ethnic/cultural bias. More attention and informed interpretation of the emotional language of the patient is a crucial element in reaching a valid diagnosis in future epidemiological studies about the incidence of schizophrenia among various groups of immigrants.

In **chapter 3**, we presented the results of our incidence study of schizophrenia among Moroccan immigrants and native Dutch people in Utrecht, the Netherlands. We compared the risk of schizophrenia and other psychotic disorders among treatment seeking Moroccan and native Dutch patients using a standard semi-structured interview (CASH) and an adapted

version of the same instrument based on the principles of cultural formulation (CASH-CS). The overall observed risks of a first contact with the mental health services because of a suspected psychotic disorder of all psychotic disorders and of schizophrenia according to the CASH was significantly higher among Moroccans compared with the ethnic Dutch population (psychosis: RR=7.9; schizophrenia: RR=7.8) and these relative risks were even higher than the ones reported in a previous incidence study in the Netherlands by Selten and colleagues (Selten et al., 2001): psychotic disorders RR=4.8 (CI 95% 3.1- 7.5); schizophrenia RR=5.0 (CI 95% 2.8- 8.9). However, in our study, the RR for broadly defined psychosis was substantially attenuated when a culturally sensitive diagnostic procedure was applied (CASH-CS) but remained statistically significant (RR=7.9 → RR=4.2), whereas the RR for schizophrenia became non-significant (RR=7.8 → RR=1.5). Our conclusion was that first contact incidence of schizophrenia in Moroccans is similar to that among ethnic Dutch people when a cultural sensitive diagnostic procedure is applied and that the results of studies failing to take into account cultural issues in the diagnostic procedure should be seriously questioned.

It is important to note that broadly defined psychosis in our study included schizophrenia, schizophreniform disorder, schizoaffective disorder, delusional disorder, brief psychotic disorder, psychotic disorder not otherwise specified and also major depression or bipolar disorder with psychotic features.

Fifty-eight percent of Moroccan and 86% of Dutch native participants with a possible psychotic disorder (cases that where referred to the central reporting office with suspected signs of psychosis during the observation period) were diagnosed to have one of the psychotic disorders based on the CASH, and 15% of the Moroccan patients and 59% of the native Dutch participant with a possible psychotic disorder received a diagnosis of schizophrenia according to the CASH-CS. Non-psychotic Moroccan patients according to the CASH-CS were diagnosed with a mood disorder without psychotic features, a factitious disorder or a dissociative disorder. Non-psychotic native Dutch patients were all diagnosed with a non-psychotic bipolar disorder.

Surprisingly during the full inclusion period of 24 months no second generation Moroccan immigrants contacted the central reporting office in Utrecht for a suspected, possible or confirmed psychosis. This was independent of the type of interview used.

In **chapter 4**, we studied the predictive validity of the culture sensitive diagnostic procedure (CASH-CS) compared to the standard diagnostic procedure (CASH). In the absence of a gold standard to ascertain which of the two diagnostic procedures renders the most "truthful'

results, we had to rely on the results of a follow-up study investigating the possible differences between the two diagnostic procedures in terms of the stability of the diagnoses and in term of the course and outcome of the disorders over 30 months. All Moroccan participants and an equal number of native Dutch patients were asked to be interviewed approximately two and a half years after the baseline assessment using the follow-up version of the standard diagnostic interview, the CASH-UP, to assess not only the subjects' level of symptoms but also psychosocial functions, medication use and hospitalization. To prevent considering patients in sustained remission as having "no diagnosis", the follow-up diagnosis was based on the combination of a structured interview (CASH-UP) and the recorded clinical information during the total follow-up period. Thus, a change in diagnosis from baseline to follow-up could not be attributed only to the (very recent) absence of psychotic symptoms during the follow-up assessment, but took into account the entire illness episode. To the best of our knowledge this is the first follow-up study assessing the impact of a systematic application of the principles of a cultural sensitive diagnosis compared to a standard diagnostic procedure in patients with a possible first episode psychosis.

Diagnostic stability according to the CASH was high for native Dutch (92%) but low for Moroccan patients (27%), whereas diagnostic stability according to the CASH-CS was high for both groups (85% and 81%, respectively). Moroccan patients who were diagnosed with schizophrenia using the standard CASH at baseline had a significantly better 30-month prognosis than native Dutch patients with the same CASH diagnosis. Prognosis of schizophrenia according to the CASH-CS was similar for Moroccan and native Dutch patients. This findings were corroborated by the comparison of the 30-months prognosis of Moroccan and native Dutch patients with a non-schizophrenic disorder at baseline: Moroccan patients showed a somewhat better prognosis than native Dutch patients according to both CASH and CASH-CS. This is remarkable because the Moroccan CASH-CS group with a non-schizophrenic disorder included many patients classified as having schizophrenia according to the standard CASH at baseline.

These findings show that in Moroccan immigrants a cultural specific diagnosis has superior stability and predictive validity compared to a standard, not culturally informed diagnosis. These data raise questions regarding the validity of the standard CASH in Moroccan immigrants in the Netherlands and support the validity of the CASH-CS. These findings also confirm our doubts regarding the validity of previous studies showing an increased incidence of schizophrenia in immigrants using standard diagnostic procedures.

In **chapter 5**, we studied whether and how the application of a culture sensitive diagnostic interview (CASH-CS) compared to a standard semi-structured interview (CASH) affects symptom profiles in Moroccan immigrant patients compared to native Dutch patients referred for the first time to a mental health service for a possible psychotic disorder. In this exploratory study, all 26 Moroccan patients and the same number of native Dutch subjects were included and were interviewed twice in random order: once with the standard Dutch version of the (CASH) and once with the CASH-CS. The CASH raters were blind for the ratings of the CASH-CS and vice versa. The data showed that in native Dutch patients, symptoms profiles were very similar for CASH and CASH-CS. In contrast, among Moroccan immigrant patients, symptom profiles for CASH and CASH-CS were very different with more depression symptoms (+23%), more mania symptoms (+30%), less delusions (-31%), and less hallucinations (-23%;) using the CASH-CS compared to the CASH. These results suggest that the previously reported overdiagnosis of schizophrenia in Moroccan immigrants with a first psychosis referral (Selten et al., 2001; Veling et al., 2006) are at least partly caused by a failure to recognize mood symptoms and a misinterpretation of stress-related expressions as psychotic symptoms.

6.2. Implications

Cultural factors relate to mental illness in several ways. For example, culture determines what is seen as normal and abnormal within a given society. In this study we put special emphasis on the cultural background of patients and the use of the principles of a cultural formulation for a valid evaluation of psychiatric symptoms in ethnic and culturally different populations. This culture-sensitive approach resulted in a substantial attenuation of the difference in the incidence of psychotic disorders and schizophrenia between Moroccan immigrant and native Dutch people and the observed higher rate of schizophrenia in Moroccan immigrants became statistically non-significant. Similar attenuations might have occurred in other studies that failed to (adequately) adjust for possible cultural bias in the diagnostic process. As a consequence, the generally accepted presence of a higher incidence and prevalence of schizophrenia in black immigrants (Saha et al., 2005; Bourque et al., 2011) should be reconsidered and popular explanations should be critically reviewed against this background. However, many studies still continue to use non-validated diagnostic procedures and serious misdiagnosis will remain the rule rather than the exception. In this regard we would like to

quote Ineichen (1991): “until the aetiology of the condition (or conditions) is clarified, and its validity well tested, epidemiological studies remain hazardous”.

The findings of our study may have a serious impact on our thinking about the causes of psychosis and schizophrenia and on the way we treat Moroccan patients with a suspected or possible psychosis

In the last decade, most studies look at schizophrenia as a multifactorial developmental disorder (Khoury, 1993) with important gene-environment interactions as a crucial mechanism in the development and the onset of the disease (van Os et al., 2003, 2008). How these factors interrelate to cause the clinical symptoms of schizophrenia is mainly unsolved. The authors in this field are often referring to the increased rates of schizophrenia among immigrants. A better understanding of the possible mechanism of the confounding factors and the source of possible misclassification influencing the diagnosis of psychotic disorders may contribute to the answer to the question whether there is a truly increased rate of schizophrenia among immigrants and what this means for future theories on schizophrenia.

The misinterpretation of symptoms may also have serious consequences at the individual patient level, including over-prescription of antipsychotics and under-prescription of antidepressants and mood stabilizers with negative effects on the prognosis in this group. Considering the increasing dissatisfaction of patients from ethnic minorities with the quality of health care, misdiagnosis only adds to this negative attitude and further hampers the therapy process (Saha et al., 1999). This may be partly due to a mismatch between patients and treatment providers based on a range of culturally embedded factors as religion, ethnic background, personal history, the experience of illness and perceptions of health (Steffenson & Colker, 1982). We therefore like to encourage the use of a cultural formulation as a central element in the assessment of the symptoms of psychotic and affective disorders in immigrant patients. Cultural sensitive training and supervision are needed to address the cultural relativity of psychopathological symptoms and syndromes (Whaley, 1997).

Finally, there is evidence of substantial variation between ethnic groups in voluntary and compulsory admissions and more complex pathways to specialist care. However. If there is no increased incidence of psychotic disorders or schizophrenia in (dark) immigrant then there is no objective reason for increases rates of compulsory admissions and there most be seriously worrying practices that are leading to disproportionate levels of compulsory admission” (Patel and Heginbotham, 2007), resulting in underserved restrictions of freedom for migrant patients with a mental disorder.

6.3. Strengths and Limitations

A very important strength of this study is that in this study we assessed for the first time the impact of a systematic application of the principles of cultural formulation in the context of a standardized diagnostic interview. We were able to compare the results of two diagnostic interviews. Despite the absence of a gold standard to ascertain which of the two diagnostic procedures renders the most "truthful' results, we were able to test the validity of each procedure using the results of a follow-up study comparing the stability of the diagnoses and the course and outcome of the disorders over an extended period of time (predictive validity). We therefore consider the absence of a significant difference between Moroccans and native Dutch patients in the treated incidence of schizophrenia according to a cultural sensitive diagnostic procedure as a valid observation. Another strength is that our cohort from Utrecht was highly representative as was shown by another research group that obtained information from the Psychiatric Case Register (Selten et al., 2011; Zandi et al., 2011b).

The limited sample size can be considered as the main limitation of this study and we are aware that no final conclusions can be drawn about the reported incidence rates of schizophrenia among Moroccans and about the significance of the difference in incidence rates between the two ethnic groups. In a larger sample the difference, although seriously attenuated, would probably have been significant. Another limitation is that our analyses were not controlled for possible differences between the ethnic groups in terms of socio-economic characteristics. Although, a previous study in the Netherlands reported only minor effects of socio economic status based on neighborhood (Selten et al., 2001), we regard socio-economic adversity as an important potential confounder of the relation between ethnicity on the presence of psychotic disorders. Therefore future studies should take both cultural sensitive diagnostic procedures and differences in socio-economic differences into account simultaneously in order to arrive at the best comparison of incidence rates of psychotic disorders and schizophrenia between different ethnic groups.

6.7. Future studies

In the last decades there are increasing claims about the importance of acknowledging ethnic identity. However, differences in cultural interpretation of symptoms is still not considered to be a crucial strategy to prevent information bias in immigrant studies in Europe. The

clinician's cultural competency in multicultural settings is an important determinant and is essential in dealing with patients with different cultural backgrounds (Alarcón et al,. 2002; Smedley et al,. 2003; Hyaman 2004; Alegria et al,. 2008; Cummings & Druss. 2011). Anthropological should help us to clarify the distinction between traditional symbols and culturally sanctioned idioms of distress and pathological phenomena. This also means that the methodology of new studies should be more subtle in addressing the issue of cultural background of the immigrant patients.

If, as most of the incidence studies argue, migration as a newly identified risk factor that can change the risk of an illness or produce new forms of the illness among a particular group, the research tools must not only be cross culturally valid but also be able to detect and differentiate these atypical cases form already existing types of psychosis (Mc Kenzie et al., 2008).

We hope that our results will inspire future methodological studies on the standardisation of diagnostic interviews and the development of new versions of these diagnostic tools for other ethnic groups. Subsequently, the equivalence of diagnostic and research tools used in different incidence studies should be tested in different populations. In addition, new incidence studies with properly adapted instruments, using long-term follow-ups, and with proper adjustments for socio-economic differences between ethnic groups may result in a better estimate of the difference in incidence rates of psychotic disorders between ethnic groups. There is no doubt that cultural differences may contribute to health disparities, but unjustified differences in diagnostic evaluation and unequal access to the mental health care system should be reduced as much as possible in order to achieve equity in terms of treatment. In order to reach this goal, the issue of cultural diversity has to be seriously addressed both in health science and in health care practice (Alegria et al,. 2010).

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Nederlandse samenvatting

Nederland is al eeuwen lang één van de Europese landen die veel immigranten aantrekt of juist doelbewust deze mensen naar het land haalt. In 2011 bestond 20.6 % van de Nederlandse bevolking uit etnische minderheden, waarvan 9.2 % westerse en 11.4 % niet-westerse immigranten. Van de niet-westerse immigranten is 18.7% van Marokkaanse afkomst, 355.883 inwoners of 2.1% van de totale Nederlandse bevolking (CBS, 2011). De eerste Marokkaanse immigranten zijn in de jaren zestig van de vorige eeuw naar Nederland gekomen, meestal vanuit het Rif gebergte, bijna allemaal moslim en grotendeels analfabeten. Opleiding en inkomensniveau van Marokkanen ligt net als bij andere immigranten lager dan dat van autochtone Nederlanders. Psychiatrische ziektes zijn nog altijd taboe binnen vele Marokkaanse families en velen kiezen er bij problemen voor om eerst naar een inheemse genezer te gaan teneinde de klachten te verminderen.

Er wordt vaak verondersteld dat immigratie een bron van stress is en dat deze stress de oorzaak is van de veel voorkomende psychische problemen bij immigranten. Er is verder weinig twijfel dat immigranten vaker geconfronteerd worden met armoede, huisvestingsproblemen, werkloosheid en discriminatie. Maar zoals bekend zijn nationale studies die immigranten - vooral niet westerse - includeren, relatief nieuw en de bevindingen over het effect van immigratiestress op de geestelijke gezondheid zijn niet consistent. Dit neemt niet weg dat er wel verontrustende berichten zijn wat betreft emotionele en gedragsproblemen en het drugsgebruik bij jeugdige immigranten in Nederland.

Cultuur, etniciteit en sociaaleconomische positie zijn belangrijke begrippen die wereldwijd niet genoeg aandacht krijgen in epidemiologische onderzoeken. De laatste decennia is er vooral vanuit Engeland onderzoek gedaan naar de hoge incidentie van psychotische stoornissen en vooral schizofrenie onder verschillende groepen immigranten. In het verlengde daarvan zijn er ook in onderzoeken met een vergelijkbare methodologie in Nederland verontrustend hoge incidentiecijfers voor schizofrenie bij Marokkaanse, Surinaamse en later bij Turkse immigranten gerapporteerd. Opvallend is dat dit niet geval lijkt te zijn voor stemmingsstoornissen bij dezelfde immigrantengroep in Nederland.

Het is belangrijk dat de onderzoekers bij veel van de studies over psychotische stoornissen er voor kiezen om de etnische achtergrond van de patiënten niet te kennen om zodoende de diagnose zo zuiver mogelijk te kunnen stellen. De gebruikte vragenlijsten kennen ook geen aanpassingen om deze enigszins voor de culturele achtergrond van de patiënten geschikt dan wel meer begrijpelijk te maken.

In dit proefschrift wordt de invloed van een cultureel sensitieve procedure onderzocht bij de vaststelling van de diagnose psychotische stoornis en vooral schizofrenie bij eerste en tweede generaties Marokkaanse immigranten wonende in Utrecht die vanwege een eerste psychose hulp hebben gezocht bij één van de geestelijke gezondheidszorg instanties in Utrecht. Eén van de belangrijkste hypothesen in de huidige studie is dat culturele verschillen in de presentatie van emotionele toestanden en psychiatrische symptomen de hoge incidentiecijfers van schizofrenie onder niet-westerse immigranten in Europa en Marokkanen in Nederland kunnen verklaren. Daartoe hebben wij de incidentiecijfers voor Marokkaanse en Nederlandse patiënten met elkaar vergeleken op basis van twee interviews: een standaard semi-gestructureerd interview (CASH) en een aangepaste versie van dit interview met bijbehorende cultuur-specifieke instructies (CASH-CS). Een onderliggend doel is daarbij om op basis van de resultaten meer inzicht te krijgen in de invloed van een cultuursensitieve blik naar klachten, klinisch beeld, en diagnose bij patiënten uit andere culturen.

Hoofdstuk 1 is een algemene inleiding, waarin behalve een beeld van de geestelijke gezondheid van Marokkanen in Nederland, de etiologie en epidemiologie van schizofrenie besproken worden. De definitie van schizofrenie en de kritische meningen daarover worden besproken waarbij ook aandacht wordt besteed aan de beschrijving en betekenis van belangrijke termen als ras, etniciteit en sociale achterstand. Als achtergrond van onze studie is een overzicht gemaakt van de verschillende onderzoeken over de incidentie van schizofrenie onder immigranten in verschillende landen. Hierbij wordt ook de methodologie van deze onderzoeken weergegeven. Ook worden de verschillende mogelijke hypotheses besproken die de vaak gemelde verhoogde incidentie van schizofrenie onder immigranten kunnen verklaren. Verder wordt de mogelijkheid van misdiagnose van schizofrenie onder immigranten uitgebreider beschreven.

In **hoofdstuk 2** wordt de procedurele validiteit van een gestandaardiseerd instrument voor de diagnose van psychotische stoornissen in Marokko beschreven. In Casablanca, Marokko, zijn 29 patiënten met een psychotische stoornis of een stemmingsstoornis met behulp van de Comprehensive Assessment of Symptoms and History (CASH) en de aangepaste cultuur-sensitieve versie ervan (CASH-CS) geïnterviewd. De vergelijking is gedaan op basis van deze twee versies van CASH en een onafhankelijke klinische diagnose gesteld door lokale psychiaters. Opvallend was dat de overeenstemming tussen CASH-CS en de gestelde klinische diagnose door de Marokkaanse psychiaters zeer hoog was, terwijl de

overeenstemming tussen de standaard CASH en klinische diagnose door de Marokkaanse psychiaters laag was. De resultaten van onze studie laten zien dat het standaard interview (CASH) dat vaker in internationale incidentie studies is gebruikt sensitief lijkt te zijn op de positieve symptomen van psychose maar niet specifiek genoeg is. Dit kan een bron zijn van overmatige registratie van positieve symptomen en kan daardoor een verhoogde kans op een misdiagnose van psychotische stoornissen in internationale studies opleveren. In deze studie concluderen wij dat een standaard instrument voor de beoordeling van een psychose zoals de CASH een bron van culturele misinterpretatie van de symptomen kan worden. Deze studie laat zien dat het weglaten van alle verwijzingen naar de culturele achtergrond van de patiënt om culturele bias voorkomen, zoals het geval was in meerdere incidentie studies in Nederland in Engeland, een bron van etnisch-culturele bias kan worden. Meer aandacht en kennis van de emotie en culturele achtergrond van de patiënten is nodig om tot een correcte interpretatie van de geobserveerde symptomen te komen en om een valide diagnose te stellen in toekomstige epidemiologische studies over de incidentie van schizofrenie onder verschillende groepen van de immigranten.

In **hoofdstuk 3** worden de resultaten van de incidentiestudie van schizofrenie onder Marokkanen en autochtone Nederlanders in Utrecht gepresenteerd. Het voorkomen van schizofrenie en andere psychotische stoornissen wordt vergeleken tussen autochtone Nederlandse patiënten en Marokkaanse patiënten die in Utrecht voor het eerst in hun leven hulp hebben gezocht vanwege het vermoeden van een psychose. Deze patiënten zijn twee keer geïnterviewd, één keer met de CASH en een keer met CASH-CS. Het risico om vanwege de verdenking van een psychose in contact te komen met de geestelijke gezondheidszorg was onder Marokkanen 5.6 keer zo groot als bij Nederlanders. De kans op een psychotische stoornis in het algemeen en van schizofrenie in het bijzonder bleek bij gebruik van de standaard versie van CASH onder Marokkanen significant hoger te liggen dan bij autochtone Nederlanders (psychose: RR=7.9; schizofrenie: RR=7.8). Bij gebruik van de CASH-CS was het verschil in het risico voor psychose en voor schizofrenie tussen autochtone Nederlanders en Marokkaanse Nederlanders veel kleiner en voor schizofrenie was dit verschil niet langer significant (psychose: RR= 4.2; schizofrenie: RR= 1.5). In dit verband is het van belang te melden dat wij bij de diagnose psychotische stoornissen ook depressie en bipolaire stoornissen met psychotische kenmerken geïncludeerd hebben. Dit om het onderzoek vergelijkbaar te maken met eerdere studies. Verrassend voor ons was dat gedurende de twee jaar inclusie van deze incidentiestudie geen tweede generatie Marokkaanse patiënten zijn aangemeld bij

het aanmeldpunt. Dit was onafhankelijk van de diagnostische procedure. In Utrecht kon de uiterst hoge RR van 9.3 (95% CI 3.7- 23.4) voor de tweede generatie Marokkaanse patiënten, zoals deze eerder gerapporteerd werd in den Haag, dus niet bevestigd worden. Dit kan niet verklaard worden door het aantal tweede generatie Marokkaanse personen in Utrecht, dat ongeveer twee keer zo hoog was als in Den Haag.

In **hoofdstuk 4**, hebben wij de voorspellende validiteit van de cultuursensitieve diagnostische procedure (CASH-CS) vergeleken met de standaard diagnostische procedure (CASH). Bij gebrek aan een gouden standaard is een follow-up studie de meest aangewezen mogelijkheid om dit te onderzoeken. In dat kader hebben wij de stabiliteit van de diagnose en het beloop van de ziekte na 30 maanden bekeken. Alle Marokkaanse deelnemers en een gelijk aantal autochtone Nederlandse patiënten werd gevraagd om deel te nemen aan de follow-up studie. Deze patiënten zijn ongeveer 2,5 jaar na het eerste diagnostische gesprek geïnterviewd met het standaard diagnostische interview, de CASH-UP. Om niet alleen naar het subjectieve niveau van de symptomen te kijken zijn ook het psychosociale functioneren, de medicatie en de mogelijke opnameduur in acht genomen. Om de patiënten die in remissie waren niet als zonder diagnose te classificeren, is de follow-up diagnose gebaseerd op de combinatie van de uitkomst van het gestructureerde interview CASH-UP en de geregistreerde klinische informatie gedurende de gehele follow-up periode. Voor zover bekend dit is de eerste follow up studie die het belang van een systematische toepassing van de principes van een cultureel sensitieve diagnostische procedure beoordeelt en deze uitkomsten vergelijkt met de resultaten van een standaard diagnostische procedure bij een eerste psychose.
Diagnostische stabiliteit was volgens de CASH voor de autochtone Nederlanders hoog (92%) maar voor de Marokkaanse patiënten opvallend laag (27%), terwijl de diagnostische stabiliteit volgens de CASH-CS hoog was voor zowel de Marokkaanse (85%) als de autochtone Nederlandse patiënten (81%). Marokkaanse patiënten die volgens de CASH een diagnose schizofrenie hadden, hadden een significant betere prognose (meer sociale contacten, beter algemeen psychosociaal functioneren, minder gebruik van antipsychotica, minder positieve symptomen, minder onvrijwillige opnames en vaker klachten in remissie) in vergelijking met autochtone Nederlandse patiënten, terwijl de prognose van schizofrenie volgens de CASH-CS zeer vergelijkbaar was voor beide groepen patiënten. Wanneer wij de prognose Marokkaanse en Nederlandse patiënten die volgens beide interviews geen schizofrenie hadden vergeleken waren de verschillen in uitkomst tussen beide interviews zeer gering.

Deze bevindingen worden bevestigd wanneer wij de prognose na 30 maanden voor de beide groepen patiënten met een geen schizofrenie diagnose volgens CASH en CASH-CS met elkaar vergelijken. Marokkaanse patiënten hebben een enigszins betere prognose. Dit is opvallend omdat de groep Marokkaanse patiënten die volgens de CASH-CS geen schizofrenie diagnose hadden vele Marokkaanse patiënten includeerde die volgens de standaard CASH wel de diagnose schizofrenie hadden gekregen. Deze bevindingen laten zien dat cultuur sensitive diagnostiek bij Marokkaanse patiënten een betere stabiliteit en een betere vooruitlopende validiteit laat zien in vergelijking met een standaard diagnostische procedure. Nu deze bevindingen de validiteit van de CASH-CS voor Marokkaanse patiënten boven de CASH bevestigen, kan de validiteit van de standaard CASH onder Marokkaanse patiënten betwijfeld worden. Deze bevindingen bevestigen onze twijfels wat betreft de validiteit van de eerdere studies die een verhoogde incidentie van schizofrenie onder immigranten met het gebruik van standaard diagnostische procedures gerapporteerd hebben.

In **hoofdstuk 5** hebben wij het symptoomprofiel onder Marokkaanse patiënten en autochtone Nederlandse patiënten vergeleken aan de hand van het CASH en het CASH-CS interview. In deze exploratieve studie, waarin alle 26 Marokkaanse patiënten en evenveel autochtone Nederlandse patiënten werden geïncludeerd, hebben wij de patiënten twee keer geïnterviewd: één keer met CASH en één keer met CASH-CS. De interviewers van beide vragenlijsten waren blind voor de resultaten van de andere groep. De studie laat zien dat bij de Nederlandse patiënten het symptoomprofiel volgens CASH en de CASH-CS zeer vergelijkbaar is, terwijl het symptoomprofiel volgens de CASH en de CASH-CS bij de Marokkaanse patiënten heel verschillend is met meer depressie symptomen (+23%) en meer manische symptomen (+30%) en met minder wanen (-31%) en minder hallucinaties (-23%) wanneer de CASH-CS was gebruikt. Deze resultaten suggereren dat de eerder bij andere auteurs gerapporteerde hoge incidentie cijfers van schizofrenie onder Marokkanen in ieder geval gedeeltelijk het gevolg kunnen zijn van een fout negatieve diagnose van stemmingsstoornissen en van een fout positieve diagnose van psychotische stoornissen.

In **hoofdstuk 6** worden de bevindingen samengevat en geïntegreerd. De bevindingen van de uitgevoerde studies laten het belang zien van cultuur-specieke diagnostiek voor het doen van epidemiologisch onderzoek, maar ook voor de behandeling van patiënten. De bevindingen roepen ernstige vragen op ten aanzien van de geldigheid van de gerapporteerde hoge cijfers van schizofrenie onder immigranten in studies die gebruik hebben gemaakt

van niet gevalideerde, niet cultuur-sensitieve interviews. De bevindingen, geven ook aan dat er ernstige fouten gemaakt kunnen worden bij de diagnostiek en behandeling van niet-autochtone patiënten met psychische klachten, waardoor de prognose negatief kan worden beïnvloed. De resultaten van de hier gerapporteerde studies maken duidelijk hoe belangrijk het is om bij de diagnostiek en behandeling van patiënten rekening te houden met hun etnisch-culturele achtergrond. Hulpverleners zullen daarin getraind en begeleid moeten worden.

Dankwoord

In 2002 bezocht ik een congres waar de eerste resultaten van een incidentiestudie in Den Haag werden gepresenteerd. Het hoge percentage immigranten dat gediagnosticeerd werd met schizofrenie, schokte mij. Kort hierna hoorde ik bij het Riagg dat er mogelijk een vergelijkbaar onderzoek in Utrecht zou beginnen en de dag daarop vroeg Annechien Limburg of ik mogelijk interesse had om deze studie te beginnen. Daarna ging alles heel snel. Maar naarmate de kans om de AGIKO-plek te krijgen groter werd, namen mijn twijfels toe. Ik was nog niet zo lang in Nederland en wist lang niet hoe alles hier werkte. Nu zie ik hier met plezier op terug en ben ik blij dat ik heb doorgezet.

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Beste René, de data van dit onderzoek werden in het UMCU verzameld en ik ben deze studie in eerste instantie onder jouw begeleiding begonnen. Ik wil je bedanken voor je scherpe blik en ondersteuning vooral tijdens de dataverzameling. Deze opmerkingen hebben mij enorm geholpen om het nodige in het onderzoeksprotocol tijdig aan te passen en om het onderzoek zo correct mogelijk te laten verlopen. Dank voor dit alles.

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Curriculum Vitae

Tekleh Zandi is geboren op 11 september 1968 in Zanjan, Iran. Vanwege politieke activiteiten moest ze haar middelbare school verlaten om later vanuit huis alsnog haar diploma te halen. Om dezelfde redenen mocht ze in Iran niet verder studeren. De studie geneeskunde is zij begonnen aan de Hacettepe universiteit in Ankara, Turkije, en heeft zij in 2000 voltooid aan het Universitair Medisch Centrum Utrecht. Na twee jaar als AGNIO bij de Willem Arntz Hoeve in Den Dolder en het RIAGG in Utrecht gewerkt te hebben is zij in 2002 haar opleiding tot psychiater bij Altrecht in Utrecht begonnen (opleiders dr. J.M. Havenaar en later Prof.dr. R. Kupka). Tegelijk begon zij een epidemiologische studie naar de incidentie en het beloop van schizofrenie met aandacht voor transculturele diagnostiek bij immigranten (Marokkanen) bij Altrecht in samenwerking met het Universitair Medisch Centrum Utrecht. Vanaf 2008 werkt ze bij GGZ Centraal in Amersfoort. In eerste instantie bij de afdeling psychotische stoornissen (kliniek en ambulant) en later bij de afdeling sociale psychiatrie. Tekleh Zandi heeft verder korte tijd bij I-psy in Utrecht gewerkt en meer dan twee jaar als psychiater rapporteur bij het Pieter Baan Centrum. Sinds begin 2013 heeft ze voor één dag per week een eigen praktijk in Utrecht.
Tekleh woont met haar man Rombout Hijma en hun twee kinderen Aida en Damon in Zeist.

Appendices

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Letter to the Editors

Incidence of schizophrenia among Moroccan immigrants to the Netherlands

To the Editors,

With interest we read the report of a psychosis incidence study in the Dutch town of Utrecht (Zandi et al., 2010). The authors hypothesized that previous reports of an increased incidence of schizophrenia among Moroccan–Dutch people in the Netherlands were due to cross-cultural bias. They examined first-onset cases using a "culturally sensitive" version of the Comprehensive Assessment of Symptoms and History (CASH; Andreasen et al., 1992) and arrived at the conclusion that the first-contact incidence of schizophrenia among the Moroccan–Dutch was no longer significantly increased when this culturally sensitive instrument was applied. The purpose of this letter is to examine whether the authors have made a strong case.

The study procedures were as follows. Patients suspected of a first psychotic episode during the period May 1st 2002–May 1st 2004 were reported to a central office and interviewed twice: (1) academic psychiatrists (or residents) administered the standard Dutch version of the CASH and made a DSM-IV diagnosis; (2) the authors applied the culturally sensitive version of this instrument (CASH-CS), discussed all findings during a diagnostic meeting and made another DSM-IV diagnosis. The Relative Risks (RRs; Moroccan–Dutch versus Dutch nationals) based on the standard CASH turned out to be much higher than those based on the CASH-CS. Using information from the CASH-CS the RR of schizophrenic disorders (DSM-IV: schizophrenia, schizophrenifom disorder or schizo-affective disorder) dropped from 7.8 (95% CI 4.0–15.2) to 1.5 (0.5–4.3). The authors also observed that they could not replicate the high RR of 9.3 (95% CI 3.7–23.4) for second-generation Moroccans in The Hague (Selten et al., 2001), because not a single second-generation Moroccan was reported to the central office of the researchers. We wish to make the following comments.

Firstly, the previous epidemiological studies found an increased incidence or prevalence of schizophrenia among Moroccan–Dutch *males*, not among Moroccan–Dutch *females* (Brook & de Graaf, 1985; Selten and Sijben, 1994; Schrier et al., 2001; Selten et al., 2001; Veling et al., 2006). Since Zandi et al. reported a RR of schizophrenic disorders for Moroccan–Dutch males of 2.4 (95% CI 0.8–7.7), the 95% confidence interval of which includes the usually reported RR of about 4 to 5 for Moroccan–Dutch males, their finding is *not significantly different* from the results obtained previously. There is an interesting parallel with the sex difference in social achievement, because it is not uncommon that within the same Moroccan family the brothers are in prison and the sisters attend university (Selten et al., 2008).

Secondly, the claim of the authors "that every patient aged 15–54 who made contact with one of the mental health services in Utrecht for a suspected psychotic disorder was reported to a central office" is pretentious. This happens only in an ideal world. Since 1999 the Psychiatric Case Register-Mid Netherlands receives anonymized information on patients who attend any of the in- or out-patient facilities for mental health care in the town of Utrecht and its surroundings. During the 5-year period 2002–2006 *fourteen* second-generation Moroccan citizens of Utrecht (11 males and 3 females) were reported to the registry for a non-affective psychotic disorder (DSM-IV: schizophrenia, schizophreniform disorder, schizo-affective disorder, delusional disorder, brief psychotic disorder, psychotic disorder not otherwise specified). Since these patients were young and had received no psychiatric treatment during the period 1999–2001, they were likely to suffer from a first episode. Using this information and population denominators of Utrecht we arrived at an age-adjusted RR of 7.7 (95% CI 3.8–15.7) for second-generation Moroccan males and of 4.2 (1.1–15.5) for second-generation Moroccan females (details of analysis in Selten et al., submitted for publication). The possibility that the authors missed potential cases is further supported by the lower rate of psychotic disorders for Dutch nationals in Utrecht (1.4 per 10,000) than in The Hague (2.2 per 10,000; 95% CI 1.7–2.7 per 10,000; Selten et al., 2001).

We do not differ in opinion with the authors that knowledge of the cultural background is required for a proper interpretation of the patient's complaints. The apparent over-diagnosis of psychotic symptoms and under-diagnosis of depressive symptoms on the part of academic psychiatrists (or residents) may be explained in part by their failure to interview relatives (clearly illustrated by vignette 1) and to discuss findings during a diagnostic meeting. Both the interview with relatives and the diagnostic meeting were standard elements of the incidence study in The Hague (Selten et al., 2001; Veling et al., 2006).

We conclude (i) that Zandi et al. have failed to undermine the validity of the findings of an increased incidence of schizophrenia among Moroccan–Dutch males, and (ii) that their non-replication of the increased risk for second-generation Moroccan–Dutch is due to a failure to include them in their study.

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Letter to the Editor

Incidence of schizophrenia among Moroccan immigrants to the Netherlands. Response to letter written by Selten et al.

Dear Editors,

In a recent paper in Schizophrenia Research we conclude that first contact incidence of schizophrenia among Moroccans in the Netherlands is no longer significantly different from native Dutch inhabitants when a validated cultural sensitive diagnostic procedure is applied (Zandi et al., 2010). This finding raises serious doubts about the validity of the frequently reported increased incidence of schizophrenia in non-Western immigrants in countries like the Netherlands and Great Britain (e.g. Harrison et al., 1997; Van Os et al., 1996; Selten et al., 2001, Veling et al., 2006). In their letter to the editor, Selten et al. (2010) claim that our conclusions are based on invalid data, inaccurate collection procedures and misinterpretations of the findings, and that we have failed to undermine the validity of the repeatedly reported increased incidence of schizophrenia in Moroccans in the Netherlands. In this rebuttal we will refute their arguments.

First, Selten et al. argue that the point estimate of the Relative Risk (RR) of schizophrenic disorders based on the cultural sensitive version of the diagnostic interview for Moroccan versus Dutch males (RR = 2.4) is indeed smaller than the generally reported RRs of about 4 to 5, but that the 95% Confidence Interval (CI: 0.8–7.7) includes these generally reported RRs. We do not agree with the authors that this proves that our results are *not significantly different* from the results obtained in previous studies. Undoubtedly, the wide and overlapping confidence intervals found in all of these epidemiological studies, including theirs and ours, are the result of the small number of incident cases of schizophrenia. We appreciate Selten et al.'s attempt to down-play the findings of our study in this way, but they missed the main point of our study, which is that the use of culturally sensitive diagnostic procedure reduced the RR for schizophrenia among Moroccans compared to native Dutch inhabitants from 7.8 (95% C.I. 4.0–15.2) to 1.5 (0.5–4.3), and was no longer significantly different from the figure for native Dutch. Also, the authors fail to point out that the relative risk of 2.4 we found using this culturally sensitive method lies outside of the 95% CI of 3.2–8.4 for first generation Moroccan versus Dutch males reported by these authors (Veling et al. 2006).

Second, Selten et al. claim that the registration of "every patient aged 15–54 who made contact with one of the mental health services in Utrecht for a suspected psychotic disorder" by the central office of the study is pretentious and can "happen only in an ideal world". We agree that detection of all new cases of psychosis in this type of study is practically impossible, but it is unlikely that this would affect Moroccan patients more than native Dutch. Also, this equally applies to the studies from the Selten group, which used a similar method. More importantly, our study produced even higher incidence rates for first generation Moroccans than their studies, as long as the same culturally insensitive diagnostic methods were used. (Selten et al., 2001; Veling et al., 2006). These authors try to strengthen this argument by stating that missing Moroccan first episode schizophrenic patients and especially second generation, is the reason for our "non-replication of the increased risk for second-generation Moroccans". In order to prove this point, they obtained information from the Psychiatric Case Register (PCR) of Utrecht. During the 5-year period 2002–2006 they found 14 second-generation Moroccan citizens of Utrecht (11 males and 3 females) that were reported to the registry for a non-affective psychotic disorder. Without providing any additional information about in- and exclusion criteria for these patients they declare that "since these patients were young and had received no psychiatric treatment during the period 1999–2001, they were likely to suffer from a first episode of schizophrenia. We have scrutinized the data from the PCR for cases in the period of our study, i.e. May 1st 2002 to May 1st 2004. In this period, only *one* second-generation Moroccan patient suspected of a first psychotic episode was definitely registered in Utrecht and in *two* other cases it was undeterminable if they were really registered in the period of our study. Theoretically, it remains possible that we missed these patients. However, we did register *two* second-generation Moroccan patients at the central reporting office during this period, but we had to exclude them after the first screening. One had received psychiatric treatment for psychosis before in another province; the other patient was excluded because it was a case of substance induced psychosis. Assuming that these are overlapping groups of patients (two of the three), this shows again that PCR data are not a valid source for incidence studies of schizophrenia, because it uses unstandardised diagnostic methods, imperfect probability linkage of anonymised cases and crude in- and exclusion criteria. This argument should perhaps be extended to other incidence studies using PCRs (e.g. Selten and Sijben, 1994).

Finally and most importantly, we are happy to see that the authors underline the importance of knowledge of the cultural background for a proper interpretation of the patient's complaints. However, in their studies so far they

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applied ambivalent strategies. For example in the first period of The Hague study (1997–1999) psychiatrists who made the diagnosis were blind to ethnicity of the patients (Selten et al., 2001), whereas in the second period of this study (2000–2002) the psychiatrists were aware of the ethnicity of the patients, but did not specifically probe for relevant cultural background information as we did (Veling et al., 2006). Thus, in both periods of The Hague study, cultural aspects were not seriously taken into account in the diagnostic process itself, and therefore it comes as no surprise that the incidence rates between the two periods of the study were almost identical. This probably explains why they repeatedly found an increased incidence of psychosis and schizophrenia among Moroccans, whereas we did not (Zandi et al., 2010).

In conclusion, Selten et al. have failed to invalidate our findings. We strongly hope that – based on the outcome of our study – researchers as well as clinicians will appreciate the importance of culturally sensitive diagnostic methods in de diagnosis of psychosis and schizophrenia among Moroccans and other immigrants.

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