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ARE THE OUTCOMES OF PSYCHOTIC ILLNESS MORE FAVOURABLE IN DEVELOPING COUNTRIES? A LITERATURE REVIEW

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Abstract
This paper reviews evidence for and against one of the most surprising hypotheses to emerge from international research into the outcomes of schizophrenia and related disorders: that recovery rates are generally more favourable in developing countries when compared with the developed world. Support for this hypothesis has emerged from a variety of international longitudinal studies, most notably a series of large-scale multi-country investigations in this field by the World Health Organization conducted over three decades. Relatively lower stress and greater social support in low- and middle-income nations have generally been proposed as explanatory factors for such findings. However, a number of researchers have seriously questioned the interpretation of the data showing more favourable outcomes. Such critics point to methodological issues that often limit the validity of cross-cultural comparisons, and argue that the wider body of research from developing countries (still comparatively small compared with that from industrialised settings) actually shows highly variable outcomes rather than favourable ones. Those on both sides of this debate advocate the need for morestudies with rigorous research designs in developing country settings in order to address gaps in the current literature and shed further light on this topic.

Background: Longitudinal Outcomes of Schizophrenia and Related Disorders

Whereas schizophrenia was previously regarded as an illness with an inevitably poor course, longitudinal studies have found that at least a substantial minority of patients do in fact recover [1-3]. In one of the largest meta-analyses on the subject, Hegarty and colleagues [4] analysed 320 studies conducted between 1895 and 1992 and reported that 40% of patients "improved" after a mean follow-up period of approximately six years. However, these findings can only be regarded tentatively due to the wide methodological variability of the studies included. Moreover, a significant issue that has been identified in the majority of research conducted before the past two decades is its use of prevalent cohorts, consisting of patients with different illness durations and dominated by people with chronically-recurring psychosis [5]. Thus, in more recent decades, longitudinal studies using incident samples of people experiencing their first episode of psychosis have emerged [6]. A systematic review of 37 such studies by Menezes and colleagues [5] confirmed the hypothesis that the outcomes of first-episode psychosis are more favourable than those previously reported. However, the researchers again stressed the need for caution in interpretation of their findings due to the highly variable methodologies used in the studies reviewed, including a lack of standard criteria for defining outcome.

A number of recently published first-episode psychosis studies with short to medium follow-up periods have employed very similar standardised operational definitions of outcomeand are thus

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better suited for comparison. A selection of these can be seen in Table 1. They appear to show that a highly variable proportion of patients achievedeither symptomatic remission (37-60%) or functional remission (26-45%) at follow-up [6-9]. A smaller proportion of individuals - 14-24% - met combined recovery criteria in the same selected studies, i.e. both symptomatic and functional remission sustained for two years. However, while these figures may appear low, they must be interpreted in the context of the stringency of the outcome definitions applied.

Table 1. Short and medium-term outcomes of first-episode psychosis from selected studies applying standardised operational definitions of remission and recovery [a]

Study	**Follow up** (years)	**Symptomatic Remission** (mild or better symptoms for 6 months)	**Functional Remission** (adequate psychosocial functioning for 6 months)	**Recovery** (combined remission for 2 years)
Robinson et al 2004	5	47%	26%	14%
Lambert et al 2008	3	60%	45%	17%
Wunderink et al 2009	2	52%	26%	19%
Henry et al 2009	7	37% [b]	31% [b]	24% [b]

a. Each study used definitions based on criteria defined by the Remission in Schizophrenia Working Group (RSWG) and Liberman et al (10).

b. Time criteria (6 months or 24 months) were not applied to definitions of remission and recovery respectively

Unfortunately, most studies with a long-term follow-up period (15 years or more) have not applied standardised outcome definitions. However, notwithstanding this limitation, they have reinforced the picture of heterogeneous rather than inevitably poor outcomes [1, 11-13]. The proportion of patients achieving broadly defined good long-term outcomes ranges from 36% to 77% [11], with a modal value of approximately 50% [1]. Findings indicate significant variability in illness course not only across outcome domains (e.g. symptoms, social roles), but also between individuals and geographic regions. This was clearly demonstrated by the World Health Organization's International Study of Schizophrenia (ISoS), which used samples from countries in both the developed and developing world followed up over at least 15 years [14]. Overall, they found rates of recovery within the range of other long-term studies. However, one remarkable finding was that developing country cohorts generally showed a more favourable course of illness than those in developed countries.

Evidence for the hypothesis of more favourable outcomes in developing countries

WHO Research

The WHO's aforementioned International Study of Schizophrenia (ISoS) provides the most notable evidence for the hypothesis that the course and outcome of psychotic illness may be better in low- and middle-income countries (LAMIC) [14, 15]. IsoS pooled together the results of several previous large research projects: two multi-country WHO studies featuring incident samples (the Determinants of Outcome of Severe Mental Disorder (DOSMeD) and the Reduction and Assessment of Severe Mental Disorders (RAPyD), one older multi-country study with a prevalent cohort (the International Pilot Study of Schizophrenia (IPSS), and three additional single-country studies. The research followed large samples of individuals (totalling 1633 subjects for ISOS) in 12 countries using standardised assessment instruments designed to be applicable across cultures. Results consistently showed that the proportion of individuals achieving a good outcome in terms of symptoms and functioning at short- and long-term follow-ups were significantly higher in developing countries such as India and Nigeria than in more developed nations such as the USA and Ireland. For example, in the DOSMeD 10-country study, Jablensky and colleagues [16] found, at two-year follow-up, a mean of 37% of

patients in developing countries were no longer experiencing symptoms, compared with 15% of patients in the developed countries sample. While 43% of those in developing countries were functioning at an unimpaired level in the community, a significantly lower proportion (32%) of their developed world counterparts were doing as well. Notably, the WHO studies found that while outcomes were on average better in developing centres, they were by no means uniformly so at all sites and for all variables [15, 17]. There was considerable variation both within and between countries, consistent with the international literature. Nevertheless, the WHO authors argue their research provides a strong case for the powerful influence on schizophrenia outcomes of a factor that can be referred to as 'culture'.

Further Evidence

Evidence supporting the hypothesis of more favourable outcomes in developing countries extends beyond the WHO research. For example, Menezes and colleagues' (5) systematic review of first-episode psychosis studies (see above) found that patients with a developing country of origin were more likely to achieve a good outcome. (The 15% of their sample that were from developing countries included the DOSMeD cohort but also those derived from other studies.) Haro and colleagues [18], in a recent prevalent-cohort study of outpatients from 37 countries, found support for the hypothesis at least in terms of clinical remission rates. These rates were higher on average in the study's Asian, Latin American and African cohorts, compared with those located in Europe. (Functional remission rates, however, showed a different pattern.) In a recent consideration of the better outcomes hypothesis, Kulhara and colleagues [19] concluded in favour of the proposition after conducting a widespread review of research from low-, middle- and high-income countries, also including the WHO work. The authors acknowledge the difficulties inherent in conducting cross-cultural research, pointing out the questionable validity of certain widely-used outcome measures. For example, occupational status will be influenced by environmental factors such as the nature of a country's economy and its general unemployment rate. Similarly, hospitalisation rates are unlikely to accurately reflect clinical status as they will be significantly affected by a country's resources, mental health system, legislative environment and other local factors. Nevertheless, in weighing up the evidence, these authors still concluded that:

a reasonably consistent finding across various foreign, cross-cultural and Indian studies, barring a few, is that the developing countries have a larger proportion of patients (50-60%) with a good outcome and lesser percentage with a worse outcome compared to developed countries at 2-year and 5-year follow-up (p. 61).

Other non-WHO research specifically from Asian low- and middle-income countries that has provided evidence for the hypothesis of better outcomes in those countries includes studies conducted in India [20-22], Hong Kong [23] and Indonesia [24].

Why Better Outcomes?

Relatively lower stress and greater social support in developing countries have generally been hypothesised to be behind such findings [25-27]. Researchers have postulated that traditional cultures may better facilitate recovery from schizophrenia due to factors including the informal nature of developing economies, the degree of support offered by traditional family structures, and the specific ways in which some traditional belief systemsinterpret mental illness.

Informal economies

Greater opportunities for individuals with schizophrenia to occupy valued social roles in agrarian economies may promote recovery, including through less demanding, flexible work roles that can accommodate disability [3, 28]. Informal economies in places such as rural China and India may offer more opportunities for patients with schizophrenia to maintain or regain their social and occupational functioning through jobs that are less organised and relatively easier to perform such as street vendors, shop assistants, individual farmers and domestic help [19, 29].

For example, in rural China, Ran (2001) found that more than three-quarters of people with schizophrenia who had never been treated were engaged in some form of employment such as housework or farm work, including those with significant psychotic symptoms. Thus, rural developing economies appear to offer a greater variety of tasks and competencies that are socially valued and accessible to people with a disability at their current level of functioning [30, 31]. Moreover, deterioration in social and occupational skills and functioning may be slowed, halted or reversed through patients being able to engage in productive work. Another factor may be that developing economies place significant economic pressure on those with psychotic disorders to earn money and contribute to family income [29]. In welfare states, disability payments reduce the necessity and potentially also the motivation to find employment. Thus, as Hopper and Wanderling [30] express it: "tightly strapped circumstances and flexible means of addressing them may provide therapeutic benefits forgone under circumstances of enforced supported dependency."

Family relationships

The family relationships that traditionally exist in developing countries may promote recovery more than those in industrialised nations in a number of ways. Traditional extended family structures may reduce the burden of illness on the individual and their immediate care givers simply via the greater availability of familial resources [26]. In addition, families in India and some other developing countries are generally highly involved in treatment and maintain a significant amount of control over the process through taking on roles that would be filled by professionals in developed nations [32]. This includes in regard to hospitalisations, during which family members often stay with patients and take on basic nursing tasks, meaning that patients effectively remain socially integrated in their family settings. Cultural attitudes towards the care giver role may also play a role, as indicated by Ohaeri and colleagues [33] findings in a Nigerian setting that family members generally feel positive about their caring role and that the task of caring appears to strengthen family emotional ties. Another factor often cited with regard to cross-cultural differences in family relationships is the construct of 'expressed emotion', which refers to attitudes and expressions of criticism, hostility or over-involvement by family members towards an individual with schizophrenia [34, 35]. Studies applied in a variety of cultural and clinical populations have consistently found one or more of these domains to be related to illness relapse. Researchers from developing country cohorts have reported lower levels of expressed emotion and proposed this to be a factor contributing to better patient outcomes. [36, 37]. The lower levels of criticism and lower demands on patients may result from the reduced burden on family carers due to extended kinship ties [26].

Belief systems and stigma

Researchers have reported that the interpretation of mental illness provided by some traditional cultural belief systems possibly enable better coping than modern medical perspectives and result in less stigma towards people with psychotic disorders [26, 31]. Rather than viewing psychiatric illnesses as a problem with the individual, traditional societies often externalise their causes, viewing them as physical and/or supernatural. This may provide a basis for reduced blame, rejection and stigma both from the self and others. Warner [31] details a number of recorded examples of traditional societies in South America, Africa and Asia in which psychotic symptoms are generally attributed to supernatural causes, apparently resulting in more tolerant social attitudes and less rejection. (However Lin and Kleinman [26] point out that Western societies can also differ considerably in attitudes towards schizophrenia and its prognosis, and that some non-Western societies such as China exhibit high levels of stigma towards people with the illness and their families.)

Questioning the findings of better outcomes

However, a number of researchers have strongly questioned the hypothesis of better outcomes in developing countries and argued

the need for further research [38-40]. Edgerton and Cohen [41] pointed out that the five centres featured in the DOSMeD study could not be regarded as representative of the developing world. Subsequently, Cohen, Patel, Thara and Gureje [38] reviewed data from 23 longitudinal studies in 11 low- and middle-income countries, revealing highly variable outcomes and what they argued was a more complex picture than suggested by the WHO studies. Clinical and/or social outcomes were found to be good for the cohorts studied in some countries such as India and Indonesia, but poorer in others such as China, Brazil and Ethiopia. The authors also highlight the finding that people with schizophrenia generally appeared to have poorer outcomes when social outcome indicators were analysed in the context of a particular country's general population data and sociocultural norms. For example, in terms of marriage and divorce rates, individuals with schizophrenia had significantly better outcomes than those in the Western world but were substantially worse than those of the general populations in their own countries. However, this review by Cohen and colleagues did not include a comparison group from developed countries and therefore could not draw conclusions about any outcome differences between the two [3, 17]. Furthermore, this review was dominated by prevalent-cohort studies with highly variable methodologies [3, 42]. One strength of the WHO research compared with many other developing country studies is its use of incident cohorts and standard methodologies across all research sites.

Methodological issues

Nevertheless, the methods employed by the WHO in their schizophrenia research have still faced significant questions in the literature. For example, Burns [39] expressed the view that their case-finding methods may have missed a significant number of ill individuals in the developing country sites. In LAMI countries, acutely psychotic and socially disruptive patients are far more likely to access formal health services than poor prognosis individuals with an illness characterised by negative symptoms and insidious onset, due to the context of resource scarcity. The latter therefore may be underrepresented in research cohorts, skewing findings to more favourable outcomes. A counter argument is that the DOSMeD study recruited participants actively via non-medical agencies such as police and traditional healers, and moreover conducted repeated "leakage" checks that showed only a very small proportion of all incident cases in each geographic area were missed [17]. Furthermore, Hopper and Wanderling [30] examined the WHO data for other potential sources of sampling bias, including differential loss to follow-up, selective outcome measuresand diagnostic ambiguities, concluding that their outcome findings were not accounted for by any of these.

Yet, the WHO research methodologies inevitably do have significant limitations, as acknowledged by the researchers themselves, particularly with respect to assessments of social functioning. In relation to their ISOS research, Hopper and colleagues [15] wrote that some of their measures were "crude at best and could be misleading". As an example, they cite the proportion of patients who were recorded as living independently in the community versus in institutions. Further investigation conducted into subjects from selected research sites including China and India revealed that while three-quarters of individuals were reported as living with family, approximately 40% of these were being maintained in institution-like conditions at least some of the time. Similarly, although rate of medication usage atfollow-up was used as an outcome measure in the DOSMeD study, this too is likely to be subject to local environmental factors and therefore dubious as a comparative indicator of illness severity.

Further Questions

Beyond these methodological issues, other questions have also been raised in relation to the hypothesis of higher recovery rates in LAMI countries. The idea that extended family support and relatively lower levels of stigma in such countries leads to better outcomes has been questioned [38, 39]. A review of Asian

research found high levels of stigma and negative stereotyping of people with schizophrenia, although expressed somewhat differently due to the collectivist nature of Asian cultures [43]. This stigma was reported as a risk factor for families abandoning members with a mental illness or subjecting them to harsh criticism and hostility [44, 45].

On another tack, Burns [39] suggests that underlying prejudices and a political agenda may lie behind the better outcomes hypothesis. Such beliefs may, if unconsciously, portray developing nations as simple and unsophisticated "paradises for…optimal recovery", thus reinforcing the sophistication and dominance of developed cultures. The political dimension of this topic can also be seen in the concern expressed by Dias [46], who contends that uncritical acceptance of the hypothesis may lead to poor health care practices, even denial of treatment, if favourable outcomes are attributed to the decreased welfare available in developing countries. (Countering this, Kulhara [47] points out that believing an illness always has a poor outcome may also have negative consequences for treatment seeking and provision.) Critics of the better outcomes hypothesis further support their perspective by citing several factors in LAMI countries that are likely to promote poor mental health, including: the high levels of poverty, income inequality and violence; poor availability of mental health services, specialists, legislation and education; and reports of severe human rights abuses within psychiatric facilities [39]. Furthermore, social changes in the developing world associated with globalisation and economic change over recent decades may have altered the trajectory of schizophrenia since the time the WHO studies were conducted. WHO researchers Jablensky and Sartorius [17] agree that this potential deterioration of support systems should be of great concern, as should the inadequacy of mental health systems in low-income countries. However, they stand by their existing views regarding the influence of culture on outcomes, stating: "(t)he sobering experience of high rates of chronic disability and dependency associated with schizophrenia in high-income countries, despite access to costly biomedical treatment, suggests that something essential to recovery is missing in the social fabric"(p.254). Thus, debate around the hypothesis of better outcomes continues.

Conclusion

While recent research appears to show that the outcomes of psychotic illnesses such as schizophrenia are generally more favourable than previously believed, the question of whether recovery rates are more favourable in the developing world remains hotly debated. Discussion of this topic is highly limited by a lack of rigorous studies conducted in low- and middle-income countries. Most existing studies have not employed consistent, up-to-date methodologies that facilitate cross-study comparisons. Even the most rigorous, such as the WHO's large-scale examination of this topic, face significant limitations including in terms of the number of LAMI sites included and the sophistication of functional measures. The complexity of conducting longitudinal research on the outcomes of psychotic illness, particularly in a cross-cultural context, is a significant barrier to examining the hypothesis of better outcomes. Both sides of the debate advocate the need for more rigorous studies in developing nations that can provide evidence regarding the course and outcomes of psychotic disorders and the sociocultural factors hypothesised to impact upon them.

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