VA/DoD Clinical Practice Guideline for the Management of First-Episode Psychosis and Schizophrenia
**Quick Reference Guide**

### Recommendations

The following evidence-based clinical practice recommendations were made using a systematic approach considering four domains as per the GRADE approach (see *Summary of Guideline Development Methodology* on page 19 in full CPG). These domains include: confidence in the quality of the evidence, balance of desirable and undesirable outcomes (i.e., benefits and harms), patient values and preferences and other implications (e.g., resource use, equity, acceptability).

<p>| Topic                                    | Sub-topic                        | #   | Recommendation                                                                 | Strengtha | Categoryb               |
|------------------------------------------|----------------------------------|-----|********************************************************************************|------------|-------------------------|
| Assessment and Evaluation                | Suspected Psychosis              | 1.  | For individuals with suspected psychosis, we suggest using evidence-based screening tools in specialty mental health settings to differentiate/identify individuals at risk for transition to psychosis. | Weak for   | Reviewed, New-added     |
|                                          |                                  | 2.  | For individuals with suspected psychosis, there is insufficient evidence to recommend for or against biomarker screening tools (e.g., magnetic resonance imaging–based prediction system, serum biomarker panels) to differentiate/identify individuals at risk for transition to psychosis. | Neither for nor against | Reviewed, New-added |
| Management of First-episode Psychosis and Schizophrenia | First-episode Psychosis          | 3.  | We recommend treatment/management with early intervention services for individuals with first-episode psychosis. | Strong for | Reviewed, New-added     |
|                                          |                                  | 4.  | We recommend the use of family interventions (including problem solving–based self-learning, education, and mutual family support) for individuals with first-episode psychosis. | Strong for | Reviewed, New-added     |
|                                          |                                  | 5.  | We suggest the use of the Individual Placement and Support model of supported employment for individuals with first-episode psychosis with a goal of employment and/or education. | Weak for   | Reviewed, New-added     |
|                                          |                                  | 6.  | There is insufficient evidence to recommend for or against any specific duration for participation in specialized early intervention services for individuals with first-episode psychosis. | Neither for nor against | Reviewed, New-added |
|                                          |                                  | 7.  | There is insufficient evidence to recommend for or against a specific duration for treatment with antipsychotic medication after response or remission for individuals with first-episode psychosis. | Neither for nor against | Reviewed, New-added |</p>
<table>
<thead>
<tr>
<th>Topic</th>
<th>Sub-topic</th>
<th>#</th>
<th>Recommendation</th>
<th>Strengtha</th>
<th>Categoryb</th>
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<tbody>
<tr>
<td>Pharmacologic Interventions for Psychosis</td>
<td></td>
<td>8.</td>
<td>We recommend the use of an antipsychotic medication other than clozapine for the treatment of an acute episode in individuals with schizophrenia or first-episode psychosis who have previously responded to antipsychotic medications. The choice of antipsychotic medication should be based on an individualized evaluation that considers patient characteristics and side effect profiles of the different antipsychotic medications.</td>
<td>Strong for</td>
<td>Reviewed, New-added</td>
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<td>9.</td>
<td>We recommend the use of an antipsychotic medication for the maintenance treatment of schizophrenia to prevent relapse and hospitalization in individuals with schizophrenia who have responded to treatment. Choice of antipsychotic medication should be based on an individualized evaluation that considers patient-specific characteristics and side effect profiles of the different antipsychotic medications.</td>
<td>Strong for</td>
<td>Reviewed, New-added</td>
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<td>10.</td>
<td>We suggest a trial of another antipsychotic medication for individuals with schizophrenia who do not respond to (or tolerate) an adequate trial of an antipsychotic medication. Choice of antipsychotic medication should be based on an individualized evaluation that considers patient-specific characteristics and side effect profiles of the different antipsychotic medications.</td>
<td>Weak for</td>
<td>Reviewed, New-added</td>
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<td>11.</td>
<td>We suggest offering long-acting injectable antipsychotics to improve medication adherence in individuals with schizophrenia.</td>
<td>Weak for</td>
<td>Reviewed, New-added</td>
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<tr>
<td></td>
<td></td>
<td>12.</td>
<td>We recommend the use of clozapine for individuals with treatment-resistant schizophrenia.</td>
<td>Strong for</td>
<td>Reviewed, New-added</td>
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<tr>
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<td>13.</td>
<td>We suggest augmenting clozapine with another second-generation antipsychotic medication for individuals with treatment-resistant schizophrenia who have not experienced an adequate response to clozapine.</td>
<td>Weak for</td>
<td>Reviewed, New-added</td>
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<tr>
<td>Pharmacologic Interventions for Side Effects</td>
<td></td>
<td>14.</td>
<td>There is insufficient evidence to recommend for or against any treatment for hyperprolactinemia-related side effects of antipsychotic medications in individuals with schizophrenia.</td>
<td>Neither for nor against</td>
<td>Reviewed, New-added</td>
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<td>15.</td>
<td>We suggest using metformin, topiramate, or aripiprazole augmentation for treatment of metabolic side effects of antipsychotic medication and weight loss for individuals with schizophrenia.</td>
<td>Weak for</td>
<td>Reviewed, New-added</td>
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<td>16.</td>
<td>We suggest a trial of a vesicular monoamine transporter 2 inhibitor for the treatment of tardive dyskinesia for individuals with schizophrenia and tardive dyskinesia.</td>
<td>Weak for</td>
<td>Reviewed, New-added</td>
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<td>17.</td>
<td>We suggest a trial of diphenhydramine for individuals with schizophrenia who are experiencing sialorrhea as a side effect of clozapine.</td>
<td>Weak for</td>
<td>Reviewed, New-added</td>
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<td></td>
<td>18.</td>
<td>There is insufficient evidence to recommend for or against augmentation with any non-antipsychotic medication for treatment of cognitive and/or negative symptoms for individuals with schizophrenia.</td>
<td>Neither for nor against</td>
<td>Reviewed, New-added</td>
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<td>19</td>
<td>We recommend the use of psychosocial interventions provided to a primary support person or family member to decrease the risk of relapse and hospitalization for individuals with schizophrenia.</td>
<td>Strong for</td>
<td>Reviewed, New-added</td>
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<td>20</td>
<td>We recommend the use of service models based on standard Assertive Community Treatment in individuals with schizophrenia evidencing severe functional impairments and/or risk for repeated hospitalizations.</td>
<td>Strong for</td>
<td>Reviewed, New-added</td>
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<td>21</td>
<td>We recommend the use of the Individual Placement and Support model of supported employment for individuals with schizophrenia with a goal of employment.</td>
<td>Strong for</td>
<td>Reviewed, New-added</td>
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<td></td>
<td></td>
<td>22</td>
<td>There is insufficient evidence to recommend any specific supported housing intervention over another for individuals with schizophrenia experiencing housing insecurity.</td>
<td>Neither for nor against</td>
<td>Reviewed, New-added</td>
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<td></td>
<td>23</td>
<td>We suggest compensatory cognitive training programs for the treatment of cognitive impairment for individuals with schizophrenia.</td>
<td>Weak for</td>
<td>Reviewed, New-added</td>
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<td>24</td>
<td>We suggest offering skills training for individuals with schizophrenia evidencing severe and persistent functional impairments and/or deficits in social, social-cognitive, and problem-solving skills.</td>
<td>Weak for</td>
<td>Reviewed, New-added</td>
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<td>25</td>
<td>There is insufficient evidence to recommend for or against transcranial direct current stimulation and repetitive transcranial magnetic stimulation for individuals with schizophrenia.</td>
<td>Neither for nor against</td>
<td>Reviewed, New-added</td>
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<td>26</td>
<td>There is insufficient evidence to recommend for or against electroconvulsive therapy for individuals with schizophrenia.</td>
<td>Neither for nor against</td>
<td>Reviewed, New-added</td>
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<td>27</td>
<td>There is insufficient evidence to recommend for or against the use of motivational interviewing or shared decision making to improve medication adherence for individuals with schizophrenia.</td>
<td>Neither for nor against</td>
<td>Reviewed, New-added</td>
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<td>28</td>
<td>There is insufficient evidence to recommend for or against the use of the Clubhouse model for vocational rehabilitation to increase employment outcomes for individuals with schizophrenia.</td>
<td>Neither for nor against</td>
<td>Reviewed, New-added</td>
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<td>29</td>
<td>There is insufficient evidence to recommend for or against the use of targeted peer-provided interventions for individuals with schizophrenia.</td>
<td>Neither for nor against</td>
<td>Reviewed, New-added</td>
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<td>30</td>
<td>We suggest adding aerobic exercise to treatment as usual to reduce symptoms and improve functioning for individuals with schizophrenia.</td>
<td>Weak for</td>
<td>Reviewed, New-added</td>
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<td>31</td>
<td>We suggest offering yoga as an adjunct to other evidence-based treatments for positive and negative symptoms for individuals with schizophrenia.</td>
<td>Weak for</td>
<td>Reviewed, New-added</td>
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<td>32</td>
<td>We suggest cognitive behavioral therapy for psychosis in combination with pharmacotherapy for individuals with prodromal and early psychosis.</td>
<td>Weak for</td>
<td>Reviewed, New-added</td>
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</table>
|       |           | 33. | We suggest the following psychotherapies and psychotherapeutic interventions in combination with pharmacotherapy for individuals with schizophrenia:  
- Cognitive behavioral therapy or cognitive behavioral therapy for psychosis,  
- Acceptance and mindfulness-based therapies,  
- Metacognitive therapy, or  
- Positive psychology interventions. | Weak for   | Reviewed, New-added             |
|       |           | 34. | There is insufficient evidence to recommend for or against Illness Management and Recovery in combination with pharmacotherapy for individuals with schizophrenia. | Neither for nor against | Reviewed, New-added          |
|       |           | 35. | There is insufficient evidence to recommend for or against virtual reality interventions, including avatar therapy, for individuals with schizophrenia. | Neither for nor against | Reviewed, New-added          |
|       |           | 36. | We suggest using telephone-based care management to reduce rehospitalization days for individuals with schizophrenia. | Weak for   | Reviewed, New-added          |
|       |           | 37. | There is insufficient evidence to recommend for or against augmenting pharmacotherapy with acupuncture to reduce negative and positive symptoms for individuals with schizophrenia. | Neither for nor against | Reviewed, New-added          |
|       |           | 38. | There is insufficient evidence to suggest case management to improve preventive screening and/or medical outcomes for individuals with schizophrenia. | Neither for nor against | Reviewed, New-added          |
|       |           | 39. | We recommend a face-to-face individualized smoking cessation intervention tailored specifically to the patient for individuals with schizophrenia. | Strong for | Reviewed, New-added          |
|       |           | 40. | We suggest the use of dietary interventions, exercise, individual lifestyle counseling, and/or psychoeducation for metabolic side effects of antipsychotic medication as well as the delivery of weight management services that are based on a chronic care model (e.g., Enhancing Quality of Care in Psychosis) for individuals with schizophrenia. | Weak for   | Reviewed, New-added          |
|       |           | 41. | There is insufficient evidence to recommend specific, integrated, non-integrated, or psychosocial treatments in addition to usual care for individuals with schizophrenia and comorbid substance use disorder. | Neither for nor against | Reviewed, New-added          |

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*a For additional information, see *Determining Recommendation Strength and Direction* on page 128 in the full CPG

*b For additional information, see *Recommendation Categorization* on page 130 in the full CPG
Algorithm

Shape          Description

Rounded rectangles represent a clinical state or condition

Hexagons represent a decision point in the process of care, formulated as a question that can be answered “Yes” or “No”

Rectangles represent an action in the process of care

Ovals represent a link to another section within the algorithm

The algorithm sidebars can be found on page 30 in the full CPG at https://www.healthquality.va.gov/

Appendix J (in the full CPG) contains the alternative text descriptions of the algorithm.
Module A: Primary Care Evaluation and Management of Suspected Psychosis or Possible Schizophrenia

1. Individual presenting with suspected psychosis (see Sidebar 1)

2. Evaluate safety concerns and other urgent needs (see Sidebar 2)

3. Are there safety concerns or urgent needs?
   - Yes → Refer to mental health or emergency department
   - No

4. Have diagnoses of a psychotic disorder because of another medical condition and substance/medication-induced psychotic disorder been excluded? (see Sidebar 3)
   - Yes → Refer to mental health specialty care
   - No

5. Complete assessment, treatment, and referrals, as appropriate, including mental health specialty care

8. Proceed to Module B as appropriate
Module B: Evaluation and Management of First-Episode Psychosis and Schizophrenia by Mental Health Providers

Individual with first-episode psychosis or an exacerbation of schizophrenia presents for evaluation/treatment

Are there urgent needs?

Yes

Consult/treat to address urgent needs (see Sidebar 2)

No

Is this a first episode of psychosis?

Yes

Refer to a coordinated specialty care program for first episode psychosis (see Sidebar 4)

No

Conduct clinical evaluation:

- Confirm diagnoses and rule out other conditions (see Sidebar 5)
- Evaluate severity and persistence of symptoms/impairments
- Identify comorbidities
- Review history
- Identify family/other supports
- Review patient treatment goals
- Provide psychoeducation about schizophrenia/psychotic disorder and its treatment

Use shared decision making to determine an individualized outpatient treatment plan; consider some or all of the following components:

- Engaging family and peer supports
- Stratifying for care management/coordinated care (see Sidebar 6) and addressing comorbidities (e.g., mental health, substance use, medical)
- Offering psychotherapy/psychosocial treatment (see Sidebar 6)
- Offering pharmacotherapy (see Module C)
- Monitoring to evaluate treatment outcomes (see Sidebar 7)

Are symptoms/impairments severe and/or persistent or have there been multiple previous episodes requiring hospitalization?

Yes

Consider referral to:

- Assertive Community Treatment (ACT) or, in VA, Intensive Community Mental Health Recovery services (ICMHR)
- Residential care programs
- Psychosocial Rehabilitation and Recovery Centers (see Sidebar 6)

No

Did the individual decline pharmacotherapy?

Yes

Revisit psychotherapy/psychosocial interventions (see Sidebar 6) along with psychoeducation and motivational interviewing

No

Go to Module C
Module C: Pharmacotherapy for Treatment of First-Episode Psychosis and Schizophrenia

1. Individual presents with a diagnosis of first-episode psychosis or schizophrenia (from Module B, Box 20)

2. Initiate/continue psychotherapy/psychosocial interventions (see Sidebar 6)

3. Is this an initial treatment of a first episode of psychosis?

4. No

5. Using shared decision making, choose antipsychotic medication, route of administration, and starting dose/rate of titration based on history of responses, adverse effects, adherence to previous treatment(s), comorbidities, and discussion of benefits versus side effects

6. Follow-up/reevaluate closely for 4–6 weeks after an initial short-term reevaluation within 1 week (including side effects); allow longer times for comorbid substance use, limited adherence, and slow titration based on aging or medical comorbidities

7. Is there an adequate treatment response?

8. Yes

9. Continue treatment with ongoing monitoring of response, side effects, and adherence

10. Evaluate at 3 months; allow longer times for comorbid substance use, limited adherence, and slow titration

11. Go to Box 37

12. No

13. Is the individual taking the medication as prescribed?

14. Yes

15. Are there side effects?

16. Yes

17. Manage side effects; consider:
   - Modifying dose
   - Changing medication(s)
   - Adding other medication directed toward side effects

18. No

19. Evaluate causes of non-adherence; address them through education, management of side effects, change to LAI, and psychosocial interventions

20. No

21. Is there an adequate treatment response?

22. Yes

23. Titrate dose; begin considering a change in medication if there is no response (go to Box 25)

24. No

25. Go to Box 37
Continued from Box 36

38 Are there significant residual positive or negative symptoms or impairments? (see Sidebar 6)

39 Have there been adequate trials of adequate dose and duration of at least two antipsychotic medications? (see Appendix E)

40 Consider change to another antipsychotic medication; go to Box 23

41 Are there significant antipsychotic medication side effects?

42 Yes

- Manage weight gain and metabolic side effects with any combination of diet, exercise, lifestyle interventions, and medication
- Manage extrapyramidal symptoms with anticholinergics/other medications
- Lower medication dose, if appropriate

43 Continue current medication with ongoing monitoring of response, side effects, and adherence

44 Consider de-prescribing unnecessary polypharmacy

45 Provide psychoeducation about clozapine, begin clozapine treatment, and mitigate risk following clozapine REMS guidelines (see Sidebar 7)

46 Has there been a response at 4–6 months? (see Sidebar 6)

47 Yes

- Continue treatment plan, follow-up, and adjust as appropriate

48 Partial response

- Consider augmentation with a second generation antipsychotic or ECT and adjust treatment plan, as appropriate

49 No response

- Consider changing to another antipsychotic medication to avoid side effects and risks of continued treatment with clozapine, adjust treatment plan, and follow-up, as appropriate

Abbreviations: ECT: electroconvulsive therapy; REMS: Risk Evaluation and Mitigation

Access to the full guideline and additional resources is available at: https://www.healthquality.va.gov/.