The management of adult psychiatric emergencies in low-income and middle-income countries: a systematic review

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The aim of this Review is to identify effective interventions and treatment guidelines to manage common types of psychiatric emergencies in non-specialist settings in low-income and middle-income countries. Mental health specialist services in low-income and middle-income countries are scarce. We did a systematic review of interventions for psychiatric emergencies and a literature search for low-income and middle-income-specific treatment guidelines for psychiatric emergencies. A dearth of high-quality guidelines and contextualised primary evidence for management of psychiatric emergencies in low-income and middle-income countries exists. Filling these gaps in present guidelines needs to be an urgent research priority in view of the adverse health and social consequences of such presentations and the present drive to scale up mental health care.

Introduction

A psychiatric emergency is a severe disturbance of mood, thought, or behaviour that needs an immediate intervention. A large proportion of people attending emergency services in high-income countries present with mental health problems needing treatment. In emergency services settings, psychiatric emergencies are reported to be as frequent as trauma-related and neurological emergencies, constituting up to 12% of emergency service attenders. Common psychiatric disorders reported in people presenting to emergency services in high-income countries include psychoses (12–29%), substance abuse disorders (6–25%), mood disorders (depression and bipolar disorders; 2–23%), and personality disorders (11–20%). Furthermore, in high-income countries, people with depression, anxiety, or substance use disorders are frequent users of emergency medical services. Many common emergency presentations, such as attempted suicide and agitated or disturbed behaviour, cut across diagnostic categories.

Most people with mental health problems living in low-income and middle-income countries do not have access to treatments that are shown to be successful and cost effective in such settings. For this reason, emergency presentations are expected to be more frequent in these populations. Owing to a variety of factors, including absence of availability of specialist services, people with mental health problems often make their first presentation to non-specialist settings. Thus, the management of psychiatric emergencies is more likely to fall to non-specialists working in non-psychiatric settings, as primary care or general hospital emergency departments. Health professionals working in general health-care settings in low-income and middle-income countries therefore need the necessary skills to handle psychiatric emergencies. An important resource that would help these health professionals is evidence-based guidelines that provide a framework for the management of psychiatric emergencies in a non-specialist, low-income and middle-income country setting. Although many such evidence-based guidelines have been developed in high-income countries, the generalisability of such guidelines to low-income and middle-income countries might be restricted because low-income and middle-income countries might differ substantially in terms of characteristics of clinical phenotypes, the available human resources for delivering the intervention, availability, and mental health legislation for involuntary treatment.

There are two aims of this Review: first, to identify and assess the evidence base for the effectiveness of interventions for psychiatric emergencies in adults in non-specialist settings in low-income and middle-income countries, and second, to review the availability, coverage, and quality of treatment guidelines for psychiatric emergencies in low-income and middle-income countries.

Data collection

Systematic review of the literature

We did this Systematic Review in line with the PRISMA statement for reporting systematic reviews and in accordance with a review protocol designed for this Review as a guide. We included randomised and non-randomised controlled trials, observational studies, pilot studies, and case series if they were done in any setting except specialist mental health settings (eg, general hospitals, emergency departments, primary care, and mental health services provided by non-governmental organisations in any low-income and middle-income country as defined by the World Bank at the time that the study took place). We excluded interventions delivered in specialist psychiatric settings (eg, psychiatric wards and psychiatric emergency departments) because the goal of the Review was to examine interventions that could be delivered in non-specialist settings. We also excluded interventions delivered to children and adolescents or delivered in post-conflict or humanitarian settings because they address issues in specific patient groups and settings that have distinct requirements, which are beyond the scope of this Review.

Our literature search focused on phenotypic presentations (eg, suicide attempts) as they are likely to have more
relevance in non-specialist emergency settings. To ensure a comprehensive search of priority phenotypes, the search terms were informed by a survey of experts. We generated a consensus list of phenotypic presentations based on discussion among the author group. We contacted World Psychiatric Association (WPA) regional and country representatives and other key informants identified by the researchers by email and invited them to respond to the survey (appendix). We asked experts to rate a list of phenotypic presentations (eg, aggression or violence, mute or uncommunicative, self-harm, and bizarre behaviour) on a three-point Likert scale of extremely relevant, moderately relevant, and not relevant for their context. We also asked WPA to suggest any other phenotypes that were relevant but not on our list. 27 experts from 17 countries (Armenia, Bangladesh, Cambodia, Egypt, Ethiopia, Georgia, India, Jordan, Kenya, Moldova, Mongolia, Niger, Nigeria, Pakistan, Sudan, Togo, and Uganda) participated in the survey.

We excluded the following presentations: seizures, acute adverse effects of psychotropic medications, and acute behavioural disturbance due to delirium (as the most common causes are not attributed to mental health problems). There were no restrictions to the delivery representative (eg, general physician, nurse, or mental health professional), type of intervention (eg, psychosocial, pharmacological, or environmental), and control groups (eg, no treatment or alternative treatment; see appendix for detailed inclusion and exclusion criteria).

Guideline search
To retrieve relevant guideline recommendations, we invited key informants (described earlier) to identify guidelines for psychiatric emergencies, which were developed or used in their country. Additionally, we did a search with Google Scholar with the search terms “emergency psychiatric clinical guidelines” and “acute psychiatric clinical guidelines”. We did a search for relevant guidelines from Latin American countries that were not published in English. We took an a-priori decision to include WHO’s Mental Health Gap Action Programme (mhGAP) intervention guide for mental, neurological, and substance use disorders in the Review as an example of high-quality guidelines developed through a systematic process and designed for low-income and middle-income country settings. We assessed the quality of guidelines on three dimensions, namely treatment efficacy, clinical use, and guideline development process with the American Psychological Association Criteria for Evaluating Treatment Guidelines. Data from English language guidelines were extracted independently by UB and CH whereas data from non-English guidelines were extracted by CR, SLdAP, and SF.

Findings
Selected studies
The database search returned 16687 reports. After excluding duplicates and ineligible manuscripts, we did a full-text assessment of the remaining 23 studies. 21 studies were excluded because they did not describe assessment of an intervention or were not based in a low-income or middle-income country or were not done in non-specialist emergency settings. We were able to identify two reports, both assessing the same intervention from the same study, the WHO Multisite Intervention Study on Suicidal Behaviours (SUPRE-MISS), which is a multicountry, individual randomised trial that assessed a brief educational intervention and periodic follow-up contacts for people who attempted suicide in Brazil, China, India, Iran, and Sri Lanka. Consecutive people who attempted suicide (defined using the 10th revision of the international classification of disease [ICD10] criteria) attending the emergency care departments were to receive either brief intervention and contact (BIC), which was a brief educational intervention, with periodic follow-up contacts (n=922) or treatment as usual [TAU] (n=945).

A person with clinical experience (eg, doctor, nurse, or psychologist) delivered the BIC and included TAU plus a 1-hour individual information session followed by nine follow-up contacts (phone calls or visits) over 18 months. The results showed that overall, at 18 months, significantly fewer deaths from suicide occurred in the BIC than in the TAU group (2 [0·2%] vs 18 [2·2%]; p<0·001). However, the difference between the proportion of patients with repeated suicide attempts in the BIC and TAU groups was not significant (66 [7·6%] vs 60 [7·5%]; p=0·909).
reports provided inadequate information for variables such as allocation concealment, blinding of personnel, and blinding of outcome assessment, thus raising concerns about potential bias. However, we thought the study had a high risk of selection bias because of selective attrition from the intervention and comparison groups (appendix).

<table>
<thead>
<tr>
<th>Common recommendations*</th>
<th>Other recommendations†</th>
<th>Source guideline or randomised control trial from which recommendation is derived</th>
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<tbody>
<tr>
<td><strong>Acute anxiety</strong></td>
<td>Clonazepam 0·25–0·5 mg sublingually</td>
<td>Diazepam 5–10 mg intravenously</td>
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<tr>
<td><strong>Conversion</strong></td>
<td>None</td>
<td>Full explanation that should be clear, coherent, and emphasise the genuineness of the disorder, which is common, potentially reversible, and does not mean that the patient has a long-term psychiatric illness; treatment of comorbid depression or anxiety if present; diazepam 5·10 mg orally, intramuscular, or intravenously, psychosocial intervention; refer to higher level for appropriate management</td>
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<tr>
<td><strong>Agitation, overactive, aggressive, violent, and excitement</strong></td>
<td>Verbal de-escalation; assess in pairs in calm settings, with or without family and friends; keep lines of communication open by talking to the patient in a firm but friendly manner until the situation is under control; diazepam 2–20 mg intravenously, 5·10 mg orally, or 10 mg intramuscularly for acute agitation secondary to anxiety; chlorpromazine 50–150 mg intramuscularly or 200 mg four times a day orally; haloperidol 5·10 mg intramuscularly; physical restraint, if used, should be temporary and in combination with sedation and close medical supervision; restrain patient when necessary without causing injuries; protect yourself, have enough people to handle patient safely, and do not immediately remove physical restraints</td>
<td>Risperidone 2 mg and clonazepam 2·4 mg; olanzapine 5 mg and diazepam 10–20 mg; quetiapine 100–200 mg; haloperidol 5 mg intramuscularly plus chlorpromazine 25 mg intramuscularly to be repeated once after 1–2 h if necessary; for patients older than 60 years, haloperidol 5·10 mg intravenously or 10·20 mg intramuscularly, or chlorpromazine 50–75 mg intramuscularly, if no response with oral medications then use lorazepam 2·4 mg intramuscularly with or without haloperidol 5·10 mg intramuscularly, or olanzapine 5·10 mg intramuscularly or clozapine (maximum 360 mg per 24 h); if no response then use diazepam 10 mg intravenously or zuclopenthixol acetate (clopoxil acuphase) intramuscularly 50–150 mg (only if detained under mental health law) refer to general hospital if haemodynamically unstable or organic cause is suspected</td>
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<td><strong>Suicidal</strong></td>
<td>Detailed assessment and risk assessment; talk with the patient to try to understand what the actual problem is and try to identify cause for suicidal behaviour; treat an underlying mental illness such as a severe depression; liaise with relevant parties and talk to important relatives or friends; if risk of harming again exists, ask relatives to spend time with the patient and ensure that they are not left alone; do not leave them unattended; carefully observe patient to minimise risk of self-harm; refer to relevant professionals; consider the need to admit to hospital and do so unless properly supervised at home</td>
<td>Brief intervention and contact; individual information session (information about suicidal behaviour as a sign of psychological or social distress, risk and protective factors, basic epidemiology, repetition, alternatives to suicidal behaviours, and referral options) before discharge followed by nine follow-up contacts (phone calls or visits); form a contract with the patient; provide emergency contacts; provide adequate psychological care, refer or call a pastor</td>
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<td><strong>Opiate intoxication</strong></td>
<td>None</td>
<td>Naloxone 0·4 mg intravenously; if no response within 2 min, repeat 0·4–0·8 mg twice more at 5·10 min interval; if antidote for opiate overdose is not available, treatment is symptomatic with analgesia and sedation</td>
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<td><strong>Opiate withdrawal</strong></td>
<td>Diazepam 10 mg orally or 10 mg intravenously as starting dose, repeat every hour until sedation; clonidine 0·15 mg orally as starting dose daily for 10 days</td>
<td>Haloperidol 5·10 mg orally three times a day or chlorpromazine 50–100 mg orally three times a day for behaviour tending towards assault; paracetamol 1 g orally every 4 h as necessary for pain with a maximum dose of 4 g or 24 h; referral to substance treatment centre; treat with reducing doses of opioids (methadone or buprenorphine) or alpha-agonist drugs (lofexidine) using either supervised dosing or daily dispensing; treat specific symptoms as needed (diarrhoea, vomiting, muscle pain, and insomnia); consider starting opioid agonist maintenance treatment; oral or intravenous rehydration, if necessary</td>
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<td><strong>Amphetamine intoxication</strong></td>
<td>Diazepam in titrated doses until the person is calm and lightly sedated; if psychotic symptoms do not respond to benzodiazepines, then consider using short-term antipsychotics; monitor blood pressure, pulse rate, respiratory rate, and temperature every 2 h</td>
<td>Chlorpromazine 25–50 mg rapidly reverses the acute intramuscular agitation; amnomium chloride to alkalise urine for the excretion of toxic amounts of ingested substances (eg, amphetamine)</td>
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<td><strong>Crack intoxication</strong></td>
<td>Diazepam fractionated doses until tranquillisation and mild sedation; short-acting antipsychotics for psychotic symptoms; monitor vital signs every 2 h</td>
<td>Watch out for suicidal thoughts; refer to hospital if chest pain, arrhythmia, or violent or aggressive behaviour</td>
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<tr>
<td><strong>Crack withdrawal</strong></td>
<td>None</td>
<td>Maintain hydration; avoid physical restraint; diazepam (for anxiety or restlessness); haloperidol intramuscularly or midazolam intramuscularly for motor agitation or psychotic symptoms</td>
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<tr>
<td><strong>Cannabis intoxication</strong></td>
<td>None</td>
<td>Maintain hydration; tranquillisation with midazolam 5 mg intramuscularly (for management of acute agitation)</td>
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### Common recommendations

<table>
<thead>
<tr>
<th>Alcohol intoxication</th>
<th>Alcohol withdrawal</th>
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<tr>
<td>Thiamine 100 mg intravenously or intramuscularly if signs of encephalopathy; diazepam 10 mg intravenously if agitated or violent, repeat if needed after 30 min</td>
<td>Haloperidol intravenously every 20–30 min for aggressiveness until patient is calm then intravenously 4–8 h depending on disorder, or hydrazepam 50–100 mg orally or rectally if possible, or lorazepam 2–4 mg orally every 4–6 h until patient is calm (repeat if needed)</td>
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### Other recommendations

<table>
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<tr>
<td>Thiamine 50 mg intravenously or intramuscularly, or 5–10 mg orally, or 5−10 mg rectally, or 100–300 mg orally four times a day, or phenytoin intravenously 10−15 mg/kg, diazepam intravenously for withdrawal seizures, or carbamazepine 600–800 mg per day for 4–8 h then taper by 200 mg per day for prophylaxis for withdrawal seizures; diazepam (orally or intravenously), various regimens; lorazepam 2–4 mg every 8 h intramuscularly to a maximum dose of 4 mg over 24 h; diazepam 10–15 mg intravenously or 10 mg intramuscularly, or lorazepam 2–4 mg orally for aggressiveness or restlessness; 50 mL of 50% dextrose for hypoglycaemia</td>
<td>Haloperidol intravenously every 20–30 min for aggressiveness until patient is calm then intravenously 4–8 h depending on disorder, or hydrazepam 50–100 mg orally or rectally if possible, or lorazepam 2–4 mg orally every 4–6 h until patient is calm (repeat if needed)</td>
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</table>

### Source guideline or randomised control trial from which recommendation is derived

- mhGAP;19 Thai–Burmese border;24 South Africa;26 Namibia;28 Malawi;30

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**Table: Summary of guidelines for the management of neuroses spectrum emergencies, externalising spectrum emergencies, suicidal behaviour, and substance use related emergency presentations in non-specialist settings in low-income and middle-income countries**

**Literature review of guidelines**

Through the grey literature search and key informants we identified 21 treatment guidelines (excluding the mhGAP-IG). We found one set of guidelines from each of the Thai–Burmese border, Namibia, South Africa, Kenya, Zambia, Ethiopia, Vanuatu, Afghanistan, and Colombia. The maximum number of guidelines from one country was from Brazil, followed by three from Peru. The mhGAP-IG were developed for use across low-income and middle-income countries. Two sets of guidelines (including mhGAP) addressed a range of mental disorders, whereas others were specific, for example on the management of opiate disorders, crack disorders, or psychotic disorders. One guideline was specific for the aggression and agitation phenotype. The remaining guidelines addressed psychiatric emergencies alongside other medical emergencies.

The appendix describes the quality criteria used to assess the guidelines and specifies which of the guidelines met many (appendix). With a few exceptions, most of the guidelines did not consider the level of methodological rigour and clinical sophistication of the evidence supporting the intervention proposed.

We organised the phenotypes under four broad groups: the neuroses spectrum (eg, acute anxiety and conversion), externalising symptoms (eg, agitation and aggression), suicidal behaviour, and substance use related presentations (eg, opiate intoxication and alcohol withdrawal). The table presents a summary of the recommendations derived from a synthesis of the recommendations from the various guidelines. Recommendations made in two or more guidelines are classified as common recommendations, and the rest are classified as other recommendations (table).

For some phenotypes there were more than one set of guidelines recommending a common intervention (eg, diazepam for alcohol withdrawal), whereas for other phenotypes only one set of guidelines recommended a particular intervention (eg diazepam for conversion symptoms). The most widely addressed phenotypes were alcohol intoxication or withdrawal and suicidal behaviour. For alcohol intoxication, the common recommendations were monitoring of vital signs, supportive interventions (eg, lateral positioning and rehydration) and management of symptoms (eg, management of hypoglycaemia). For
alcohol withdrawal, the common recommendations included sedation with diazepam, prophylaxis against Wernicke Korsakoff syndrome with thiamine, multi-vitamin supplementation, rehydration, and symptomatic treatment (eg, antipsychotics for psychotic symptoms, and benzodiazepines or antiepileptics for withdrawal seizures). Finally, for suicidal behaviour, the common recommendations included detailed risk assessment, management of risk (eg, treat underlying mental illness and liaise with support networks), and referral to specialist professionals as appropriate.

The management of other phenotypes was as follows: for acute anxiety, clonazepam is recommended; for agitation and aggression, recommendations included interventions that were verbal (eg, de-escalation through firm but friendly communication), mechanical (eg, physical restraint), and pharmacological (eg, benzodiazepines like diazepam and antipsychotics like haloperidol); for opioid withdrawal, diazepam and clonidine were recommended; and for both crack and cocaine intoxication and amphetamine intoxication the principles of treatment were the same (ie, benzodiazepine for management of agitation, antipsychotics for management of psychotic symptoms, if any, and monitoring of vital signs).

Discussion

We noted only one study in which researchers empirically assessed a treatment of a psychiatric emergency in non-specialist settings in low-income and middle-income countries. Results showed that a brief psychosocial intervention delivered to patients who had attempted suicide was associated with a significant reduction in completed suicide, but not in repeated suicidal behaviour. Additionally, we were able to retrieve 22 treatment guidelines for psychiatric emergencies in low-income and middle-income countries; however, only WHO’s mhGAP-IG was based on context-relevant evidence or developed after rigorous procedures to ensure clinical usefulness.

The approach we took in this Review to the problem of psychiatric emergencies was based on phenotypic presentations rather than on syndromal diagnoses. Our rationale for this method was that the immediate management of psychiatric emergencies, particularly in non-specialist settings, needs treatment of the presenting symptoms that are causing distress, and that this management is often distinct from the longer-term management driven by the syndromal diagnosis.

Data from high-income countries show an increasing trend of psychiatric emergencies presenting to general hospitals. No evidence suggests that this rise would be any different in low-income and middle-income countries, and indeed the burden might be higher on such services for several reasons. The shortage of specialist human resources in low-income and middle-income countries makes it imperative that non-specialist health-service providers are adequately trained and equipped to deliver evidence-based treatment guidelines. Experiences from high-income countries show that the use of short, focused training programmes for general health-care professionals improves knowledge, diagnostic accuracy, and treatment of psychiatric emergencies in non-specialist settings. Such training needs to be supplemented by contextualised and evidence based guidelines to ensure sustained delivery of high-quality care. However, our Review reported an almost complete absence of empirical evidence about management of psychiatric emergencies in non-specialist settings in low-income and middle-income countries. Furthermore, the few guidelines to manage psychiatric emergencies in low-income and middle-income countries had notable flaws in the methodology used for their development. The synthesis of recommendations from the guidelines and the randomised control trial (table) shows that, although treatment guidelines for some of the phenotypes exist (eg, suicidality and alcohol withdrawal), many phenotypes are not represented at all (eg, stupor, catatonia, and mutism). The overall quality of the guidelines was weak and we noted some variation in the recommendations for specific phenotypes, for example in terms of drugs and dosages.

One of the American Psychological Association criteria that we used to examine the guidelines was whether the guidelines considered patients’ willingness and ability to participate in recommended interventions. None of the guidelines included in our Review fully met that criterion, which is a substantial shortcoming for guidelines that are to be used to treat psychiatric emergencies, since many of the patients might have reduced capacity to give informed consent for treatment. Hence, consideration of the legal provisions and protection provided in a specific country to patients with reduced capacity to consent is essential to draft treatment guidelines. This objective is particularly important, in view of the findings made by the UN Committee on the Rights of Persons with Disabilities that laws authorising the involuntary treatment on the basis of mental disability are non-compliant with the Convention on the Rights of Persons with Disabilities.

Our Review shows an absence of empirically based and contextually appropriate guidelines on how to manage psychiatric emergencies in non-specialist settings in low-income and middle-income countries. In the short term, mental health systems could follow the recommendations synthesised in the guidelines reviewed in our report, but ultimately should adapt these proposals through rigorous guideline development processes. Additionally, high-quality evidence from robust designs, ranging from clinical cohorts to randomised trials of the management of psychiatric emergencies in specialist mental health settings in low-income and middle-income countries, is essential to assess recommendations and novel approaches.

Guidelines for the management of psychiatric emergencies in non-specialist health-care settings also need

recommendations on the management of patients who have reduced capacity to consent, which are compliant with both local laws and international conventions. One of the concerns about doing trials in psychiatric emergencies is to do with ethical issues, particularly in relation to the involvement of patients with restricted capacity. However, results from the TREC trials, which compared two drug treatments for people with aggression or agitation due to mental illness in low-income and middle-income countries, have shown that rigorous yet pragmatic randomised trials can be done in people presenting with psychiatric emergencies in middle-income country settings and provide a suitable model for future trials in non-specialist settings.

The guidelines should be based mainly on a framework of contextualy relevant phenotypic presentations with the goal of providing quick relief from distressing psychiatric events. The guidelines should be graded according to their feasibility (eg, the cost of medications and competencies needed to deliver interventions) and acceptability (eg, the regulatory restrictions on their use in specific settings). Although some contextual specificities are expected, these are likely to be smaller than the universal principles of management of psychiatric emergencies, and an mhGAP-IG styled set of guidelines might be an appropriate format for synthesis of these recommendations (panel).

Our Review has several strengths. To the best of our knowledge, this report is the first attempt to synthesise evidence on the types and management of psychiatric emergencies in non-specialist settings in low-income and middle-income countries. We have synthesised data from two sources, thereby increasing the generalisability of our findings. Although we have presented the synthesised recommendations, we would like to specify that this is by no means an endorsement of the quality of the source guidelines, and the synthesised recommendations are only as good as the guidelines from which they are derived. Finally, we tackled the problem with a phenotypic approach, on the grounds that this would be of more practical value to front-line health professionals, as compared with the conventional syndromal diagnosis approach taken by mhGAP-IG. One limitation of our Review is that our scientific literature search was limited to studies written in English, although our guidelines search covered many languages. Additionally, the summary treatment recommendations that we have presented are based on the synthesis of guidelines which are themselves restricted by the weak quality of the evidence base and method used for their development.

In conclusion, a dearth of high-quality guidelines and contextualised primary evidence for management of psychiatric emergencies in low-income and middle-income countries exists. Existing guidelines are restricted to a small number of emergency presentations of uneven quality and neglect to provide guidance about the management of people with reduced capacity to consent. Ample well documented evidence exists on the assessment and management of psychiatric emergencies in non-specialist settings. However, this evidence mainly comes from high-income countries, which differ contextually from low-income and middle-income countries on various dimensions (eg, availability of trained human resources and drugs). Because much of the visible morbidity, and possibly mortality, associated with mental disorders is due to such presentations, our findings call for an urgent investment in the expansion of the evidence base for management of psychiatric emergencies in low-income and middle-income countries and the development of contextualised guidelines following a rigorous methodology.

Panel: Recommendations for the management of psychiatric emergencies in non-specialist settings in low-income and middle-income countries

- Guidelines to be developed immediately based on the best available global evidence
- Guidelines should be developed at a consistent quality and should be based on clear recommendations on management of patients without capacity to consent
- Low-income and middle-income countries should generate high-quality primary evidence which will address gaps in the evidence and enable the continuing assessment and refinement of contextualised guidelines

Search strategy and selection criteria

We searched the following databases for publications in English with no restriction on date of publication: Medline, Embase, PsycINFO, CINAHL (Cumulative Index to Nursing and Allied Health Literature), Cochrane library, Web of Knowledge, LILACS (Literatura Latino Americana en Ciencias da Saúde; comprehensive index of scientific and technical literature from Latin America and the Caribbean), Indmed (indexes peer-reviewed medical journals published from India), and ELDIS (Electronic Development and Environment Information System). We searched title, abstract, and keywords for the topics of mental disorder (eg, schizophrenia, depression, and mania), phenotype (eg, aggression and bizarre behaviour), presentation (eg, acute, emergency, and crisis), management (eg, treatment, intervention, and therapy), type of country (eg developing, underdeveloped, and low income), and country (eg, Bhutan, Sudan, and Vietnam). The detailed search strategy is included in the appendix.

One investigator (AN) did the literature search in October, 2014. Three investigators (AN, DF, and UB) double-screened titles and abstracts of all studies to establish eligibility for full-text screening. RS and EK resolved any disagreement about eligibility for inclusion in the Review by discussion among themselves. Two investigators (UB and CH) extracted the data independently with a data extraction form designed to achieve study objectives. One investigator (AN) checked the extracted data for consistency and any gaps addressed. Criteria for data extracted included country, study design, phenotype, diagnostic criteria, sampling strategy, sample size, intervention and intervention components, intervention representative, and comparison group. We assessed the quality of the included randomised trials using the Cochrane Risk of Bias instrument to rate the randomised trials on dimensions of allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias. We planned to do a meta-analyses if there were enough homogeneous studies.
Review

Contributors

AN was the lead author coordinating the review process, developed the search strategy, did database search, screened and selected studies, wrote the first draft of the manuscript and co-ordinated further drafts. DF helped develop search strategy and review protocol. UB and DF independently screen search results of reports for full-text screening and independently screened full text of papers for final inclusion. CR, SF, and SLdAP searched for guidelines from Latin American countries and extracted data from such guidelines. TR mentored the author group. VP originated the idea for this Review, commented on search strategy and review protocol, and mentored the authors’ group. RS and EK independently did grey literature search. CH and UB independently did data extraction. RS, CH, EK, and TR commented on search strategy and review protocol. SF, RH, CH, UB, EK, TR, and VP commented on all drafts. All authors read and approved the final draft of the manuscript.

Declaration of interests

We declare no competing interests.

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References


