Introduction to VA/DoD Clinical Practice Guideline for the Management of Schizophrenia

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Grading Recommendations - GRADE

- Evidence-based clinical practice recommendations were developed based on the:
  - Evidence review, which was informed by 20 key questions
  - GRADE (Grading of Recommendations Assessment, Development and Evaluation) methodology and use of four decision domains to determine strength (*Strong* or *Weak*) and direction (*For* or *Against)* of each recommendation:
    - Confidence in the quality of evidence
    - Balance of desirable and undesirable outcomes
    - Values and preferences
    - Other implications, as appropriate (e.g., resource use)

Strength of a Recommendation

- Strength of a recommendation on a continuum:
  - ***Strong for*** (or "*We recommend*…")
  - ***Weak for*** (or "*We suggest*…")
  - ***Neither for nor against*** (or "*There is insufficient evidence*…")
  - ***Weak against*** (or "*We suggest against*…")
  - ***Strong against*** (or "*We recommend against*…")

Epidemiology and Impact on the General Population

- Globally, 24 million people (1 in 300) are living with schizophrenia.
- The age of onset in men is usually between 18 and 25, and in women onset occurs between age 25 and 30.
- In the U.S., individuals living with schizophrenia are also two to three times more likely to die prematurely than the general population, with individuals dying an average of 15 years sooner.
- Nearly 50% of individuals diagnosed with schizophrenia have co-occurring mental or behavioral health disorders.
- Schizophrenia is linked to higher rates of co-occurring medical conditions, potentially related to under-detection and under-treatment of underlying physical illnesses, especially chronic diseases such as coronary heart disease, stroke, type 2 diabetes, respiratory diseases, and some cancers.

Description of Schizophrenia

- Positive symptoms: deficits in perceptual, motor, cognitive, and emotional functioning. Perceptual deficits involve distortions in the reception of stimuli, such as hallucinations and delusions.
- Negative symptoms, referred to as deficit symptoms: cluster into two main components: diminished emotional expression and severe reduction in goal-directed activities because of lack of interest or drive. Negative symptoms are associated with detrimental effects on an individual's clinical and functional outcomes and QoL
- Cognitive dysfunction is a core feature of schizophrenia, observed much earlier in the course of the disorder and before the onset of psychotic symptoms. The cognitive impairments experienced by individuals with schizophrenia include non-social cognitive domains and social cognitive domains.
- A diagnosis of schizophrenia does not encompass all clinical presentations of psychotic symptoms.

VA patients with schizophrenia - 2021

- N=73,867 or 1.21% of total system users
- Age
  - 7.5% ≤ 35 years
  - 50.1% 35-65 years
  - 42.4% ≥ 65 years
- 90.3% men
- 54.5% White, 35.4% Black
- 68.4% service-connected disability
- 22.4% PTSD
- 28.0% drug or alcohol use dx
- 20.6% tobacco use disorder
- 30.5% diabetes
- 10.2% inpt MH past year
- 10.2% intensive case mgt
- 11.1% homeless services
- 3.9% high risk flag suicide
- 3.4% clozapine

Early episode patients in VA

- 4.1% of Veterans with schizophrenia
- Average age 26.7

Compared to those with schizophrenia, those with early episode had:

- More MH inpatient care (32.0% vs 10.2%)
- More PTSD (41.3% vs 22.4%)
- More drug and alcohol use disorder (48.1% vs 28.0%)
- More homeless services (19.6% vs 11.1%)
- More high risk flags-suicide (13.9% vs 3.9%)

Early episode patients in DoD

- FEP Incidence Rate (per 100,000) was 91.26 in 2020
- Incident diagnosis of first episode psychosis between October 2016 and September 2021 yielded a cohort of 3,857. Medical and personnel records from the year prior to and year after the diagnosis were analyzed.
  - Sex: Male (76.7%), Female (23.3%)
  - Race/ethnicity: White (68.2%), Black (10.6%), Hispanic (38.2%)
- Diagnostic outcomes among subsets without diagnosis in 12 months prior to index diagnosis
  - Anxiety – including PTSD (61.2%)
  - AUD (81.6%), SUD (90.7%)
  - Suicidal ideation (93.3%), Suicide attempt (56.6%)
  - Obesity (89.3%), Hyperlipidemia (95.9%)
- Of the 3,943 cohort members, 57% were separated from service by the close of the study observation window in 2020

Recommendations for First Episode Psychosis

Recommendations for the management of FEP

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

Selected Pharmacological Interventions and Somatic Treatments for Schizophrenia

Pharmacological Interventions for Treatment of Schizophrenia

- Basic principle:
  - 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.
- Recommendations for treatment of acute episodes
  - 8. We recommend starting treatment with a medication other than clozapine
  - 10. We suggest a trial of another antipsychotic if individuals who do not respond to an initial treatment
  - 11. We suggest use of a long-acting injectable medications to improve adherence
  - 12. We recommend use of clozapine for individuals with treatment-resistant schizophrenia
  - 13. We suggest augmenting clozapine with another 2nd generation antipsychotic if there has not been and adequate response to it.
- Recommendation for maintenance treatment
  - 9. After response, we recommend maintenance treatment with antipsychotics to prevent relapse and rehospitalization

Pharmacological Interventions -Other

- Pharmacological management of side effects
  - 14. We cannot recommend for or against any treatment for prolactin-related side effects.
  - 15. We suggest metformin, topiramate, or aripiprazole augmentation for metabolic side effects.
  - 16. We suggest vesicular monoamine transporter 2 inhibitors for tardive dyskinesia.
  - 17. We suggest diphenhydramine for clozapine-related sialorrhea.
- Other strategies for addressing side effects
  - 40. We suggest dietary interventions, exercise, lifestyle counseling, and/or psychoeducation for metabolic side effects of antipsychotic medication
- Management of coexisting conditions
  - 41. We cannot recommend for or against any treatments specifically for individuals with schizophrenia and comorbid substance use disorders.

Clozapine

- The guideline includes a “strong for” recommendation for use of clozapine for treatment-resistant schizophrenia.
- In addition, it is FDA-approved for reducing suicidal behavior in individuals with schizophrenia or schizoaffective disorder.
- However, clozapine use in VA (and most other systems) is low.
- All mental health providers should know how to prescribe clozapine, as outlined in sidebar 7 from the algorithm.
- Members of the workgroup believe that other mental health providers should be aware of the unique benefits and should advocate for its use when appropriate.

Sidebar 7: Clozapine Management

1. Provide the patient (and, where appropriate, the family) education about the benefits and risks of clozapine, and ensure their understanding and consent.
2. Ensure that the prescriber and the pharmacy are registered with Clozapine REMS.
3. Confirm indications for clozapine: treatment-resistant schizophrenia; schizophrenia or schizoaffective disorder with suicidality; or, possibly, schizophrenia with persistent aggressive behavior.
4. Evaluate symptoms and impairments with standardized assessment instruments.
5. Consider whether the patient might have BEN as defined by Clozapine REMS.
6. Register the patient with Clozapine REMS (NCCC).
7. Obtain and provide Clozapine REMS with a within-range absolute neutrophil count before prescribing and dispensing.
8. Prescribe clozapine starting at low doses with gradual titration to therapeutic doses and blood levels.
9. Monitor absolute neutrophil counts weekly for six months, then once every two weeks for six months, then monthly, thereafter; report results to Clozapine REMS.
10. Follow Clozapine REMS protocols for below-threshold absolute neutrophil counts indicating neutropenia or agranulocytosis

Other Somatic Treatments

- Although
  - The evidence review conducted to support development of these guideline identified promising early findings supporting the effectiveness and safety of transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS).
  - There is some evidence suggesting that augmentation with electroconvulsive therapy (ECT) may reduce symptoms in individuals with clozapine-resistant schizophrenia
- We cannot at this time recommend for or against the use of transcranial direct current stimulation (recommendation 25), or transcranial magnetic stimulation or electroconvulsive therapy (recommendation 26).

Selected Psychosocial Interventions for Schizophrenia: Highlights from the CPG

Overview

- There are effective psychosocial interventions for schizophrenia
- Treatment planning should
  - Use shared decision making
  - Be matched to individual goals
- Psychosocial interventions should be coordinated with
  - Other providers, including medication providers
  - Family, friends, and others of the individual's choosing
- Medication adherence is not a prerequisite for participation
- The goal is to promote recovery

Psychosocial Interventions

- Psychiatric Rehabilitation (PSR) practices
- Psychotherapies
- Other psychosocial treatments
- Supportive services

Principles of PSR

- Hope and empowerment
- Pragmatic
- Strengths-based
- Person-centered
- Comprehensive

How does the CPG methodology influence the PSR recommendations?

Methodology:

- CPG evidence is diagnosis specific (80% individuals with schizophrenia)
- PSR practices target non-symptom domains
- Much research on PSR is not specific to a diagnosis
- Foundational research is older than the search window
- Limited to 20 key questions

What does this mean?

- Important and relevant research may not be included
- Some practices considered by others to be evidence-based may not be included
- Recommended practices have a robust and rigorous evidence base

Psychiatric Rehabilitation practices

Strong for

- Assertive Community Treatment (and ICMHR)
- Individual Placement and Support (IPS, part of VHA Voc Rehab)

Weak for

- Skills training (e.g., social skills training, SST)
- Compensatory cognitive training

Insufficient evidence

- Peer support
- Housing First

Psychotherapies

Strong for:

- Family and caregiver interventions

Weak for:

- Cognitive Behavioral Therapy
- Cognitive Behavioral Therapy for psychosis
- Acceptance and mindfulness-based therapies
- Metacognitive therapy
- Positive psychology interventions

Other interventions

Strong for:

- Tailored smoking cessation

Weak for:

- Aerobic exercise
- Yoga
- Telephone-based care management

Supportive services

- Case management
- Housing supports
- Benefits counseling
- Support for financial literacy (banking, budgets, bill paying, etc.)
- Parenting assistance
- Legal support

Hypothetical Example

- XX is a 26-year-old man who comes to the VA for the first time 2 years after a medical discharge from the Army for schizophrenia.
  - He has been living with his parents and has been treated by a community psychiatrist with insurance coverage through his parents. Coverage terminated on his 26th birthday.
  - Treatment was limited to medications and supportive therapy.
  - He was treated for 1 year with olanzapine but he experienced weight gain. It was switched to aripiprazole. He says his hallucinations have decreased by 90%, but his still hears voices when he is stressed -- when his parents or (when he is working) his supervisors are critical. The voices are very distressing, and he avoids situations that provoke them.
  - Treatment adherence has been good, but he hasn't felt really okay since he was discharged from the Army.
  - He started in community college but dropped out because he couldn't concentrate. He got several entry-level jobs, but lost them because attendance and performance was erratic.
  - He feels awkward when he is with people.
  - Currently, he spends most of his time in his room in his parents' basement playing video games, avoiding his parents when possible because they are critical of him.
  - He smokes heavily but does not drink heavily or use other drugs.
  - He is depressed and has been thinking about suicide.
- What should be considered in planning his treatment?

Poll Question: Treatment considerations

A. treatment/management with early intervention services.
B. use of family interventions (including problem solving based self-learning, education, and mutual family support).
C. individuals with a goal of employment and/or education, use of the individual placement and support model of supported employment.
D. A. and C.
E. All of the above

What psychosocial and recovery-oriented treatments should be considered in treatment planning?

What psychosocial and recovery-oriented treatments should be considered in treatment planning?

What are the Veteran's goals?

What interventions would help this Veteran meet these goals?

Enter your answers in the chat!

- Earn a college degree
- Work at a job he finds meaningful
- Develop friendships
- Stop or reduce smoking
- Reduce symptoms of depression
- Better cope with hallucinations
- Live independently
- Improve relationship with parents

Poll Question
What is the next somatic treatment approach?

- Which recommendation is most relevant:
  - 9. After response, we recommend maintenance treatment with antipsychotics to prevent relapse and rehospitalization.
  - 10. For individuals with schizophrenia who do not respond to (or tolerate) an adequate trial of an antipsychotic medication, we suggest a trial of another antipsychotic medication. Choice of antipsychotic medication should be based on an individualized evaluation that considers patient characteristics and side effect profiles of the different antipsychotic medications.
  - 12. For individuals with treatment-resistant schizophrenia, we recommend the use of clozapine.
  - 25/26. Initiate a trial of tDCS, rTMS, or ECT.

Treatment Planning

- What other issues should be considered in treatment planning/shared decision-making?
  - Should the family be included in shared decision-making? (Covered in “Approach to Care …”)
  - Coordinating mental health w. primary medical care (? Rec. 38)
  - Suicidal ideation (Sec VII.C. Refers to the CPG for Assessment/ Management of Risk for Suicide)

Poll Question

When should the treatment plan be revised?

- (Check all that apply)
- When a course of treatment has been completed
- When adverse effects or non-adherence is observed
- When new interventions (or new evidence) emerges
- When there is a significant change in symptoms or functioning (improvement or worsening)
- When requested by the patient
- When the program I work in requires it
- At regular intervals to ensure that the Veteran's goals are being met
- Other (specify by chat)

Resources

Provider Education Resources

- SMI Adviser https://smiadviser.org/
- VA VISN 2 MIRECC https://www.mirecc.va.gov/visn2/
- VA VISN 5 MIRECC https://www.mirecc.va.gov/visn5/
- VA VISN 22 MIRECC https://www.mirecc.va.gov/visn22/

Consumer Education Resources

- NIMH https://www.nimh.nih.gov/health/topics/schizophrenia
- SMI Adviser https://smiadviser.org/
- VA Office of Mental Health and Suicide Prevention https://www.mentalhealth.va.gov/schizophrenia/index.asp

Support

- NAMI https://www.nami.org/home
- National Suicide Prevention Lifeline https://www.veteranscrisisline.net/

Resources

Treatment Locators

- Get Help from a TRICARE Provider or Treatment Facility https://tricare.mil/
- Get Help at VA https://www.va.gov/find-locations/
- Get Help in the Community https://findtreatment.samhsa.gov/
- Get Help for Recent Onset SMI https://www.samhsa.gov/esmi-treatment-locator
- Get Help for At-Risk/Early Psychosis https://med.stanford.edu/peppnet.html
- inTransition https://www.health.mil/Military-Health-Topics/Centers-of-Excellence/Psychological-Health-Center-of-Excellence/inTransition

Other

- VA Moving Forward https://www.veterantraining.va.gov/movingforward/
- Personal Story of Mental Illness https://youtu.be/usI6PDwMjcw

Audience Questions?