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## Post-print version

### Global mental health and schizophrenia

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## **Abstract**

### **Purpose of review**

The aim was to synthesise recent evidence on schizophrenia illness experience and outcomes and models of care in low and middle-income countries (LMIC).

### **Recent findings**

There is a plurality of explanatory models for psychosis and increasing evidence that context influences experiences of stigma. People with schizophrenia in LMIC are vulnerable to food insecurity, violence and physical health problems, in addition to unmet needs for mental healthcare. Family support may help to improve outcomes if present, but caregivers may be overwhelmed by the challenges faced. Despite efforts to increase availability, evidence-based care remains inaccessible to many people with schizophrenia. Non-randomised evaluations in South Africa and Mexico indicate that psychosocial support groups for people with schizophrenia and caregivers may be acceptable and useful. Randomised controlled trials in Pakistan and China show that culturally-adapted cognitive-behavioural therapy can reduce symptom severity. There is emerging evidence that traditional and alternative medicine, such as Tai Chi, may be beneficial, but to date most studies are of low quality. The challenges of biomedical-traditional provider collaborations have been highlighted. Evaluations of integrated mental health care in primary care are underway and promise to provide vital information about how to scale-up quality care.

### **Summary**

Acceptable and effective responses to schizophrenia in LMIC should be cognisant of both cultural context and universal concerns. Efforts to enhance the quality of family support should be central to models of care.

## **Key words**

Schizophrenia, low and middle-income countries, global mental health, mental health Gap Action Programme

## **Introduction**

The field of global mental health has emerged in the last decade, with the primary agenda of scaling up services for people with mental health problems, especially in low and middle-income countries (LMIC) [1]. Schizophrenia has been identified as a priority disorder due to its association with high levels of disability and premature mortality, human rights violations and loss of productivity [2]. There is consensus that in both LMIC and high-income countries (HIC), optimal care for schizophrenia comprises 1) a combination of anti-psychotic medication and psychosocial support and 2) community-based care with access to inpatient care for acute crises [2]. However, a severe shortage of mental health specialists means that an estimated 69% of people with schizophrenia in LMIC do not access any evidence-based care; referred to as the ‘treatment gap’ [3]. Family members are typically the main source of support. Accordingly, efforts to scale up care focus on delivery by trained non-specialists, an approach known as task-sharing. The World Health Organization (WHO) mental health Gap Action Programme (mhGAP) represents the most widely disseminated model of task-sharing for the treatment of schizophrenia, and other priority mental disorders, in primary care [4]. Given their wide availability and acceptability for the treatment of mental health problems, collaboration with traditional and faith practitioners is also proposed as a promising approach [5].

A refined understanding of explanatory models, risk factors, illness course, and social impact of schizophrenia is paramount for the development of acceptable and effective interventions to address the treatment gap. The notion that people with schizophrenia in LMIC experience superior outcomes than those in better-resourced settings is perhaps the most influential and enduring finding from a series of multi-country studies conducted by the WHO [6]. However, a number of commentators have challenged the validity of these findings, highlighting, for example, the high mortality rates in LMIC, which could have caused differential attrition of severe cases, and the variation in outcomes between LMIC settings [7, 8]. The aim of this review was to synthesise recent evidence on schizophrenia illness explanations, impact and outcomes and the accessibility, feasibility and effectiveness of models of care in LMIC.

### **Explanations and attitudes**

Recent research has consolidated the rich literature on the ways cultural and social settings shape understandings of psychotic symptoms [9, 10]. Qualitative work in India, Nigeria and Trinidad found that disruptive behaviours, wandering and decline in functioning are more often considered signs of psychosis than distorted perceptions and beliefs. Across settings, psychosis was attributed to multiple, sometimes contradictory, causes; whilst supernatural beliefs were most prominent, biological factors, substance misuse, and psychosocial factors were also important [9]. These findings strengthen the recognition of a plurality of explanatory models for psychosis in both HIC and LMIC settings.

The implications of context have also been explored in relation to the content of delusions [11], help-seeking behaviour [9, 12], and stigma [10, 13, 14]. Campbell et al.'s findings echo the axiom that whilst the form of psychotic symptoms is universal, the content is dependent on cultural milieu [11]. In this large qualitative study amongst South African Xhosa, the majority of persecutory delusions related to bewitchment, which was perceived to be caused by the jealousy of friends or family [11]. Recent multi-country cross-sectional surveys have built on previous findings that supernatural explanatory models for schizophrenia tend to be associated with greater self-stigma [13] and public stigma [10]. Using rich qualitative and quantitative data, Koschorke et al. concluded that, in India, caregivers' experience of stigma is underpinned by their own and their relatives' lack of achievement in gendered role expectations relating to marriage, work and social standing [14]. In a cross-sectional survey (n=4476) Angermeyer et al. found that amongst members of the public in Germany, there was a greater desire for social distance from people with schizophrenia in remote relationships, in contrast to Tunisia where social distance was desired for family relationships. The variation in the form of stigma was attributed to differences in the social role that 'matters most' (understood as 'what is most at stake for actors in a local social world' [15]) between settings, with family life being more important in Tunisia [10].

### **Social and health impact**

New research has broadened our understanding of the ways in which people with schizophrenia in LMIC represent a uniquely vulnerable group. In rural

Ethiopia, 32.5% of people with severe mental disorders had severe household food insecurity, compared to 15.9% of comparison households (n= 576)[16]. In a small cross-sectional survey (n=77), 75% of women with schizophrenia in a Nigerian outpatient clinic had experienced intimate partner violence, with around three quarters reporting verbal abuse, half reporting physical abuse and a quarter reporting sexual violence [17]. This compares to 3.1% of women in a general population sample reporting sexual violence in the last 12 months [18]. In a qualitative study in rural Ethiopia, people with schizophrenia were found to be commonly physically restrained by family members as a strategy to manage the illness in the absence of other support [19].

In an analysis of 2002-2004 World Health Survey data (n= 242,952), significantly higher multi-morbidity was observed in people with self-reported psychosis (36.0% (95% CI, 32.1–40.2%)) compared to those with no psychotic symptoms (11.4% (95% CI, 11.0–11.8%)) across 48 LMICs [20]. There are indications of a universal pattern of physical health problems amongst people with schizophrenia. The pooled prevalence of metabolic syndrome in people with schizophrenia across 14 Indian studies was found to be 29.8%, which is comparable to HIC [21]. Liu et al. propose a multi-level model of risk, comprising individual factors, health systems and social determinants of health, to explain excess mortality in people with schizophrenia across LMIC and HIC [22]. Growing interest in the prevalence of underweight in people with schizophrenia [23], given the known association between underweight and excess mortality in the general population [24] , may have particular relevance for LMIC.

## **Risk factors and illness course**

The apparently superior outcome of schizophrenia in LMIC has been hypothesised to arise from better social support. Indirect evidence for this notion comes from three recent papers of the 14-year outcomes of the Chengdu Mental Health Project cohort study of schizophrenia conducted in rural Southwest China (n=510) [25-27]. Individuals who were either unmarried or had no family caregiver at baseline had higher rates of homelessness and suicide, and a lower rate of survival after 14 years of follow-up [25, 26]. Individuals with family caregivers also had significantly higher functioning scores, lower symptoms scores and lower relapse rates at 14 years [25]. However, it is established globally that it is not simply the presence but the nature of family support that influences outcomes. In common with findings across LMIC and HIC settings, a recent study in Pakistan (n=53) found the relapse rate for people with schizophrenia in high-expressed emotion households was 72% as compared with 36% in low-expressed households ( $p < 0.05$ ) [28].

Two small-scale but in-depth qualitative papers from South Africa contest some assumptions around the nature of informal care for people with schizophrenia in LMIC. Whilst care was readily and flexibly provided by family and community members in most cases [29], this was often because they felt obligated to do so [30]. One study found that family members used non-confrontational care strategies, including unrestricted mobility, to avoid conflict with care recipients [29]. These findings contrast with the restrictive practices, including restraint, identified as part of informal care in other settings [19]. Gaps and difficulties were also identified: informal care was sometimes not available due to caregiver

employment, sickness or death [29] and caregivers experienced substantial obstacles in supporting medication adherence, especially in the context of violence, food insecurity and substance abuse [30].

Recent exploratory research has proposed universal mechanisms for the development of psychotic symptoms and further challenged the notion of a more supportive family environment in LMIC. An online community-based survey in Chile, Columbia, Indonesia, Germany and US found that, whilst participants from LMIC were more likely to report that they had any family support, they also perceived more criticism compared to participants from HIC (n=1317).

Moreover, the association between criticism and psychosis proneness was stronger in LMIC compared to HIC [31]. Jaya et al. used cross-sectional survey data (n=2350) to demonstrate that cognitive vulnerability, particularly negative schemas, mediates the relationship between social adversity and self-reported psychotic symptoms in a similar way in the US, Germany and Indonesia [32][33].

### **Models of evidence-based care and access to care**

A systematic review identified 33 papers relating to mhGAP implementation in LMIC across disorders, including training evaluations and country contextualisations [4], demonstrating the importance of mhGAP for global mental health practitioners and researchers. There are indications that care delivered by primary healthcare workers can support clinical improvements in people with schizophrenia but most studies to date, such as a 12-month cohort study in Nepal, have been small (n=85) and non-randomised [34]. The forthcoming results of more rigorous evaluations, including the TASCs non-inferiority RCT in

rural Ethiopia [35] and the five-country Programme for Improving Mental healthcarE treatment cohorts and facility detection studies [36], promise to shed more light on the impact of the mhGAP model.

It is increasingly recognised that alongside improved availability, services must be of high quality to achieve improved patient outcomes [37]. Reflecting growing efforts to consult people with schizophrenia in service design, Mayston et al. developed and validated the Mental Health Service Satisfaction Scale for rural Ethiopia [37, 38]. Given the limited coverage of community-based services, psychiatric hospitals remain an important source of care for people with schizophrenia in LMIC, particularly for those who are destitute [39]. The WHO QualityRights initiative aims to improve human rights conditions in mental health facilities [40], though evaluations of the impact of such initiatives have so far been of low quality [41]. A new multi-level model for interventions to reduce excess mortality in persons with severe mental disorders, comprising individual, health system, community and policy-level interventions, can be readily applied to both LMIC and HICs [22]. However, implementation and evaluation of such interventions in LMIC is limited to date.

There is mounting recognition that even where biomedical services are available, people with schizophrenia may not access treatment. Descriptions of service utilisation have tended to assume that biomedical care is the ‘final destination’ in the treatment journey [42]. Labys et al. consulted 83 stakeholders (traditional healers, religious leaders and caregivers) in rural KwaZulu Natal, South Africa, to gain richer insights into patterns of help-seeking [12]. Nearly half of the people

with psychosis discussed had never accessed biomedical care, whilst half had accessed a traditional healer. In some cases, care was sought in parallel. In qualitative studies in Ethiopia and Tanzania, people with schizophrenia, caregivers and healthcare workers reported substantial barriers to engagement with care [43, 44]. In both settings there were erratic anti-psychotic medication supplies and difficulties paying for medication, due to poverty. In Tanzania whilst free mental health services are mandated, this is not usually the case in practice [44]. Other reasons for disengagement were the long illness course and unmet expectations of cure. Differing explanatory models were rarely noted as reasons for disengagement [43].

### **Psychosocial interventions**

Previous research has demonstrated the benefits of family and psychosocial interventions for people with schizophrenia in LMIC, particularly in China [45]. Current developments include a greater emphasis on feasibility, such as delivery by non-specialists [46, 47] and peers [48], and a growing interest in rehabilitation-focused interventions [46, 47]. Using a pretest-posttest design, a 12-week family-to-family psychoeducation intervention in Mexico City produced small reductions in expressed emotion amongst caregivers of people with schizophrenia (n=230 family members) [48]. In Jordan, Al Hadihasan et al. found that even an extremely low-intensity intervention comprising psychoeducational leaflets with follow-up phone calls is acceptable and may impact on patient outcomes through improving knowledge, coping skills and self-confidence [49]. Participants in a pilot of group psychosocial rehabilitation in South Africa

likewise reported improvements in knowledge and self-esteem, and also social support and self-care. However, a substantial acceptability issue was the absence of income-generating opportunities [46]. Delivery by auxiliary social workers, a non-specialist cadre, was found to be feasible [46]. Results from the Rehabilitation Intervention for people with Schizophrenia in Ethiopia cluster-randomised trial, will provide insights into the effectiveness of community-based rehabilitation delivered by lay health workers [47].

eHealth approaches offer exciting scope for intervention scalability. To date in LMIC there is little experience of delivering psychosocial interventions for schizophrenia via eHealth platforms. However, an RCT in rural China will evaluate the effectiveness of a multicomponent intervention comprising medication reminders via mobile text and voice messaging supported by an e-platform, an award system to incentivise medication adherence and support for family members [50]. A pilot study set in Cape Town assessed the feasibility of a single psychoeducation session and text message appointment reminders amongst people with severe mental illness (n=77). Substantial problems were identified; 41.2% did not receive the text messages as phones were lost, stolen or numbers were changed [51]. Although it was not explored in this paper, it is conceivable that difficulties using electronic devices may disproportionately affect the poorest. This pilot therefore highlights that an unintended negative consequence of eHealth interventions may be to widen health inequalities.

A recent RCT has demonstrated the effectiveness of brief culturally-adapted CBT delivered by community clinicians in improving outcomes in people with

schizophrenia in China. Guo et al. found a clinically significant improvement in symptoms in 37.3% in the CBT plus treatment as usual (TAU) arm vs 19.1% in TAU alone arm ( $p=0.003$ ) [52]. RCTs in Pakistan and China also demonstrated the effectiveness of CBT delivered by psychiatrists and psychologists in hospital settings [53, 54]. Qualitative studies in China and Pakistan have explored potential cultural adaptations to CBT for non-Western settings, including a bio-psycho-spiritual-social model for managing psychosis [55, 56].

### **Traditional, faith and alternative medicine**

Nortje et al.'s systematic review examined evidence for the effectiveness of any type of traditional healing (including holy water and herbal remedies) across HICs and LMICs. Evaluations were generally of poor quality, included mixed psychiatric diagnoses, and utilised non-randomised designs [57]. The authors concluded that whilst acute relapses of schizophrenia may improve whilst individuals are under the care of traditional healers, these improvements cannot be distinguished from the natural illness course [57]. A large effect of adjunctive Tai Chi on negative symptoms of schizophrenia (five RCTs;  $n=451$ ) was found in a systematic review and meta-analysis (Standardised Mean Difference 0.87 (95% CI -1.51, -0.24),  $p=0.007$ ) [58]. A Cochrane Review concluded Wendan decoction (a Chinese herb formula) may produce short-term improvements in psychotic symptoms compared to placebo, and whilst the formula is no better than anti-psychotic medication in improving mental state it has fewer side effects [59]. However, the quality of evidence was low in both reviews [58, 59].

There are few evaluations of biomedical-traditional provider collaborations. Van der Watt's qualitative study provides fascinating insights into the views of biomedical and alternative mental healthcare providers on potential collaboration in Ghana, Kenya and Nigeria [60]. Several barriers were identified, including a mutually strong sense of distrust towards, and superiority over, the other provider groups. The incompatibility of different belief systems and the perceived intention of biomedical providers to siphon expertise from traditional healers without acknowledgement or compensation, were also cited [60]. The Collaborative Shared care to Improve Psychosis Outcome RCT will compare the effectiveness of a collaborative care programme with usual care at improving symptom severity in people with psychosis in Nigeria and Ghana [61].

## **Conclusion**

Social and cultural contexts continue, rightly, to be considered important forces shaping the illness experience of schizophrenia. Yet there is increasing appreciation of universal influences on schizophrenia outcomes and the problems associated with the illness, such as physical co-morbidities. Acceptable and effective responses to schizophrenia in LMIC should be cognisant of both sets of factors. Efforts to enhance the quality of family support should also be central to models of care, given the influence of the family in outcomes, and their typical role as primary care provider. Learning in this area may have wider relevance to HIC. Alternative treatment approaches such as Tai Chi may be a vehicle for the shift of global mental health from 'delivery science to discovery science' [62]. Some topics have received little attention in LMIC including involuntary treatment, early intervention and how to address excess mortality.

The evolution of global mental health into a truly global discipline will benefit people with schizophrenia in low, middle and high-income country settings [62].

### **Key points**

- There is a plurality of explanatory models for psychosis across settings and context influences experiences of stigma. People with schizophrenia in LMIC are vulnerable to food insecurity, violence and physical health problems.
- Being married or having close family may be associated with better outcomes in LMIC. However social support is not always available and caregiving is challenging.
- Evidence-based care remains inaccessible to many people with schizophrenia. Psychosocial support groups appear to be acceptable and culturally-adapted cognitive-behavioural therapy can reduce symptom severity.
- Most research on traditional and alternative treatments for schizophrenia is of low quality, but some modalities, such as Tai Chi, may be beneficial. The challenges of biomedical-traditional provider collaborations have been highlighted and forthcoming evaluations will evaluate their effectiveness.

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## Conflicts of interest

LA and AF are co-principal investigators, and CH is co-investigator, of the RISE trial. CH is principal investigator, and AF is co-investigator, of the TASCs trial. CH is the research director of PRIME and AF is the principal investigator of PRIME Ethiopia.

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