

## Schizophrenia outcome measures in the wider international community

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**Background** Outcome of schizophrenia has been described as favourable in low- and middle-income countries. Recently, researchers have questioned these findings.

**Aims** To examine the outcome studies carried out in different countries specifically looking at those from low- and middle-income countries.

**Methods** Long-term course and outcome studies in schizophrenia were reviewed.

**Results** A wide variety of outcome measures are used. The most frequent are clinical symptoms, hospitalisation and mortality (direct indicators), and social/occupational functioning, marriage, social support and burden of care (indirect indicators). Areas such as cognitive function, duration of untreated psychosis, quality of life and effect of medication have not been widely studied in low- and middle-income countries.

**Conclusions** The outcome of schizophrenia appears to be better in low- and middle-income countries. A host of sociocultural factors have been cited as contributing to this but future research should aim to understand this better outcome. There is a need for more culture-specific instruments to measure outcomes.

**Declaration of interest** None.

Schizophrenia may have a better outcome in low- and middle-income countries. The initial evidence for this came from the International Pilot Study of Schizophrenia (IPSS; World Health Organization, 1979) and was further strengthened by two subsequent studies, the Determinants of Outcome of Severe Mental Disorders (DoSMED; Jablensky *et al*, 1992) and the recently concluded International Study on Schizophrenia (ISoS; Harrison *et al*, 2001). A host of sociocultural factors have been cited as contributing to the better outcome in these countries, including lower expressed emotion, closely knit family structures and family interactions (Kulhara & Chakrabarti, 2001). However, there is little evidence for the beneficial influence of these factors. The World Health Organization (WHO) follow-up studies of the past 25 years have been unable to tease out the specific patterns and timing of cultural influences that determine a better prognosis in these countries. The strongly held belief in a better outcome in these countries has been questioned in recent times (Patel *et al*, 2006).

The ISoS study, coordinated by the WHO, addressed the outcome and related issues in a 15- to 25-year follow-up of 14 culturally diverse schizophrenia cohorts. Although the outcome results were consistently more favourable from low- and middle-income countries, there was marked heterogeneity across the centres (Hopper & Wanderling, 2000). Removing Hong Kong left three centres in this category from India (one in Madras and two in Chandigarh). It might be helpful to examine which cultural aspects of the Indian subcontinent contribute to an improved outcome in people with schizophrenia (Patel *et al*, 2006).

### DIMENSIONS OF OUTCOME MEASUREMENT

Outcome is a multidimensional construct consisting of several independent domains,

including clinical symptoms and their improvement, and social functioning, especially the ability to relate to people and performance at work (including employment, housework and tasks). Cognitive function, family burden and quality of life are other outcome measures. Outcome is also influenced by the course of schizophrenia. The possible contribution of factors to the good prognosis observed in low- and middle-income countries is shown in the Appendix.

### Clinical symptoms

The Present State Examination-9 (PSE-9; Wing *et al*, 1974) has been used as the measure of clinical symptoms at baseline and during follow-up in almost all long-term studies from low- and middle-income countries. The PSE-9 assesses 140 symptoms grouped into 36 syndromes and measures the presence of symptoms in the previous month. In a 20-year longitudinal study from India (Thara, 2004), all syndromes registered decline, although slowness, loss of interest, concentration and simple depression registered an increase over the second 10 years whereas positive symptoms showed little difference. In this cohort only 5 out of 61 patients (8%) were continuously ill. Using a similar methodology, 10-year clinical outcome was reported as favourable in three-quarters of the sample (Thara & Eaton, 1996).

Outcome was classified into broad categories in the DoSMED cross-cultural study (Jablensky *et al*, 1992). The outcome criteria used were: good, remitting course with full remission; poor, continuous/incomplete remission. A more recent long-term study from Singapore (Kua *et al*, 2003) described final outcome measures in similar broad domains – good, patient not receiving treatment, well and working; fair, patient not receiving treatment and not working, or receiving out-patient treatment and working; poor, patient receiving treatment and not working, or receiving in-patient treatment. This study included treatment, employment and hospitalisation as indicators of severity of clinical symptoms for patients with schizophrenia. Over two-thirds of patients had a good/fair outcome.

Measurement of positive or negative symptoms/syndromes has been used by most studies. However, neurocognitive symptoms were not properly covered in the outcome measures used. This domain

**Table 1** Important outcome studies from low- and middle-income countries<sup>1</sup>

Source	Study/ follow-up	Design	n at beginning/end	Instruments	Outcome, %
Thara <i>et al</i> (1994), India	Madras Longitudinal Study, 10-year follow-up	Prospective, three follow-up assessments at 2, 5 and 10 years	90/76	PSE, PPHS, IFS	Death, 11.84 No symptoms, 65 Good, 72.3 Psychotic, 22 (7% continuously since inclusion) Complete recovery, 14.5 Complete remission with one or more relapses, 48.7 Incomplete remission, 27.6
Thara (2004), India	Madras Longitudinal Study, 20-year follow-up	Prospective, four follow-up assessments at 2, 5, 10 and 20 years	90/61	PSE, PPHS, IFS (first 10 years), GAF	Asymptomatic at syndromal level, 59 Complete recovery, 8.2 Continuously ill, 8.2 Death, 17.7
Tirupati <i>et al</i> (2004), India	Untreated psychosis, 1-year follow-up	Prospective follow-up	49/49	PSE, PPHS	Good Clinical, 29 Social, 35 Occupational, 51 Global, 31
Kurihara <i>et al</i> (2000, 2005), Bali <sup>2</sup>	Treatment-naïve schizo- phrenia, 5- and 11-year follow-up	Prospective	59/51, 5 years 59/46, 11 years	PANSS, ESAS	Remission, 23.9 Partial remission, 19.6 Self-supportive, 39.1
Kua <i>et al</i> (2003), Singapore	20-year follow-up	Assessment at 5, 10, 15 and 20 years	402/216	Clinical interview on treatment and work status, no scales	Good/fair, 66 Working, 32
Lee <i>et al</i> (1998), Hong Kong	15-year follow-up	File review	100/70	PSE-9, DAS, LCS, PIRS-II, SFD, BRS	Recovered, 53 GAF score > 60, 71 Working, 74

PSE, Present State Examination; PPHS, Psychiatry and Personal History Schedule; IFS, Interim Follow-Up Schedule; GAF, Global Assessment of Functioning; PANSS, Positive and Negative Syndrome Scale; ESAS, Eguma's Social Adjustment Scale; DAS, Disability Assessment Schedule; LCS, Life Chart Schedule; PIRS, Psychological Impairment Rating Schedule; SFD, Schedule for the Deceased; BRS, Broad Rating Schedule.

1. Excluding World Health Organization multicentre studies.

2. 5-year outcome strongly predicted long-term outcome; minority needed maintenance medications.

has been receiving increased attention because of its association with functional recovery. Although there continues to be wide heterogeneity in cognitive functioning in individuals with schizophrenia, a number of recent studies from the West have suggested that cognitive deficits once established are relatively stable over time.

#### Acute psychosis debate

Several researchers have argued that many patients with acute psychosis might have been included in samples of people with schizophrenia from low- and middle-income countries (Kulhara & Chakrabarti, 2001). They argue that by including diagnostic criteria of 1 month's duration people with acute psychosis which remits

completely might have been included, contributing to good outcomes. Non-affective acute remitting psychoses are far more common in low- and middle-income countries (Susser & Wanderling, 1994). However, reanalysis of the data excluding patients with these psychoses did not change the results to any appreciable extent (Hopper & Wanderling, 2000). Indeed, such patients had slightly better outcomes in the high-income countries and excluding them increased the differences between high-income countries and India. Furthermore, other studies (Kulhara & Chandiramani, 1988) using more than one diagnostic definition and criteria for schizophrenia, also supported better outcome in low- and middle-income countries irrespective of diagnostic criteria.

#### Duration of untreated psychosis

Studies from the West have shown that the duration of untreated psychosis (DUP) is associated with poorer outcome, with the relationship being strongest in the initial months of psychosis (Drake *et al*, 2000). This is particularly relevant in low- and middle-income countries where a significant number of patients come late to treatment. Reasons for this include lack of awareness, a strong belief in magical or religious causes, poor accessibility of healthcare systems and lack of community care (Isaac *et al*, 1981; Padmavathi *et al*, 1998). A cross-cultural study on pathways to psychiatric care (Gater *et al*, 1991) replicated these findings. Most patients are brought for treatment after a significant delay from the onset of symptoms.

Out of 75 patients in India who were treatment naive and living with their family, 60% had a DUP of over 5 years and 36% over 12 years. Following treatment for 1 year, patients with a DUP of 5 years or less had shown good clinical outcome (Tirupati *et al*, 2004). All were treated with antipsychotics on an outpatient basis and none needed hospital admission. An encouraging observation was the notable treatment response despite many years of untreated illness. Short-term studies using score on the Positive and Negative Syndrome Scale (PANSS) as an outcome measure corroborated these findings (Philip *et al*, 2003).

The PSE-9, which is used in most studies, measures the presence of symptoms only for the past month, which is probably too brief for outcome assessment in a chronic illness such as schizophrenia. Moreover unanchored global judgements such as good, fair or poor are crude parameters. One method for maximising specificity and generalisability is the use of structured instruments for interviews, defining core symptom variables with clearly outlined operational criteria and incorporating relevant existing scales with established psychometric credentials (McGlashan *et al*, 1988).

This has been reflected in studies such as ISOs (Harrison *et al*, 2001), in which the PSE-9 has been supplemented in most cases by the Schedule for the Assessment of Negative Symptoms (SANS; Andreasen, 1983), the Schedule for Clinical Assessment in Neuropsychiatry (SCAN; World Health Organization, 1998), and the Scale for Assessment of Positive Symptoms (SAPS; Andreasen, 1984) for outcome measurement with respect to clinical symptoms (Petersen *et al*, 2005).

### Hospitalisation/treatment-seeking

Hospitalisation has been used as an outcome measure in several studies, generally as a proxy for acuteness of symptoms and functional disability (Burns, 2007, this supplement). In low- and middle-income countries, hospitalisation is more a reflection of policy and resource availability than an indication of need (Harrison *et al*, 2001). Many people with schizophrenia have never been treated or hospitalised, and assuming that they are asymptomatic or symptoms are not severe is unjustified (Isaac *et al*, 1981; Padmavathi *et al*, 1998). The lack of hospital beds and

alternative systems of 'residential care' that exist in high-income countries limits the use of hospitalisation as a reliable outcome measure. According to the World Health Organization 2005 figures (<http://globalatlas.who.int>), the median number of hospital beds per 10 000 population in low- and middle-income countries is around 0.2 (India, 0.25) whereas it is 7 in high-income Western countries (UK, 6; Switzerland, 13.20).

Social factors such as unemployment in males, family awareness of the nature of illness and family type are strongly related to treatment-seeking in low- and middle-income countries (Srinivasan *et al*, 2001). Gender, level of literacy and economic status appear to be unrelated. Surprisingly, more florid positive symptoms (such as delusions, hallucinations or aggressive behaviour) were not associated with seeking treatment or hospitalisation. However, self-neglect seems to lead to treatment; an unhygienic, unkempt person was more noticeable in public or to visitors to the house, and family embarrassment stimulated treatment-seeking for the patient.

The use of complementary medicines and consultations with traditional healers is widely acknowledged in low-income countries such as India (Raguram *et al*, 2002), but their impact, apart from a likely placebo effect, has not been adequately studied.

### Mortality

The mortality rate is often neglected in outcome studies, but recently high mortality rates have been reported from low- and middle-income countries (Patel *et al*, 2006). In schizophrenia outcome studies spanning 15–25 years, the proportion of patients who died or were lost to follow-up ranged from 23% in Chennai to over 50% in Chandigarh and Agra (Harrison *et al*, 2001). Thara's (2004) study found a mortality rate of 10% at 10 years, which increased to 17% at 20 years. The mean age at death was 34.2 years, which is well below the national average life span of 60.5 years. A much higher mortality of 47% was reported in a 15-year follow-up study of patients from North India with early poor outcome. Out of 15 patients with a poor course of schizophrenia during the first 2 years, 7 had died before completion of follow-up (Mojtabai *et al*, 2001). A high mortality rate of over 10% has been reported from Ethiopia during follow-up

periods of 1–4 years (Kebede *et al*, 2005). Suicide accounted for nearly half of the deaths of those under 35 years.

### Social functioning

In low- and middle-income countries schizophrenia has been shown to have better outcome in terms of social and occupational functioning; social functioning more than clinical status influences the functional competence of people with schizophrenia (Verghese *et al*, 1990; Harrison *et al*, 2001).

The development of measures for the assessment of impaired social functioning lags behind clinical rating. This relative neglect of a standardised assessment of social adaptation may reflect an assumption that symptomatology is closely tied to impairment in social functioning. This pattern is repeated in research in low- and middle-income countries. Most social outcome measures are derived from scales measuring psychopathology (i.e. the PSE) or from the course of the illness (e.g. the Psychiatric and Personal History Schedule, PPHS; Verghese *et al*, 1985) (Srinivasan *et al*, 2001; Thara, 2004). Social functioning outcomes that were measured from PSE items could not distinguish social impairment from prevailing neurotic or psychotic conditions. The PPHS rates the availability and frequency of a patient's social contact during 1 month preceding evaluation. These items refer to living in a household, close friends, casual friends and the presence or absence of social activity groups. Few studies have used locally derived scales (e.g. Eguma's Social Adjustment Scale; Kurihara *et al*, 2000, 2005) to assess social and vocational outcome.

Several measures have been developed and validated for use in these populations. Scales from low- and middle-income countries include the Schedule for the Assessment of Psychiatric Disability (SAPD; Thara *et al*, 1988) and the SCARF Social Functioning Index (Padmavathi *et al*, 1995); and from high-income countries the Groningen Social Disability Schedule (GSDS; Wiersma *et al*, 1988), the Life Skill Profile (LSP; Rosen *et al*, 1989), the Social Function Scale (SFS; Birchwood *et al*, 1990), the Social Adaptive Functioning Evaluation (SAFE; Harvey *et al*, 1997), and the Independent Living Scale Survey (ILSS; Wallace *et al*, 2000). For most cross-cultural studies the Disability Assessment Schedule (World Health Organization, 2000) and

Global Assessment of Functioning (GAF; American Psychiatric Association, 1987) have been used.

Some measures of social functioning include items reflecting clinical symptoms which need to be distinguished from those of functioning. In the West, many patients reside in assisted living facilities whereas in low- and middle-income countries the majority live in the community and are cared for by family members. This important component has not been adequately represented in instruments for assessment of social functioning (Saraswat *et al*, 2006).

Recently the Social Occupational Functioning Scale (SOFS) has been developed and validated in India, and has been found suitable for use in multiple settings such as out-patient clinics, facilities and rehabilitation centres (Saraswat *et al*, 2006). A younger age at onset but not gender was associated with greater impairment in social functioning. Although none of the items was related to overall psychopathology, the item scores were correlated with positive and negative symptoms (Saraswat *et al*, 2006).

A neurocognitive study from India showed a lack of association of cognitive deficits with social functioning, employment and work performance (Srinivasan & Tirupati, 2005). At the same time there is an association of negative symptoms with these parameters. Measures of social functioning (i.e. communication and interest) are strongly associated with work functioning.

Currently there are few studies using social functional outcome measures from low- and middle-income countries. Social functioning is an important domain and, although sometimes cumbersome to measure, urgently needs to be incorporated as a regular outcome measure.

## Employment

People with schizophrenia in low- and middle-income countries are more likely to be employed than their Western counterparts. Srinivasan & Thara (1997) found an annual rate of employment of 63–73% in the first 10 years of follow-up in a cohort of 90 people with first-episode schizophrenia. Moreover, among untreated Indian people with schizophrenia almost one-third were employed (Padmavathi *et al*, 1998). Moreover, almost half obtained employment within a year of starting treatment with antipsychotics (Srinivasan *et al*, 2001). Generally, high employment

rates (up to 75%) have been found in India (Thara, 2004). A similar trend is described among Chinese patients; nearly half were able to work after 5, 10 and 15 years of follow-up (Tsoi & Wong, 1991). These rates of employment are markedly higher than those in similar populations in high-income countries (Mueser *et al*, 2001). The employment rate in the UK over the past 20 years among people with schizophrenia ranges from 4 to 31%, with most Western studies reporting a rate of between 10 and 20% (Marwaha & Johnson, 2004).

Workplace colleagues are found to be generally supportive in low- and middle-income countries (Srinivasan & Tirupati, 2005). They rarely make an issue of the unusual behaviour of the person with schizophrenia, in contrast to the West where a 'hostile social climate' may confront persons with schizophrenia, whose diagnosis denies them access to employment (Marwaha & Johnson, 2004). After treatment for an episode of illness their return to work is often accompanied by criticism and a denial of their skills.

This discrepancy derives in part from the easy availability of work in informal sectors, differences in socio-economic status and economic pressure owing to a lack of disability benefits in low- and middle-income countries. Employment is a critical factor for perceived recovery from illness in countries where families are reliant on the members for support. Future outcome studies need to incorporate in-depth analysis of these factors (i.e. type of job, sectors, performance, financial gain, absenteeism, etc.) to understand such significant variations.

## Marriage

Marriage requires certain social abilities to be successful. In countries such as India, marriage is a once-in-a-lifetime event and is associated with a high degree of social approval. The sociocultural factors determining marriage and its maintenance are vastly different from those in Western societies.

Marital state can be considered an outcome measure, as its maintenance depends on stability and functioning of both partners. Schizophrenia manifests maximally at a marriageable age (i.e. around the 20s). Most studies from the West have reported low rates of marriage for people with schizophrenia (Nanko & Moridaria, 1993; Hutchinson *et al*, 1999). In contrast, a 10-year follow-up study from India found a high marital rate of 70% (Thara &

Eaton, 1996). Good marital outcome in terms of marrying and maintaining the marriage was associated with good overall outcome in people with schizophrenia. Similarly, good marital outcome is related to a decrease in symptoms and a lower relapse rate.

There are conflicting reports on marital status and outcome as few follow-up studies have studied this in detail. A few studies found that being married favours a good outcome and others found no such relationship (Thara *et al*, 2003a). Outcome when schizophrenia develops after marriage, or in those who marry without disclosing their illness (which is common in low- and middle-income countries), needs further study.

Patients whose marriages have broken down, in addition to the stress of their mental illness, face hostility from family members and rejection by society. This can be a significant contributing factor to outcome in traditional societies (Thara *et al*, 2003a). In a qualitative study of 75 divorced/separated women with mental illness (57% of whom had developed their illness after marriage), Thara *et al* (2003a) found that many did not get any maintenance from their husbands and were fully dependent on their parents for both social and financial security. They initially felt helpless and lost, but most ultimately reconciled themselves to their fate and were pessimistic about the future. However, few had contemplated suicide. Concerns of being a burden to their aged parents, and hostile criticism from parents and siblings further reinforced their plight. In the current era of rapid globalisation, the effects of diminishing social support and the increasing prevalence of the nuclear family warrant close examination of the effects of these social changes on outcome.

## Social/family support

Social support as a predictor of outcome in low- and middle-income countries has attracted considerable attention. Recent studies propose that supportive and favourable attitudes among family members and the community contribute to the improved outcomes (Kurihara *et al*, 2000, 2005). The mean time spent in hospital by people with schizophrenia is approximately a fifth in Bali compared with Tokyo (Kurihara *et al*, 2000). Studies from Asian countries showed that less than 10% were hospitalised during follow-up, suggesting high levels of family involvement in patient care



(Ganev *et al*, 1998). It is suggested that social support is increased for both patients and caregivers from the extended family. This minimises the damaging effects of the illness and improves outcome.

Migration, urbanisation, changes in family structure and social support networks, plus the increase in economic insecurity and widening social inequalities which are evident in low- and middle-income countries will change the social support available for people with schizophrenia and influence their outcome (Patel *et al*, 2006).

### Illness beliefs

Research from low- and middle-income countries consistently shows that there is a significant delay in seeking treatment for people with schizophrenia. Misconceptions of illness, superstition and ignorance have been proposed as reasons. However, recent studies have shown that very few people still named supernatural factors alone as a cause of schizophrenia (Srinivasan & Thara, 2001). In a study of Indian patients (Srinivasan & Thara, 2001), supernatural cause was named by only 12% of families with a member with schizophrenia.

### Burden of care

Although the overall burden of care might be comparable across cultures, there are different patterns reflecting different socio-cultural factors. The issue is particularly relevant in low- and middle-income countries where the majority of patients stay with their caregivers. Pai & Kapur (1982) developed a semi-structured instrument covering six broad areas of burden (financial, family routine, leisure, interaction, effect on physical health and effect on mental health). They found that caregiver burden decreases with a reduction in the patient's symptoms and improving drug adherence. Reduction of family burden is associated with better outcome and social functioning (Pai & Kapur, 1982). The Burden Assessment Schedule (BASS; Thara *et al*, 1988), which was developed and standardised in India, also indicated significant burden among caregivers, including inability to care for others, unpredictable behaviour of patients and dissatisfaction with the help from healthcare professionals (Thara *et al*, 2003b). Some family members have considered leaving their ill relatives in psychiatric hospitals for long-term institutionalisation.

### Substance misuse

Comorbid substance misuse in schizophrenia has been described as a high-risk factor for poor outcomes, including treatment non-adherence, relapse, rehospitalisation, violence, victimisation, criminal justice involvement, HIV and hepatitis C (Swartz *et al*, 2006). Estimates of the prevalence of substance use disorders are up to 70%, depending on diagnostic assessment methods. Comorbid substance misuse (nicotine excluded) has been reported in about half of people with schizophrenia in the USA (Regier *et al*, 1990).

There are few epidemiological studies from low- and middle-income countries on the prevalence of substance misuse in the general population, and even fewer on prevalence among people with schizophrenia. A study in a psychiatric hospital showed that the prevalence of alcohol disorders among patients with severe mental disorders was much lower than in the general population (Carey *et al*, 2003). An out-patient study in Chennai showed that only 38% of males with schizophrenia were current smokers, which was not significantly different from the general population (Srinivasan & Thara, 2002). Srinivasan & Thara (2002) have argued that comorbidity with nicotine use is not entirely biological; 'culture' plays a major determinant role.

Substance misuse may thus be an important cultural factor among a host of others that may mediate the course and outcome of schizophrenia in low- and middle-income countries.

### CONCLUSIONS

Low- and middle-income countries are characterised by a poorly organised healthcare sector, limited access to psychiatrists and longer duration of untreated psychosis. Yet the outcome of schizophrenia appears to be better. What has contributed to the better outcome in these countries is difficult to say. Prevailing cultural factors and the nature of care and support might in part contribute to outcome. Factors such as the role of family and caregivers need further study as they play a vital and dynamic role in the care and rehabilitation of people with schizophrenia in low- and middle-income countries. The measures for diagnosis and assessment of outcome used in Western countries might not be suitable. A simple example is that translations of measuring instruments are often unreliable. For any

multicentre research, money, manpower and technical expertise are essential, and these have always been scarce in low- and middle-income countries, especially for mental health. This is one of the reasons for the few studies on outcome in these countries. In the majority of these studies, the various outcomes were not studied using standardised and culturally appropriate instruments. Longitudinal studies using parameters such as neurocognitive function and quality of life are almost non-existent. Most studies are hospital based and there is a need for well-designed community-based outcome studies in these countries. India, like many other low- and middle-income countries, represents a society in transition. Whether the current sociocultural patterns associated with good outcome will themselves change and in turn alter the outcome of schizophrenia needs to be examined through prospective studies.

### APPENDIX

#### Factors apparently contributing to good prognosis of schizophrenia in low- and middle-income countries

##### *Established*

Less expressed emotion  
Good social support  
Tolerance of odd behaviour by society and family  
Marriage

##### *Doubtful*

Less industrialisation and urbanisation  
Early death of those with bad outcome  
Increased prevalence of acute psychosis

##### *Needs to be studied*

Comorbid substance use  
Duration of untreated psychosis  
Pharmacological interventions

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