World Health Organization

mhGAP

Mental Health Gap Action Programme (mhGAP) guideline for mental, neurological and substance use disorders

3.10 Psychosis and bipolar disorder (PSY)

PSY1. In adults with psychotic disorders (including schizophrenia) is antipsychotic medicine safe and effective?

Recommendation (update):		
	1.1 Oral antipsychotic medicines – namely aripiprazole, chlorpromazine, haloperidol, olanzapine, paliperidone, quetiapine, risperidone – should be offered for adults with a psychotic disorder (including schizophrenia), carefully balancing effectiveness, side-effects and individual preference.	
	Strength of recommendation:	Strong
	Certainty of evidence:	Moderate
	1.2 Clozapine should be considered for adults with a treatment-resistant psychotic disorder (including schizophrenia) under mental health specialist supervision, carefully balancing effectiveness, side-effects and individual preference.	
	Strength of recommendation:	Conditional
	Certainty of evidence:	Moderate

Justification

- Evidence was extracted from three systematic reviews: Ceraso et al., 2020 (75 RCTs on antipsychotic medicines in schizophrenia) *(191)*; Leucht et al., 2017 (167 RCTs on antipsychotic medicines in schizophrenia) *(192)*; and Schneider-Thoma et al., 2018 (596 RCTs on second-generation antipsychotic medicines in individuals with severe mental illness) *(193)*.
- Antipsychotics showed moderate effects for overall efficacy (low-certainty evidence) and large effects for prevention of relapse (high-certainty evidence). Differences in efficacy between medicines were either small or uncertain.
- Overall, for the medicines with data available, social functioning (moderate-certainty evidence) and quality of life (very low-certainty evidence) were also improved.
- Antipsychotics were associated with various side-effects (very low- to low-certainty evidence) including movement disorders, weight gain, metabolic side-effects, prolactin increase, sexual side-effects, QT prolongation, sedation, which all appear in varying degrees. The propensity to produce these side-effects differed between the agents, but the differences were overall less pronounced than the efficacy differences.

Remarks

- The medicines included in the recommendation correspond to the WHO EML *(13)* and are listed in alphabetical order.
- Clozapine should be offered for treatment-resistant psychosis, defined as psychosis that has not shown improvement after receiving treatment from two alternative antipsychotics with adequate dose and time. Clozapine should only be offered where lab tests are available to monitor white blood cell count, and under a mental health specialist supervision.
- Evidence regarding the safety and effectiveness of fluphenazine is mainly concerning the long-acting injectable formulations. Please refer to **PSY4** recommendations for further information.
- This recommendation does not suggest that only medicine should be offered, but medicine may be offered in combination with psychotherapy. Please refer to **PSY11** for further information.

Research gaps

- Data on first-generation antipsychotics with few exceptions such as haloperidol and chlorpromazine were very limited. As these medicines are of lower cost, further trials on some of them with relevant pharmacological properties would be warranted.

Implementation considerations

- People living with psychotic disorders should be involved in medicine choice in a supported decision-making process, without coercion and in line with human rights instruments.
- Treatment with antipsychotic medicines should be combined with psychosocial interventions (see other PICO questions in this module).
- Acquisition costs can differ substantially and also throughout the world. Recent antipsychotics may have currently higher costs than some older antipsychotics.
- Disruption in medicine supply (common in LMICs) may interfere with continuation of treatment.
- For the treatment of psychotic disorders, the WHO EML *(13)* includes the following oral medicines:
  - haloperidol (therapeutic alternative: chlopromazine);
  - risperidone (therapeutic alternatives: aripiprazole, olanzapine, paliperidone, quetiapine);
  - complementary list: clozapine.

PSY2. In adults with a first psychotic episode (schizophrenia) with full remission, how long should antipsychotic medicine be continued after remission in order to allow for the best outcomes?

Recommendation (update):	**Maintenance therapy with antipsychotic medicine for a minimum of 7–12 months should be offered in adults with a first episode of psychosis (including schizophrenia) in remission, carefully balancing effectiveness, side-effects and individual preference.**	
	Strength of recommendation:	Strong
	Certainty of evidence:	Moderate

Justification

- Evidence was extracted from three systematic reviews: Ceraso et al., 2020 (75 RCTs on maintenance treatment with antipsychotic medicines in schizophrenia) *(191)*; Kishi et al. 2019 (10 RCTs on discontinuation versus maintenance of antipsychotic medicines in schizophrenia) *(194)*; and Schneider-Thoma et al., 2018 (596 RCTs on second-generation antipsychotic medicines and short-term somatic serious adverse events in individuals with severe mental illness) *(193)*.
- Maintenance therapy was significantly superior to discontinuation with a follow-up of up to 12 months as well as up to 24 months. However, antipsychotics were associated with side-effects.
- The certainty of evidence was high for relapse at 12 and 24 months and low for leaving the study early due to adverse events.

Remarks

- Discontinuation of antipsychotics should always be done by gradually and slowly reducing the medicine dose. When medicines are discontinued, people living with schizophrenia and family members need to be educated to detect the re-emergence of symptoms early to allow for close clinical monitoring of relapse.

PSY11. In adults with psychotic disorders (including schizophrenia), are psychological interventions (such as psychoeducation, family interventions and CBT) effective in the maintenance phase?

Recommendation (update):	**Psychosocial interventions – namely family interventions, family psychoeducation, psychoeducation and cognitive behavioural therapy (CBT) – should be offered to adults with psychosis (including schizophrenia) during the maintenance phase, either alone or in combination.**	
	Strength of recommendation:	Strong
	Certainty of evidence:	Moderate

Justification

- Data were extracted from an NMA: Bighelli et al., 2021 (72 RCTs on the use of psychosocial and psychological interventions for relapse prevention in schizophrenia) *(210)*.
- Most of the psychological interventions were significantly superior to TAU for relapse prevention. CBT, family intervention and relapse prevention programmes showed large effects.
- Family psychoeducation, integrated intervention and psychoeducation showed medium effects.
- The efficacy for relapse prevention remained robust across different subpopulations for family interventions, family psychoeducation and CBT.
- Overall symptoms were reduced by many of the interventions investigated.
- Family intervention, mindfulness and CBT were associated with improvements in functioning. Integrated intervention was associated with improvement in quality of life.
- Regarding adherence: mindfulness, CBT, integrated intervention and psychoeducation were all superior to TAU and showed large effects.

Remarks

- Although, as described under justifications, many psychosocial interventions had beneficial effects in maintenance therapy, the efficacy of family interventions, family psychoeducation and CBT were most robust *(210)*. Moreover, a subsequent analysis examining only family interventions found that simple family psychoeducation is the most recommendable one.
- *Acceptance and commitment therapy (ACT)*: A manualized third-generation behavioural therapy that incorporates acceptance and mindfulness-based strategies to help individuals in overcoming negative thoughts and feelings.
- *Assertive community treatment:* An intensive, highly integrated approach for community mental health service delivery. The teams visit the individuals at home and provide clinical assessments and crisis interventions, along with psychosocial and functional assistance. This can be considered as a more active form of case management, because it is more holistic and integrated with coordinated services that promote increased wellness for the person.
- *Case management:* Usually each person is assigned to a case manager who contacts them regularly (e.g. once a week) and can provide more intensive support in case of particularly acute needs.
- C*ognitive behavioural therapy (CBT):* CBT for psychosis is usually based on an individualized case formulation and the establishment of collaborative goals with the person requiring the therapy. Therapy components include the improvement of existing coping strategies, the development and practice of new ones, the modification of delusional beliefs and beliefs about hallucinations and the challenge of dysfunctional schemas. Adaptive views of self are strengthened, including the re-evaluation of negative beliefs about the self.
- *Family interventions:* An intervention involving the individual's relatives, which can have several different aims. These include construction of an

alliance with relatives who care for the person with a psychotic disorder, reduction of adverse family atmosphere, enhancement of the capacity of relatives to anticipate and solve problems, maintenance of reasonable expectations for the person's performance, and attainment of desirable change in relatives' behaviour and belief systems.

- *Family psychoeducation:* Similar to psychoeducation for individuals, the following areas are usually covered for families: symptoms of psychosis, pharmacological and psychosocial treatments, and prevention of relapse, with a special focus on the role of the family. The intervention might be delivered to the relatives alone, involve the individual, or be delivered in a multifamily context. More active aspects such as coping skills might be involved, but the primary focus is the provision of information.
- *Integrated interventions:* Interventions that were explicitly defined as a combination of different treatments, for example individual CBT plus family intervention plus assertive outreach.
- *Mindfulness-based interventions (MF)*: The intervention consists of guided meditation followed by reflective group discussion aimed at facilitating understanding, or metacognitive insight. During meditation, participants bring full awareness to difficult voices, feelings, thoughts and images, and also become aware of habitual coping reactions, safety behaviours and their effects. In meditation they practice letting go of these reactions and learn to observe and allow psychotic experiences to come and go without reacting. Meditation and discussion lead to insight that struggling, judging and ruminating on psychotic experience creates distress, while mindful observation and acceptance of psychotic experience is empowering and calming.
- *Psychoeducation:* Psychoeducation can be defined as the education of a person with a psychiatric disorder in subject areas that serve the goals of treatment and rehabilitation. In individuals with a psychotic disorder, it usually covers the following topics: symptoms of psychosis, models of psychosis, effects and side-effects of medicine, maintenance medicine, psychotherapy for psychosis, early symptoms of relapse and relapse prevention.
- *Rehabilitation:* Usually includes a prevocational day programme, recreational and social activities, apartment living and transitional employment opportunities with the aim of increasing the ability of the person to function independently in the community.
- *Relapse prevention programmes:* Interventions that generally include education for recognizing early symptoms of relapse, a system of symptoms monitoring, and a crisis plan and intervention in case the symptoms increase over a certain threshold.
- *Telemedicine:* Individuals and their family members are regularly contacted via SMS or telephone call with the main aim of monitoring symptoms. If the symptoms appear to be above a certain threshold, an alert is activated and a visit with the clinician is organized.

Research gaps

- Most of the research is from HICs and, in general, psychological interventions have been developed in HICs. Further research is needed in LMICs.
- Many interventions have so far been investigated in only a few trials and individuals, and thus deserve further study.

Implementation considerations

- Not all forms of psychological interventions may be available in LMICs.
- Attempts should be made to involve family and carers in maintenance treatment.
- Family psychoeducation, a relatively simple intervention that has been proven effective, should be offered in all settings.
- Differences in mental health infrastructure and resources should be considered.
- Variations in cultural context should be considered. There may be acceptability issues.
- Country adaptation and translation of training materials and tools for the provision of psychological interventions is essential.
- Face-to-face psychological interventions delivered by service providers is human resource-intensive as they require substantial provider time, training and supervision.
- Integrating the provision of psychological interventions into primary care provides many advantages, including more holistic health care, increased accessibility of mental health services for people in need of care, opportunities for reducing the stigma of mental health problems and reduced costs.