2023–2024

FLORIDA BEST PRACTICE
Psychotherapeutic Medication Guidelines
FOR ADULTS

UNIVERSITY of SOUTH FLORIDA
College of Behavioral & Community Sciences
Florida Center for Behavioral Health Improvements and Solutions

2023–2024 Florida Best Practice Psychotherapeutic Medication Guidelines for Adults

For treatment of mood disorders in pregnant and post-partum women visit https://floridabhcenter.org and see the Florida Best Practice Recommendations for Women of Reproductive Age with Serious Mental Illness and Comorbid Substance Use Disorders.

For more information, visit us at https://floridabhcenter.org.

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Purpose of the Guidelines

Introduction

Social and environmental factors are increasingly recognized for their impacts on health outcomes. Healthy People 2030 defines social determinants as "the conditions in the environments where people are born, live, learn, work, play, worship, and age that affect a wide range of health, functioning, and quality-of-life outcomes and risks" (U.S. Department of Health and Human Services Office of Disease Prevention and Health Promotion, Healthy People 2030, "Social Determinants of Health," 2021). Individuals who suffer from severe behavioral health disorders are at greater risk for lower educational achievement, decreased productivity, poverty, homelessness, substance use, involvement with the justice system, poorer physical health status, and overall lower quality of life. Conversely, individuals who experience social inequities such as poverty, housing instability, food insecurity, and lack of access to health services are at greater risk for developing mental health conditions such as depression and anxiety and for suffering from poorer physical health. Low social support has been linked to higher rates of post-partum depression in women, and studies on loneliness have found that feeling lonely at baseline has been associated with higher risk of major depressive disorder, depressive symptom severity, and generalized anxiety disorder. In addition, meta-analyses have shown associations between social connection and mortality, even when controlling for the effects of biological (e.g., age, initial health status, body mass index, blood pressure), psychological (depression, anxiety), and socioeconomic (education, income level) risk factors (Rico-Uribe, et al., 2018; Holt-Lunstad, 2018; Holt-Lunstad, 2022).

Prevalence of mental health conditions the United States is increasing; the most recent statistics estimate that more than one in five U.S. adults, or 57.8 million individuals, are living with mental illness. In 2021, approximately 14.1 million adults 18 years or older in the United States were diagnosed with a serious mental illness (SMI). The highest prevalence of serious mental illness was among young adults between 18 and 25 years old (National Institute of Mental Health, "Mental Illness," 2021). Young adults have been identified as a particularly vulnerable population because of higher rates of behavioral health concerns, emergence of new or worsening chronic health conditions, and low healthcare utilization. Supporting youth as they transition from pediatric to adult care involves emphasis on self-management, family and caregiver engagement, effective communication, recognition of cultural beliefs, health equity, and need for caregivers and parents to support youth and young adults as they develop the knowledge and skills to make their own healthcare decisions (White, et al., 2018). Yet, access to care is an ongoing concern due to the shortage of specialists required to address the growing need for behavioral health services. According to the most recent data published by the National Institute of Mental Health, the percentage of young adults 18-25 years with serious mental illness (SMI) who received mental health treatment was lower than adults with SMI aged 26-49 years and aged 50 years and older (National Institute of Mental Health, "Mental Health Services—SMI," 2023). To address these gaps in care, primary care clinicians are increasingly tasked with providing behavioral health services in the primary care setting, particularly in areas of critical need, since they serve as the first point of contact into the healthcare system. In the context of these challenges, providing quality care is especially challenging in the absence of clear, concise, evidence-based treatment recommendations.

Purpose

The purpose of the ***2023–2024 Florida Best Practice Psychotherapeutic Medication Guidelines for Adults*** is to guide clinicians who manage adults diagnosed with behavioral health conditions. These guidelines have evolved to reflect the most recent state of evidence, together with expert consensus when evidence is lacking. The guidelines cover a range of conditions that providers encounter in their clinical practice, including treatment of bipolar disorder, major depressive disorder, and schizophrenia. In this most recent iteration of the best practice guidelines, special considerations were given to transitions of care, treatment of behavioral health conditions in the primary care setting, and addressing the social factors that impact behavioral health status and treatment outcomes.

Process for Creating the Guidelines

The Florida Center for Behavioral Health Improvements and Solutions organizes a diverse group of stakeholders known as the Florida Expert Panel every two years to update the Florida Best Practice Psychotherapeutic Medication Guidelines for Adults. This year's Expert Panel was comprised of nationally recognized experts, academicians, medical directors of Florida Medicaid Managed Medical Assistance (MMA) health plans and community mental health centers, primary care providers, and pharmacists.

The 2023-2024 Florida Expert Panel met on April 8, 2023 to review and update the Florida Best Practice Psychotherapeutic Medication Guidelines for Adults. For each behavioral health condition, a psychiatrist who is a nationally recognized content expert conducted a full literature review, presented findings to the expert panel, and suggested revisions based on the current scientific evidence base. The panel then discussed the guidelines, proposed changes, and reached a consensus about whether or not to revise and adopt a particular set of revisions. The final guidelines are therefore a product of a thorough literature review with an emphasis on the highest level of clinical evidence (e.g., randomized controlled trials, systematic reviews), expert consensus, and consideration of safety and efficacy. The names of the meeting attendees and meeting presentations are available on the Florida Center for Behavioral Health Improvements and Solutions website at https://floridabhcenter.org. Financial disclosures are available upon request.

Organization

The ***2023–2024 Florida Best Practice Psychotherapeutic Medication Guidelines for Adults*** are based on a thorough literature review of the latest evidence, and, when evidence is lacking, clinical consensus on best practice recommendations. When scientific evidence is absent or findings are mixed, the guidelines note the absence of clear evidence and advise caution in treatment.

The guidelines are organized by levels of treatment recommendations, beginning with Level 1. Recommendations for each section (Levels 1, 2, 3, and 4) are categorized hierarchically based on the strength of evidence for the efficacy and safety regarding a particular treatment option. Thus, Level 1 has stronger empirical evidence for efficacy and/or safety than Level 2, and so forth.

A description of the guideline process and assignment of levels of recommendation are provided below to explain the bases for each level of treatment recommendations:

Level 1: Initial treatment for which there is established efficacy and relative safety for the treatment recommendations based on replicated, large randomized controlled trials and/or meta-analyses.

Level 2: Considered if Level 1 is ineffective and/or not well tolerated. Compared to Level 1, data on efficacy and/or safety in Level 2 are less robust based on smaller randomized controlled trials, cohort studies, or systematic reviews of Level 2 studies.

Level 3: Considered if Levels 1 and 2 are ineffective and/or not well tolerated. Treatments at this level have more limited efficacy data and/or more tolerability limitations than Levels 1 and 2. Data are from case-control studies, case series, or systematic reviews of Level 3 studies.

Level 4: Considered if Levels 1 through 3 are ineffective and/or not well tolerated; treatments are not well supported and are listed because of expert opinion and/or use in clinical practice.

Disclaimer

The ***2023–2024 Florida Best Practice Psychotherapeutic Medication Guidelines for Adults*** are based on the current state of scientific knowledge on the safety and effectiveness of various treatment options, as well as on clinical consensus judgements when research is lacking. The inevitable changes in the state of scientific knowledge require that periodic review, updates, and guideline revisions will be necessary. Treatment recommendations may not apply to all patients and must be tailored to the individual patient.

Proper use, adaptation, modifications, or decisions to disregard these or other guidelines, in whole or in part, are entirely the responsibility of the clinician who uses these guidelines. The authors and expert panel members bear no responsibility for treatment decisions and outcomes based on the use of these guidelines.

Treatment guidelines are available on the Program website: https://floridabhcenter.org.

- Best Practice Psychotherapeutic Medication Guidelines for Adults
- Autism Spectrum Disorder & Intellectual Developmental Disorder: Psychotherapeutic Medication Recommendations for Target Symptoms in Children and Adolescents
- Best Practice Recommendations for Women of Reproductive Age with Severe Mental Illness and Comorbid Substance Use Disorders
- Best Practice Psychotherapeutic Medication Guidelines for Children and Adolescents
- Monitoring Physical Health and Side-Effects of Psychotherapeutic Medications in Adults and Children: An Integrated Approach

If you would like hard copies of the guidelines, please email sabrinasingh@usf.edu.

Comprehensive Assessment

Conduct a comprehensive assessment. Rule out medical causes of behavioral symptoms. Use validated measures to assess and track psychiatric symptoms and impairment.

A comprehensive mental health assessment includes:

- Assessment of risk of harm to self or others
  - Assessment of the full range of psychiatric symptoms and disorders, including co-morbid substance use, as well as impairment from these symptoms and disorders
  - A thorough mental status exam
  - A full medical history
  - A relevant medical work-up and physical examination
  - Assessment of substance use, including tobacco use
  - Assessment of family psychiatric history, which includes psychiatric symptoms/treatment of family members, including substance use and treatment
  - During initial evaluation, when appropriate and with permission, contact a family member or close friend for additional history (past psychiatric history and additional psychosocial history)
  - Assessment for social determinants of health (e.g., housing instability/homelessness, food insecurity, education level, employment status)
- Ongoing management of behavioral health conditions includes:
  - Use of measurement-based care to measure and monitor symptoms and side effects
  - Close follow-up after psychotherapeutic medication prescribing to assess medication tolerability
  - Assessment of benefits and risks of treatment, including review of boxed warnings
  - Patient education of the benefits and risks of treatment, including review of boxed warnings
  - Monitoring of physical health parameters (See Program publication *Monitoring Physical Health and Side-Effects of Psychotherapeutic Medications in Adults and Children: An Integrated Approach* available at http://floridabhcenter.org/)
  - Assessment of social support system (housing, family, other caregivers)
  - Evaluation of threats to continuity of care (financial burden, housing instability, access to medication, medication adherence, etc.)
  - Provision of patient tools/support for recovery and self-management
  - For any individual who presents with a depressive component to their psychiatric symptoms, we strongly recommend routine and systematic screening for bipolar disorders. We advise the use of either the Rapid Mood Screener or the Mood Disorder Questionnaire.

Notes:

- *Effort should be made to communicate between primary care providers, psychiatrists, case workers, and other team members to ensure integrated care*
- *Incorporate collaborative/shared treatment decision-making with patients, family and caregivers*
- *Written informed consent should be obtained from the patient or the individual legally able to consent to medical interventions (e.g., pharmacotherapy), and documented in the chart*

Adjunctive Psychosocial Treatments (As Indicated)

- Individual and family psychoeducation
- Cognitive-behavioral therapy (CBT)
- Interpersonal psychotherapy (IPT)
- Interpersonal and social rhythm therapy (IPSRT)
- Family-focused therapy
- Group psychoeducation (especially for bipolar disorder)
- Social skills training (especially in schizophrenia)
- Cognitive remediation/rehabilitation (to improve attention, memory, and/or executive function)

Note on pharmacogenomics testing: Limited data exists examining whether patient care that integrates pharmacogenomic test information results in better or safer treatment.

Measurement-Based Care

Questionnaires and rating scales are useful tools for diagnostic assessment and evaluation of treatment outcomes, and such instruments can be helpful in providing information to supplement clinical judgement. The integration of measurement scales into routine clinical practice is suggested for each of the conditions covered in this document. Clinicians should use rating scales to assess symptom severity during the initial evaluation/treatment, when medication changes are implemented, and/or when the patient reports a change in symptoms.

- Treatment targets need to be precisely defined.
- Effectiveness and safety/tolerability of the medication treatment must be systematically assessed by methodical use of appropriate rating scales and side-effect assessment protocols.

Internet links to the following scales are available on the Program website: https://floridabhcenter.org/.

- Beck Depression Inventory (BDI)
- Brief Psychiatric Rating Scale (BPRS)
- Clinical Global Impression (CGI) Scale
- Clinician-Rated Dimensions of Psychosis Symptom Severity (CRDPSS)
- Hamilton Rating Scale for Depression (HAM-D)
- Montgomery-Asberg Depression Rating Scale (MADRS)
- Patient Health Questionnaire (PHQ-9)
- Positive and Negative Syndrome Scale (PANSS)
- Quick Inventory of Depression Symptomatology (QIDS)
- Young Mania Rating Scale (YMRS)

Table 1. Assessment Scales for Adult Behavioral Health Conditions

Measures	Bipolar Acute Depression	Bipolar Acute Mania	Bipolar 1 Cont/Main Therapy	Major Depression	Major Depression with Mixed Features	Major Depression with Psychosis	Schizophrenia
Beck Depression Inventory (BDI)	✔	—	—	✔	✔	✔	—
Brief Psychiatric Rating Scale (BPRS)	—	—	—	—	—	✔	✔
Clinical Global Impression (CGI) Scale	—	—	—	—	✔	—	✔
Clinician-Rated Dimensions of Psychosis Symptom Severity (CRDPSS)	—	—	—	—	—	✔	✔
Hamilton Rating Scale for Depression (HAM-D)	—	✔	—	—	—	✔	—
Montgomery-Asberg Depression Rating Scale (MADRS)	✔	✔	✔	—	✔	✔	—
Patient Health Questionnaire (PHQ-9)	✔	—	✔	✔	✔	—	—
Positive and Negative Syndrome Scale (PANSS)	—	—	—	—	—	✔	✔
Quick Inventory of Depression Symptomatology (QIDS)	✔	—	✔	✔	✔	—	—
Young Mania Rating Scale (YMRS)	✔	✔	✔	—	✔	—	—

Notes: The recommendations in this table are based on the evidence-base and clinical consensus. The Montgomery-Asberg Depression Rating Scale (MADRS) and Hamilton Rating Scale for Depression (HAM-D) can also used to assess symptoms of depression in major depressive disorder. Although the MADRS and HAM-D do not assess manic symptoms, these scales are recommended to evaluate depression symptoms in individuals presenting with bipolar mania (e.g., to rule out bipolar disorder – mixed features) and to assess for depressive symptoms among individuals on maintenance treatment for bipolar disorder.

List of Antipsychotic Medications Available in the United States:

- **First Generation Antipsychotics (FGAs):** chlorpromazine, fluphenazine*, haloperidol*, loxapine, perphenazine, thioridazine, thiothixene, and trifluoperazine
- **Second Generation Antipsychotics (SGAs):** aripiprazole*, asenapine, brexpiprazole, cariprazine, clozapine, iloperidone, lurasidone, lumateperone‡, olanzapine*‡, paliperidone*, quetiapine, risperidone*, and ziprasidone

Notes:

Medications indicated by a single asterisk (*) are available in long-acting injectable formulations (refer to list below).

‡Lumateperone was introduced in 2019. Olanzapine/samidorphan was introduced in 2021.

List of Long-Acting Injectable Antipsychotic (LAI) Medications Available in the United States:

- **First Generation Antipsychotics (FGAs):** fluphenazine decanoate, haloperidol decanoate
- **Second Generation Antipsychotics (SGAs):** aripiprazole monohydrate, aripiprazole lauroxil, olanzapine pamoate, paliperidone palmitate, risperidone microspheres

Treatment with Antipsychotic Medication

Selection of antipsychotic medication with well-informed patients should be made on the basis of evidence-based guideline recommendations for a particular behavioral health condition, prior individual treatment response, side-effect experience, medication side-effect profile, and long-term treatment planning. Treatment with antipsychotic medications should take into account the following:

- First generation antipsychotics (FGAs) and second generation antipsychotics (SGAs) are heterogeneous within the class and differ in many properties, such as efficacy, side-effects, and pharmacology.
- Antipsychotics carry extrapyramidal symptoms (EPS) liability and metabolic effects. Caution should be used in prescribing antipsychotic medication in the context of dementia, anxiety disorders, and impulse control disorders. For these conditions, antipsychotic utilization should be:
  - Aimed at target symptoms
  - Prescribed only after other alternative treatments have been tried
  - Used in the short-term
  - Monitored with periodic re-evaluation of benefits and risks
  - Prescribed at the minimal effective dose

Note: The Food and Drug Administration (FDA) has issued a boxed warning that elderly patients with dementia-related psychosis treated with FGAs or SGAs have an increased risk of death.

Achieving Optimal Outcomes with Currently Available Antipsychotics

STEP 1. Considerations for selecting the most appropriate antipsychotic for a particular patient:

- Broadly equivalent efficacy across agents for psychotic symptoms (note clozapine exception in schizophrenia)
- Individual variability in response
- No reliable pre-treatment predictor of individual response to different agents
- Different agents have different side-effects and safety profiles
- Individual patients have different vulnerabilities and preferences
- Potential risk of non-adherence to oral antipsychotics
- Objective is to achieve therapeutic objective without EPS

STEP 2. Good practice guidelines for ongoing antipsychotic treatment:

- Measurement-based individualized care
- Repeated assessment of efficacy using reliably defined treatment targets for psychotic symptoms (use standard rating scales, e.g. CRDPSS, CGI, BPRS, PANSS)
- Careful assessment and measurement of adverse effects
- Care consistent with health monitoring protocols
- Standard protocols customized to individual vulnerabilities/needs and specific agent
- Ongoing collaboration with patient in decision-making

Notes:

CRDPSS = Clinician-Rated Dimensions of Psychosis Symptom Severity; CGI = Clinical Global Impressions Scale; BPRS= Brief Psychiatric Rating Scale; PANSS = Positive and Negative Syndrome Scale

Box 1. Factors that Contribute to Poor Medication Adherence

Remember to Assess for Medication Adherence

Factors that contribute to poor medication adherence include:

- Poor health literacy
- Lack of involvement in the treatment decision-making process
- Complex drug regimens
- Ineffective communication about adverse effects
- Limited access to care

Considerations in Managing Inadequate Treatment Response

- Re-assess symptoms and diagnosis, including use of standardized diagnostic tools
- Assess treatment adherence, including tolerability of medications and potential drug-drug interactions
- Assess for adequate treatment trials, including dose/duration of treatment
- Switch treatment if initial trials are inadequate after re-assessment of symptoms, diagnosis, tolerability, and adequacy of treatment
- For schizophrenia spectrum disorders, consider LAI if nonadherent to oral medication; consider clozapine if refractory to treatment (see sections on Treatment of Schizophrenia and Treatment of Schizophrenia with LAIs)

Considerations for Transition from Pediatric to Adult Care

- Transition is the process that involves preparation steps before an individual leaves pediatric care and moves to an adult provider.
- Poor care coordination, lack of resources, and inadequate planning are some factors identified as obstacles to a smooth transition of care.
- Both pediatric and adult providers play a role in supporting individuals to ensure a smooth transition.
- Initiate conversation early to ease the transition.
- Recognize the role of developmental differences through adolescence and young adulthood on patient engagement and treatment adherence.

Resources

Below is a list of national and local resources for adults with serious mental illness (SMI).

National Resources:

- American Psychiatric Association: https://www.psychiatry.org/
- American Psychological Association: https://www.apa.org/
- Brain and Behavior Research Foundation: http://bbrfoundation.org/
- National Alliance on Mental Illness (NAMI): https://www.nami.org/
- National Council for Behavioral Health: https://www.thenationalcouncil.org/
- Depression and Bipolar Support Alliance (DBSA): http://www.dbsalliance.org/
- National Institute of Mental Health: https://www.nimh.nih.gov/index.shtml
- Mental Health America (MHA): http://www.mentalhealthamerica.net/
- Substance Abuse and Mental Health Services Administration (SAMHSA): http://www.samhsa.gov/
- Suicide Prevention Resource Center: http://www.sprc.org/
- U.S. Department of Health and Human Services: https://www.mentalhealth.gov/
- Hearing Voices Network: http://www.hearingvoicesusa.org/

Local Resources:

- Florida Center for Behavioral Health Improvements and Solutions: https://floridabhcenter.org/
- Aunt Bertha Web-Based Resource Guide: https://www.findhelp.org/
- Florida Academy of Family Physicians (FAFP): http://www.fafp.org/
- Florida Association of Nurse Practitioners (FLANP): http://flanp.org/
- Florida Council for Community Mental Health (FCCMH): http://www.fccmh.org/
- Florida Medical Association (FMA): http://www.flmedical.org/
- Florida Osteopathic Medical Association (FOMA): http://www.foma.org/
- Florida Psychiatric Society (FPS): http://www.floridapsych.org/
- Florida Society of Neurology (FSN): https://fsneuro.org/
- National Alliance on Mental Illness (NAMI) Florida: http://www.namiflorida.org/
- Peer Support Coalition of Florida: https://www.peersupportfl.org/

For updated links to resources, visit floridabhcenter.org.

Summary: Transition from Pediatric to Adult Care

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1. **Transition is different from transfer**
   a. Transition is a long process that involves preparation steps before leaving pediatric care, a move to an adult provider (if necessary) and some time getting integrated into adult care.
   b. Transfer is the name we give to the move to adult care.
   c. Because transition involves both the preparation to get ready for adult care and some time integrating into adult care, both pediatric and adult providers play a role.
2. **For medical care, the general framework for addressing transition in the clinical setting is called the Six Core Elements of Transition.**
   a. This was developed by Got Transition®, a program of The National Alliance to Advance Adolescent Health, supported by Health Resources and Services Administration (HRSA) and Maternal and Child Health Bureau (MCHB).
   b. They were also endorsed in the transition guidelines developed by the American Academy of Pediatrics (AAP), the American College of Physicians (ACP), and the American Academy of Family Physicians (AAFP), published in 2018.
   c. Many of the published studies to improve transition in medical settings has used all or part of this framework as the foundation for the intervention.
3. **The Six Core Elements are:**
   a. Transition Policy – to be introduced between 12 years old and 14 years old.
      i. This introduction can be brief but removes some of the shock of talking about transfer too late.
      ii. Should be introduced at a time of calm.
   b. Transition tracking and monitoring – from 14 years old until transfer
      i. Clinics should be aware of how each adolescent patient is moving through the recommended preparation steps for transition and tracking this to help patients who are behind and using completion of the steps as a guide for determining transfer.
   c. Transition readiness – from 14 years old until transfer
      i. Adolescents should have a readiness assessment completed periodically (at least once a year) to monitor their readiness.
      ii. This is one of the elements that should be tracked in part (b)
   d. Transition planning – from 14 years old until transfer
      i. Includes helping patients assume more responsibility for their care, such as getting refills and scheduling appointments.
      ii. Also includes giving patients/families time to identify a preferred adult provider.
      iii. Should include getting a care summary ready, like keeping the problem list and medication list up-to-date.

e. Transfer to an adult provider – generally expected between 18 years old and 21 years old
    i. Pediatric provider roles: 1) Assist with scheduling with an adult provider, 2) Prepare a brief care summary for the patient to take to the new provider, 3) Remain available to the patient/family and the adult care team for questions.
    ii. Key Care Summary Components for Primary care:
        1. Up-to-date problem list
        2. Accurate medication list
        3. Allergies and serious intolerances
        4. Vaccines
    iii. Care summary components to consider for mental health
        1. Recent diagnostic or monitoring results [such as the last 2-3 Patient Health Questionnaire (PHQ-9) scores or recent IQ testing]
        2. Other members of the care team (if known), such as the patient's counselor
    iv. Adult provider roles: 1) Review any materials sent by the pediatric provider or patient/family in advance, 2) Consider having a "welcome packet" for new young adult patients (and perhaps all new patients) with information like how to schedule appointments, how to call the on-call provider, how to call for refills, etc.), 3) Consider scheduling new young adult patients in the early or late visits of a clinic session to allow them to have more time.
f. Integration into Adult Care – from the first adult appointment until about age 26 years old
    i. May involve some back-and-forth between pediatric and adult care for a period of time
    ii. Adult providers should be prepared to provide developmentally appropriate care for young adults, including being patient with questions, recognizing that full adult decision-making ability is not reached until 25-30 years of age, and supporting young adults if they bring parents/caregivers to appointments.
    iii. Adult providers should give the young adult time alone regularly, and especially during the first visit.
    iv. Adult providers should acknowledge the lived experience of the young adult and their caregiver with respect to their medical history, especially if the patient has a diagnosis with which the provider is less familiar.

4. Transition considerations more specific to mental health care

a. Having clear roles for care providers for students who are away at college (ex. Is campus health going to be refilling medications or not? Does the patient need/have a pharmacy at school?)
b. Transferring during a time of stability so as not to further exacerbate a mental health crisis
c. Making accommodations for those with new-onset conditions, particular serious mental illnesses like schizophrenia

5. Transition considerations more specific to those with developmental disabilities

a. Discuss Individualized Education Plan (IEP) transition planning through school as part of transition planning and tracking during the adolescent years
b. Addressing guardianship / supported-decision making (ideally before transfer)
c. Assessing for resource needs, such as navigating changes in insurance and the Social Security Disability Insurance (SSDI) program
d. Making sure family has considered back-up caregiving if the main caregiver is unavailable

Resources

- Moving Into Adulthood Resource Center (aacap.org) – Resources for young people and their families as they make the move to adulthood, both healthcare-related and covering other topics. Specifically from the American Academy of Child and Adolescent Psychiatrists; last updated in 2019.
- Got Transition® – Resources for young people, their parents and caregivers, and clinicians who care for adolescents and young adults and want to address transition more consistently in their practice. Site for materials related to the Six Core Elements and how to implement them. Seeks to be a repository for all patients and the providers who care for them, so not specifically focused on mental health care. Does give some consideration regarding developmental disabilities. Updated regularly.
- The Transitions to Adulthood Center for Research | Transitions ACR (umassmed.edu) – Rocused on the education-to-work transition for youth with mental health conditions.
- Types of Guardianship - Disability Rights Florida – Reviews guardianship and guardianship alternatives and is specific to Florida, which is helpful because states vary in how they address certain guardianship issues.
- Aunt Bertha (https://www.findhelp.org/) – Provides a number of resources for people with all sorts of social needs; for transition, contains links to the county board of developmental disabilities and offices of vocational rehabilitation.
- Florida Education Transition Resources (https://fcsua.org/K_transition.php) – Reviews the requirements and recommendations for transition planning in the education system and links to some other Florida-specific and national resources to support the move from education to the work force for adolescents with disabilities.

Summary: The Social Determinants of Mental Health

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What Are Social Determinants of Mental Health?

Social determinants of health are societal problems affecting communities, families, and individuals that interfere with achieving optimal health and that increase risk for illnesses. Extensive research documents the social determinants that underpin diseases like diabetes, cardiovascular disease, chronic obstructive pulmonary disease, and sexually transmitted infections. The same societal problems that comprise social determinants of health are also social determinants of mental health. That is, the determinants that increase risk for diabetes, for example, also increase risk for psychiatric disorders such as major depressive disorder, and for substance use disorders like alcohol use disorder and opioid use disorder. While the social determinants are seen as "the causes of the causes" (predating and predicting onset of illness), they are also drivers of poorer course and outcomes among those with existing conditions.

Before further defining the social determinants of mental health, three conceptual points are noteworthy. First, the social determinants are responsible for health inequities—defined as differences in health status that are the result of unjust, unfair, and avoidable social and economic policies—as well as mental health inequities. Thus, effectively working to address the social determinants of mental health will not only reduce risk and prevalence, but will lead to the reduction and ultimately the eradication of mental health inequities. Second, the social determinants perspective gives us a path for pursuing prevention. That is, in addition to the usual categorizations of prevention (primary, secondary, and tertiary, as well as the more recent framework of universal, selective, and indicated preventive interventions), the social determinants framework gives the mental health field an additional set of lenses for understanding how to engage in the prevention of mental illnesses and substance use disorders, and the promotion of mental health. Third, although it is difficult to prove, it is likely that the social determinants have a more potent effect on mental health and mental illnesses than they do on physical health and physical illnesses. This is partly because the mechanism is relatively easy to trace (e.g., from ongoing psychological stress that the social determinants cause to altered physiologic functioning). It also relates to the unfortunate fact that, because of stigma and discrimination against individuals with serious mental illnesses, those individuals tend to experience the very social outcomes (e.g., unemployment, housing instability, poor access to healthcare) that are the social determinants of course and outcomes of both mental and physical conditions.

Enumerating the Social Determinants of Mental Health

- In considering the social determinants of mental health more specifically, at least 16 different types of social determinants (although many are interconnected and interact closely with one another) can be identified, which can be placed into four broad categories. The first includes pervasive, highly detrimental U.S. societal problems that should be top priorities, from a health perspective, of policymaking and policy change:
  - Adverse early life experiences (traumatic events) and childhood maltreatment
  - Discrimination (based on race and ethnicity, gender, LGBTQ status, religion, immigrant status, disability, age, etc.) and the related social exclusion and social isolation

- Exposure to conflict, violence, shootings, war, forced migration, immigration trauma, and related issues
- Involvement and interaction with the criminal justice system

- Another category pertains to socioeconomic status and is intimately related to opportunities for accruing wealth (and thus for optimizing health):
  - Low educational attainment, poor quality of education, and educational inequalities
  - Unemployment, under-employment, and job insecurity
  - Poverty, income inequality, and wealth inequality
  - Area-level poverty and concentrated neighborhood poverty
- Yet another category relates to basic needs in terms of housing, food, transportation, and health care:
  - Homelessness, poor housing quality, and housing instability
  - Food insecurity and poor dietary quality
  - Poor or unequal access to transportation
  - Being uninsured, being under-insured, loss of insurance, and poor access to health care
- The final category concerns the immediate and global physical environment:
  - Adverse features of the built environment (e.g., the transportation infrastructure, the energy infrastructure, building design, city planning, extent of access to natural environments and green space)
  - Neighborhood disorder, disarray, and disconnection
  - Exposure to pollution (air, water, and soil pollution)
  - Exposure to the impacts of global climate change

The social determinants underpin physical health and mental health conditions through diverse mechanisms. For example, at the individual level, struggling with social needs (such as food insecurity) leads to chronic psychological stress, which can impact upon physiological stress response systems. They are also associated with reduced options (which are sometimes naively referred to as "poor choices"); food insecurity is associated with a reliance on an energy-dense, micronutrient-deficient diet (as limited food dollars are used to purchase the most calories in the most efficient and cost-effective way). In addition to their direct effects, social determinants likely interact with genetic constitution in complex ways, including gene-by-environment interactions and epigenetics.

Understanding the Underpinnings of the Social Determinants of Mental Health

Each of the 16 types of social determinants can have a negative impact on health, can increase risk for illnesses, and can worsen outcomes among those with existing illnesses; each can also make it harder to attain optimal mental health, which is more than just the absence of mental illness. The social determinants of mental health increase risk for and prevalence of mental illnesses and substance use disorders, and among those living with a behavioral health disorder, they complicate the course and worsen outcomes. As noted, the social determinants of mental health are interconnected—individuals, families, or communities are often affected by multiple social determinants at the same time. That co-occurrence suggests common underlying factors that, if addressed at a deeper level, would likely help to address many social determinants rather than one at a time. Based on one conceptualization (Compton & Shim, 2015), the common, unifying foundation setting the stage for each of the social determinants is unfair and unjust distribution of opportunity. Opportunity pertains to power, empowerment, voice, access to resources, and advantages. At an even deeper level, two

fundamental elements consistently drive the unfair and unjust distribution of opportunity: public policies (those societal conventions that are codified, such as laws, ordinances, rules, regulations, and court decisions), and social norms (those societal conventions that are imprinted upon minds rather than being printed on paper: the attitudes, biases, and opinions that groups of people have toward other groups of people). Addressing the social determinants of mental health ultimately requires changing public policies and changing social norms. Importantly, public policies shape social norms, and social norms shape public policies. As such, although both must be addressed for us to achieve most robust results, changing one is likely to have some impact on the other.

Reference:

Compton MT and Shim RS, Ed. The Social Determinants of Mental Health. Washington, DC: American Psychiatric Publishing; 2019. ISBN-13: 978-1-58562-477-5.

Box 2. Assessment Scales for Adult Acute Bipolar Depression

- Beck Depression Inventory (BDI)
- Montgomery-Asberg Depression Rating Scale (MADRS)
- Patient Health Questionairre-9 (PHQ-9)
- Quick Inventory of Depression Symptomotology (QIDS)
- Young Mania Rating Scale (YMRS)

**Notes: The recommendations are based on the evidence-base and clinical consensus. The Montgomery-Asberg Depression Rating Scale (MADRS) and Hamilton Rating Scale for Depression (HAM-D) can also be used to assess symptoms of depression in major depressive disorder.*

Note: Treatment recommendations are based on levels of evidence and expert opinion. For a description of the criteria for each level, see pages 2-3.

Conduct comprehensive assessment and use measurement-based care. Refer to Principles of Practice on pages 4-9.

The primary therapeutic objectives of bipolar disorder care are to achieve symptomatic remission, promote syndromal recovery, prevent recurrence, and facilitate full functional recovery.

- Selection of acute treatment should take maintenance treatment goals into account.
- Be aware of safety and tolerability concerns, evidence for maintenance use, and acute efficacy.
- Revisit the appropriateness of current regimen (e.g. inappropriate polypharmacy)

Strongly recommend psychiatric consultation prior to initiation of therapy + psychotherapeutic medication using a multi-disciplinary approach if treated by a non-psychiatrist.

Level 1 Options for initial treatment:

- More than one Level 1 trial is recommended before moving to Level 2. (See tables 2 - 4.)

Note: Only quetiapine and lumateperone are FDA approved in bipolar disorder II (BD-II) depression. Both are efficacious in BD-II but inferior tolerability with quetiapine largely due to sedation and weight/metabolic adverse events.

- Lurasidone or cariprazine monotherapy*

**Note: Lurasidone, lumetaperone, and cariprazine have better metabolic profiles than quetiapine.*

- Lumateperone as monotherapy or adjunctive in bipolar disorder I (BD-I) or bipolar disorder II (BD-II) depression
- Lamotrigine monotherapy
- Quetiapine or quetiapine XR monotherapy if the patient has bipolar I or bipolar II depression
- Lithium monotherapy
- Lurasidone or lamotrigine, like lumetaperone, can be considered adjunctive to lithium or divalproex if index agent (lithium or divalproex) has been previously prescribed and optimized. Adjunctive data for cariprazine not available, but cariprazine could be considered as alternative adjunct.

***Caution: There is a drug-drug interaction with use of lamotrigine and divalproex together that requires reducing the lamotrigine dose by 50% of the typical lamotrigine dose. For dosing recommendations, refer to Table 3 on pages 22-23.*

- Do not utilize conventional antidepressants (e.g., SSRIs, SNRIs, TCAs, MAOIs) as a first-line therapy.

Table 2. Second Generation Antipsychotic Drugs in Bipolar Depression

	Monotherapy		Adjunctive (to lithium or valproate)	
	Bipolar I	Bipolar II	Bipolar I	Bipolar II
Lumateperone	X	X	X	X
Quetiapine	X	X		
Olanzapine/Fluoxetine	X			
Lurasidone	X		X	
Cariprazine	X			

Level 2 If multiple Level 1 trials are ineffective and/or not well tolerated:

- Divalproex + lurasidone
- Olanzapine + fluoxetine (bipolar I disorder)

**Note: Tolerability limitations include weight gain and metabolic concerns.*

- Two (2) drug combination of Level 1 medications but NOT TWO antipsychotic medications.

**Note: Efficacy limitations, relatively few positive randomized controlled trials.*

Level 3 If Levels 1 and 2 are ineffective and/or not well tolerated:

- Electroconvulsive therapy (ECT)

**Note: Consideration is merited due to clinical need, despite even greater efficacy/tolerability limitations than Level 1 and 2 treatments.*

- Repetitive transcranial magnetic stimulation (rTMS) [Less robust evidence for efficacy compared to ECT; accumulating evidence for use in bipolar depression.]

Level 4 If Levels 1 – 3 are ineffective and/or not well tolerated:

- Intravenous racemic ketamine and/or esketamine
- FDA-approved agent for bipolar disorder + conventional antidepressant (e.g., SSRI)*
- Pramipexole
- Adjunctive: Armodafinil or modafanil, thyroid hormone (T3), or stimulants
- Three (3) drug combination

**Notes:*

- *Antidepressant monotherapy is not recommended in bipolar I depression; recommendation is for adjunctive mood stabilizer with antidepressant.*
- *The safety and efficacy of antidepressant monotherapy in bipolar II depression is uncertain but may be appropriate in select circumstances.*

Treatment of Acute Bipolar Disorder – Mania

Box 3. Assessment Scales for Adult Acute Bipolar Mania

- Hamilton Rating Scale for Depression (HAM-D)
- Montgomery-Asbergy Depression Rating Scale (MADRS)
- Young Mania Rating Scale (YMRS)

**Notes: The recommendations are based on the evidence-base and clinical consensus. Although the MADRS and HAM-D do not assess manic symptoms, these scales are recommended to evaluate depression symptoms in individuals presenting with bipolar mania (e.g., to rule out bipolar disorder – mixed features) and to assess for depressive symptoms among individuals on maintenance treatment for bipolar disorder.*

Note: Treatment recommendations are based on levels of evidence and expert opinion. For a description of the criteria for each level, see pages 2-3.

Conduct comprehensive assessment and use measurement-based care. Refer to Principles of Practice on pages 4-9.

The primary therapeutic objectives of bipolar disorder care are safety, symptomatic improvement, and patient psychoeducation.

- Selection of acute treatment should take maintenance treatment goals into account.
- Be aware of safety and tolerability concern, evidence for maintenance use, and acute efficacy.

Strongly recommend psychiatric consultation prior to initiation of therapy + psychotherapeutic medication using a multi-disciplinary approach if treated by a non-psychiatrist.

Level 1A Options for initial treatment:

Mild to moderate severity and/or not requiring hospitalization

- Lithium* monotherapy
- Monotherapy with aripiprazole, asenapine, divalproex*, quetiapine, risperidone, ziprasidone, or cariprazine
- Lithium* or divalproex* + aripiprazole, asenapine, quetiapine, risperidone, or cariprazine
- Electroconvulsive therapy (ECT) is recommended if medical emergency/patient welfare at risk and pharmacotherapy is insufficient
- Olanzapine/samidorphan monotherapy or adjunct to lithium or valproate

Level 1B If multiple Level 1A trials are ineffective and/or not well tolerated:

Mild to moderate severity

- Monotherapy with either haloperidol or olanzapine

Level 2 If Levels 1A and 1B are ineffective and/or not well tolerated:

- Combination treatment with lithium* + divalproex*
- Combination with lithium* and/or divalproex* + second generation antipsychotic (SGA) other than clozapine
- Carbamazepine* monotherapy

Level 3 If Levels 1 and 2 are ineffective and/or not well tolerated:

- Electroconvulsive therapy (ECT)
- Clozapine + lithium* or divalproex*
- Lithium* + carbamazepine*
- Divalproex* + carbamazepine*

Level 4 If Levels 1 – 3 are ineffective and/or not well tolerated:

- A three (3)-drug combination of Level 1, 2, and 3. Drugs may include first generation antipsychotic (FGA) or second-generation antipsychotic (SGA) but NOT TWO antipsychotic medications.

Example: Lithium* + (divalproex* or carbamazepine*) + antipsychotic

Notes:

**Caution should be used when prescribing lithium, lamotrigine, divalproex or carbamazepine to women of reproductive age due to increased risk to the fetus with use during pregnancy, including neural tube and other major birth defects. The risk of divalproex use during pregnancy may be higher in reference to pregnancy-associated safety risk. Please see Florida Best Practice Recommendations for Women of Reproductive Age with Serious Mental Illness and Comorbid Substance Use Disorders and online guideline on the Pharmacological Treatment of Mood Disorders During Pregnancy available at https://floridabhcenter.org.*

***Side-effect concerns with these agents include weight gain, metabolic syndrome, and extrapyramidal symptoms (EPS). Side-effects warrant vigilance and close monitoring on the part of the clinicians.*

Data for use of paliperidone to treat bipolar mania are mixed. Paliperidone greater than 6mg has some data supporting efficacy.

Benzodiazepines may be used as an adjunct treatment for acute treatment of bipolar mania.

Box 4. Assessment Scales for Adult Bipolar I Disorder Continuation/ Maintenance Therapy

- Montgomery-Asberg Depression Rating Scale (MADRS)
- Patient Health Questionairre-9 (PHQ-9)
- Quick Inventory of Depression Symptomatology (QIDS)
- Young Mania Rating Scale (YMRS)

**Notes: The recommendations are based on the evidence-base and clinical consensus. Although the MADRS and HAM-D do not assess manic symptoms, these scales are recommended to evaluate depression symptoms in individuals presenting with bipolar mania (e.g., to rule out bipolar disorder – mixed features) and to assess for depressive symptoms among individuals on maintenance treatment for bipolar disorder.*

Note: Treatment recommendations are based on levels of evidence and expert opinion. For a description of the criteria for each level, see pages 2-3.

Conduct comprehensive assessment and use measurement-based care. Refer to Principles of Practice on pages 4-9.

The list of possible treatments in the prevention of bipolar disorder is comprised of many treatment options; therefore, the regimen that stabilizes a patient should be strongly considered for continuation and maintenance (monitoring for efficacy and adverse events).

Strongly recommend psychiatric consultation prior to initiation of therapy + psychotherapeutic medication using a multi-disciplinary approach if treat by a non-psychiatrist.

Level 1 Options for initial treatment:

- Periodic evaluation: frequency based on clinical needs
- Continue with effective and well-tolerated treatment
- Lithium* monotherapy
- Quetiapine monotherapy
- Lamotrigine* (evidence strongest for prevention of depression)
- If initially stabilized on divalproex*†, maintain.
- Oral aripiprazole or aripiprazole long-acting injectable, long-acting risperidone monotherapy
- Quetiapine (for recurrence prevention) or ziprasidone (for relapse prevention) adjunctive to (lithium* or divalproex*†)
- Asenapine monotherapy
- Olanzapine/samidorphan monotherapy
- Manual-based psychotherapy (e.g., interpersonal social rhythm therapy, CBT, mindfulness best evidence along with psychoeducation during the maintenance phase)

†Note: Be aware that there are limited data on long-term efficacy of divalproex.

Level 2A If multiple Level 1 trials are ineffective and/or not well tolerated:

- Olanzapine monotherapy
- Olanzapine adjunctive to lithium* or divalproex*†

Level 2B If Levels 1 and 2A are ineffective and/or not well tolerated:

- Continue effective and well-tolerated acute treatment(s) if not listed in Level 1
- Lithium* and divalproex*† combination
- Follow acute mania/bipolar depression guidelines to achieve remission or partial remission

Level 3 If Levels 1 and 2 are ineffective and/or not well tolerated:

- Adjunctive clozapine (avoid combining with another antipsychotic)
- Electroconvulsive therapy (ECT)†

Notes:

** Caution should be used when prescribing lithium, lamotrigine, divalproex or carbamazepine to women of reproductive age due to increased risks to the fetus with use during pregnancy, including neural tube and other major birth defects. Please see Florida Best Practice Recommendations for Women of Reproductive Age with Serious Mental Illness and Comorbid Substance Use Disorders available at https://floridabhcenter.org.*

***Side-effect concerns with these agents include weight gain, metabolic syndrome, and extrapyramidal symptoms (EPS). Side-effects warrant vigilance and close monitoring on the part of the clinician.*

†Long-term efficacy data are limited for the following: divalproex monotherapy, carbamazepine (drug interaction risk), antidepressants, and electroconvulsive therapy (inconvenience/expense).

Table 3. Recommended Medications for the Treatment of Bipolar Disorder – Mood Stabilizers

Medication	Dosage	Comments
Lithium	In acute mania: 1,200–2,400 mg/day (serum level 0.8–1.2 mEq/L)	▶ Initial titration for tolerability: » Start 600–900 mg/day, increase 300 mg/day every 5 days. » Check levels 5 days after initiation/dose change (ideally, trough lithium levels 12 hours after last dose). ▶ Check blood levels more frequently if signs or suspicion of clinical toxicity. ▶ Lower doses/levels may be necessary in non-manic compared to manic patients. ▶ Monitor renal and thyroid functions. ▶ For maintenance, some patients require serum levels of 0.8 to 1.2 mEq/L, others can be maintained with lower levels, but not below 0.6 mEq/L. ▶ In older individuals, start with lower lithium dose, titrate more slowly, and target lower serum lithium levels.
Divalproex	In acute mania: 5–60 mg/kg/day; 1,000–2,500 mg/day (serum level 85–125 µg/mL)	▶ Initial dosing: » Initial loading may be tolerated, but some patients need initial titration for tolerability. » Lower doses/levels may be necessary in non-manic compared to manic patients. » Check levels 48 hours after initiation and adjust dose accordingly. ▶ Side-effects (especially gastrointestinal) are more evident above 100 µg/ml. ▶ More teratogenic than other mood stabilizers. ▶ Serious side effects include hepatotoxicity, thrombocytopenia, pancreatitis, and hyperammonemic encephalopathy.
Carbamazepine	In acute mania: 200–1,600 mg/day (serum level 6–12 µg/mL)	▶ Initial titration for tolerability due to hepatic auto-induction: » Start 200–400 mg/day and increase 200 mg/day every 3 days. Lower doses/ levels may be necessary in non-manic compared to manic patients. » Monitor for blood dyscrasias and serious rash. » Screen individuals of Asian descent for HLA-B*1502 (serious rash risk indicator) due to high risk for Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN). » Patients testing positive for the HLA-B*1502 allele should not be treated with carbamazepine unless benefits clearly outweigh risks. ▶ Carbamazepine decreases serum levels of multiple other CYP450-metabolized drugs due to induction of CYP450 enzymes 3A4, 1A2, 2C9, and 2C19.

Medication	Dosage	Comments
Lamotrigine	In bipolar maintenance: 100–400 mg/day	▶ Initial titration to reduce risk of Stevens-Johnson syndrome and Toxic Epidermal Necrolysis (TEN) [serious rash]: » Start 25 mg/day (12.5 mg/day if taken with divalproex). » Increase by 25 mg/day (12.5 mg/day if taken with divalproex) after 2 and 4 weeks and weekly thereafter. Initial target dose 200 mg/day, but final doses may be 100–400 mg/day. ▶ May be used in some patients with acute bipolar depression (despite acute efficacy limitation) due to good tolerability and depression prevention efficacy.

**mg/day= milligrams per day; mEq/L = milliequivalents per Liter; mg/kg/day = milligram per kilogram per day; µg/ml = microgram per millimeter*

Table 4. Recommended Medications for the Treatment of Bipolar Disorder—Second Generation Antipsychotics (SGAs) and Antidepressants

Medication	Dosage	Comments
Second Generation Antipsychotics (SGA)	**In acute mania:** ▶ Aripiprazole: 15–30 mg/day ▶ Asenapine: 10–20 mg/day ▶ Olanzapine: 6–20 mg/day ▶ Olanzapine/samidorphan: 5mg/10mg–20mg/10mg per day; 10mg/10mg–20mg/10mg if adjunct to lithium or valproate. ▶ Paliperidone: 3–12 mg/day ▶ Quetiapine: 400–800 mg/day ▶ Risperidone: 2–6 mg/day ▶ Ziprasidone: 80–160 mg/day **In acute bipolar depression:** ▶ Quetiapine: 200–600 mg/day ▶ Olanzapine/Fluoxetine: 3 mg/12.5 mg–12 mg/50 mg per day ▶ Lurasidone: 40–120 mg/day ▶ Clozapine: 50–400 mg/day (if treatment resistant)	▶ Initial titration may be necessary for tolerability. Lower doses may be necessary in depressed patients (e.g. quetiapine 300 mg/day). Ziprasidone should be taken with food. Asenapine is sublingual. ▶ Monitor for side effects, including sedation (especially with quetiapine and clozapine), weight gain (especially with olanzapine and clozapine), akathisia (especially with aripiprazole and ziprasidone) and extrapyramidal symptoms (EPS), especially with risperidone. Monitor weight and body mass index (BMI) at each visit and laboratory metabolic indices at baseline, 3 months, and yearly thereafter.
Antidepressants	**In acute bipolar depression:** As dosed for major depression. (No specific dosing recommendations can be given for bipolar depression.)	▶ Larger trials have not found a benefit of antidepressant when added to mood stabilizers/antimanics for bipolar depression (other than olanzapine/ fluoxetine combination). May be used in combination with antimanic drugs in some patients with acute bipolar depression, but should not be prescribed as monotherapy in patients with bipolar I disorder due to manic switch risk. ▶ Serotonin-norepinephrine reuptake inhibitors (SNRIs) and tricyclic antidepressants (TCAs) may have greater manic switch risk. ▶ Antidepressant carry an FDA boxed warning for increased suicidality risk in pediatric and young adult patients (under age 25). May be continued in patients who are on antidepressants and have stable mood.

**mg/day = milligrams per day*

Note: Samidorphan is an opioid receptor antagonist approved for use in combination with olanzapine to mitigate olanzapine-associated metabolic side effects.

Summary: Treatment of Bipolar Disorder

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Introduction

Bipolar disorders (BD) are a group of severe lifelong disorders that are associated with staggering loss of human capital, loss of healthy living years as well as lifespan. Although mania is the defining feature of bipolar I disorder, and hypomania with at least one depressive episode defining bipolar II disorder, it is well-established that depressive symptoms and episodes are the predominant illness presentation. The predominance of depressive symptoms across bipolar subtypes is apparent not only at the first illness presentation but also along the longitudinal course.

An unmet need in bipolar disorder remains the staggering misdiagnosis rate and the delay in determining that the diagnosis is present. This prolongs human suffering, increases morbidity and mortality, service utilization, healthcare costs and necessarily fosters progression of the illness. As most individuals with bipolar disorder are initially incorrectly diagnosed, treatment selection is often inappropriate, further promoting negative health outcomes.

The predominance of depression in bipolar disorder and high misdiagnosis rate provides the impetus for routine screening for bipolar disorders in all persons initially presenting with depression and for subsequent visits if characteristics of bipolar disorder become manifest and/or response to treatment is inadequate. A quantity of screening tools for bipolar disorder exist which differ in their items, psychometrics, time to completion and feasibility in busy clinical practice. The Rapid Mood Screener (RMS; https://www.rapidmoodscreener.com/) has been recently validated as a brief, validated screening tool with validation completed and satisfactory psychometrics in adults with bipolar I and bipolar II disorder. The RMS has improvements in psychometrics in time to administration as well as end-user satisfaction relative to other screening tools for bipolar disorder.

Principles of Treatment

The use of measurement to track symptoms (e.g., mood diaries) is encouraged and attempts to prevent comorbidities should be a clinical focus at initial presentations. Recognition that BD is an independent risk factor for cardiovascular disease further underscores the importance of holistic approaches to the assessment, prevention, and management of BD. Individuals with BD report much higher rates of physical and sexual trauma in the recent or distant past as well as describe psychosocial stressors as associated with episode recurrence. In addition to targeting key features of BD, the management of BD also needs to include psychoeducation, improvement of diagnosis and treatment literacy, conflict and stress management skills, as well as lifestyle improvement with focus on diet as well as sleep hygiene.

Pharmacologic Treatment of Acute Bipolar Mania/Mixed States

The pharmacologic treatment of acute bipolar mania/mixed states has been augmented with the combination of olanzapine-samidorphan. Olanzapine-samidorphan combination is FDA-approved for the treatment of acute mania/mixed states in adults with bipolar I disorder as monotherapy or adjunct to lithium or valproate. It was the panel's view that olanzapine-samidorphan would be prioritized ahead of olanzapine in the treatment of acute mania or mixed states as monotherapy or adjunct to lithium or valproate due to a lower

weight gain liability of olanzapine-samidorphan relative to olanzapine. Moreover, available evidence indicates that although samidorphan mitigates weight gain liability attributable to olanzapine, it does not mitigate olanzapine's efficacy.

Pharmacologic Treatment of Acute Bipolar Depression

The panel recommends cariprazine, lumateperone and lurasidone monotherapy as initial treatment for bipolar I depression. Lumateperone and lurasidone are also approved as adjuncts to lithium or valproate in bipolar I depression. Lumateperone is additionally approved as monotherapy or adjunct to lithium or valproate in the treatment of bipolar II depression. Quetiapine is approved as monotherapy in bipolar II depression but not as adjunctive treatment. The panel recognizes that cariprazine, lumateperone and lurasidone have lower propensity to weight gain and are metabolically similar to placebo in the treatment of adults with BD. These observations differentiate these second-generation antipsychotics (SGAs) from quetiapine and olanzapine-fluoxetine combination which have greater susceptibility to clinically significant weight gain and/or metabolic shift. It was the view of the panel that consideration of weight gain and metabolics is paramount in selecting treatments for bipolar depression. The panel also recommends lithium or lamotrigine as possible first-line treatments for bipolar depression. The anti-suicide effects of lithium, not seen with other FDA-approved treatments for BD, are an important attribute of lithium.

The panel recognizes that antidepressant monotherapy in bipolar I disorder is to be discouraged. Conventional antidepressants are not recommended in bipolar I disorder for adults manifesting mixed features, rapid cycling, and/or histories of previous antidepressant-associated emergence of hypo/mania. For adults with bipolar II disorder, preliminary evidence suggests that some adults may be safely and effectively treated with antidepressant monotherapy. Antidepressant monotherapy however would not be recommended for persons with bipolar II disorder presenting with mixed features, rapid-cycling and/or history of antidepressant-associated affective switching/cycle acceleration/dysphoria. The lack of empirically supported response predictors to antidepressant monotherapy in BD implies that it is unknown *a priori* which individuals with bipolar II disorder may be safely treated with antidepressant monotherapy. The panel also recognizes that there is a paucity of long-term treatments with antidepressants in BD. The recommendation to continue antidepressants will be determined on an individual basis.

The ***2023-2024 Florida Best Practice Psychotherapeutic Medication Guidelines for Adults*** has retained similar guidance with respect to pharmacologic treatments of bipolar mania. Bipolar mania is recognized as a medical emergency requiring, in many cases, a higher intensity of treatment. Safety is of paramount importance of mania and, where applicable, inpatient stay and specialist consultation is encouraged. The panel also recognizes that for many adults with bipolar mania, the predominant presentation is dysphoric and mixed with many adults manifesting non-specific symptoms (e.g., anxiety, agitation, irritability, anger) that often obscure the underlying diagnosis of mania. SGA monotherapy as well as lithium or divalproex are recommended in cases of mania of milder severity (e.g., non-psychotic mania). In situations where patients have severe mania (e.g., psychosis, need for hospitalization), combination SGA and additional mood stabilizing agent (e.g., lithium) is recommended.

Maintenance Pharmacological Treatment of Bipolar Disorder

More than 90% of individuals with BD will experience recurrence of illness. Episode recurrence in BD is highly associated with progressive changes to brain structure and function, as well as the accumulation of multiple comorbidities. Further evidence also suggests that greater episode frequency is associated with more pronounced cognitive deficits in BD. Moreover, it is not frequent in BD to witness a phenomenological shift across time where patients manifest increasing depressive symptom burden. A clinical impression awaiting cogent empirical confirmation is that, increasingly, clinicians are encountering a higher percentage of individuals with BD presenting with mixed features during the acute or maintenance phase. It is uncertain what is causing this, but, certainly, antidepressant utilization, drug and alcohol misuse and obesity are contributing causes.

The combination of olanzapine-samidorphan has been approved as a maintenance monotherapy in adults with bipolar I disorder. The approval of olanzapine-samidorphan was based on legacy studies in maintenance treatment of bipolar disorder with olanzapine. The combination of olanzapine-samidorphan exhibits a lower propensity to weight gain and waist circumference enlargement when compared to olanzapine when studied in adults with schizophrenia. It was the panel's view that a lower weight gain liability with olanzapine-samidorphan relative to olanzapine would prioritize olanzapine-samidorphan over olanzapine in the selection sequencing of maintenance treatments in bipolar disorder.

For most adults with BD, multi-year/lifetime pharmacotherapy is recommended, integrated with lifestyle interventions targeting healthful living, diet, exercise, and sleep hygiene. For many adults, manual-based psychosocial treatments (e.g., cognitive therapy), interpersonal social rhythm therapy and psychoeducation, are critical adjuncts to pharmacotherapy to improve overall psychosocial function and wellbeing. During the acute and maintenance phase of BD, careful attention to suicidality is paramount.

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3. McIntyre RS, Alda M, Baldessarini RJ, et al. The clinical characterization of the adult patient with bipolar disorder aimed at personalization of management. World Psychiatry 2022;21(3):364–87.
4. McIntyre RS, Berk M, Brietzke E, et al. Bipolar disorders. Lancet 2020;396(10265):1841–56.

Box 5. Assessment Scales for Adult Major Depressive Disorder

- Beck Depression Inventory (BDI)
- Patient Health Questionairre-9 (PHQ-9)
- Quick Inventory of Depression Symptomatology (QIDS)

**Notes: The recommendations are based on the evidence-base and clinical consensus. The Montgomery-Asberg Depression Rating Scale (MADRS) and Hamilton Rating Scale for Depression (HAM-D) can also be used to assess symptoms of depression in major depressive disorder.*

Note: Treatment recommendations are based on levels of evidence and expert opinion. For a description of the criteria for each level, see pages 2-3.

Conduct comprehensive assessment and use measurement-based care. Refer to Principles of Practice on pages 4-9.

The therapeutic objectives of acute treatment are to assure safety, measure response to therapy, provide psychoeducation to patient and circle of care, and to begin the process of symptomatic, syndromal, and functional recovery.

Strongly recommend psychiatric consultation prior to initiation of therapy + psychotherapeutic medication using a multi-disciplinary approach if treated by a non-psychiatrist.

Assess for:

- Current/prior hypomania/mania, symptoms/episodes*
- Psychiatric and medical comorbidities (e.g., substance-related disorders, anxiety disorders, obesity, diabetes)
- Presence of specifiers, notably: psychosis, mixed features, suicidality
- Presence of cognitive dysfunction (e.g., memory complaints; difficulty with concentration, making decisions, and thinking clearly)
- Assess for recurrence vulnerability factors (e.g., symptom severity, age of onset, number of depressive episodes)
- Manual-based psychotherapy (e.g., CBT) or exercise therapy may be an appropriate treatment option for mild depression (e.g., PHQ-9 score 5 through 9). Guided online protocolized psychotherapy may be appropriate where accessible.

**Note: Rule out the possibility of bipolar disorder in individuals presenting with depressive symptoms.*

Level 1 Options for initial treatment:

- Antidepressant Monotherapy trial at adequate dose and evaluate*:
  - Selective serotonin reuptake inhibitor (SSRI)**, serotonin-norepinephrine reuptake inhibitor (SNRI), vortioxetine, dextromethorphan-bupropion
  - Bupropion monotherapy or mirtazapine
- Consider brexanolone in persons with postpartum depression
- In adults with acute suicidal ideation or actions, intranasal esketamine co-administered with a conventional antidepressant can be initiated at any level of treatment.
- If partial response at 2 to 4 weeks, may continue for another 2 to 4 weeks or go to Level 2.

If no response at 4 weeks, ensure dose optimization and go to Level 2.

**Medication response is more pronounced in moderate to severe depression.*

***Consider propensity for drug-drug interactions and differential risk for teratogenicity.*

Initiate combination therapy for individuals with recurrent depression, persistent depressive disorder, and history of trauma. Be vigilant of emergence of hypomanic symptoms.

Level 2 If multiple Level 1 trials are ineffective and/or not well tolerated:

- Evaluate adherence
- Ensure dose optimization of medication used in Level 1.
- Switch to different monotherapy agent from different or same class (SSRI, SNRI, bupropion, or mirtazapine).
- Combine existing monotherapy with:
  - Evidence-based psychotherapy (e.g., CBT, IPT)
  - Second-generation antipsychotic FDA-approved for augmentation therapy for major depressive disorder (MDD) (i.e., aripiprazole or brexpiprazole or cariprazine; quetiapine is Level 3 due to tolerability concerns)
  - Intranasal esketamine or intravenous racemic ketamine. In the case of intranasal esketamine, co-administration with a separate antidepressant.
  - An antidepressant (avoid SSRI and SSRI/SNRI combinations)
- Accelerated TMS protocol. Consider MRI-guided TMS where accessible.

Note: FDA-approved adjunctive agents for MDD are select atypical antipsychotics. Preliminary evidence evaluating comparative effectiveness of adjunctive antidepressant versus adjunctive atypical antipsychotic medications indicates superior efficacy for adjunctive antipsychotics and superior tolerability for adjunctive antidepressants.

Level 3 If Levels 1 and 2 are ineffective and/or not well tolerated:

- Evaluate adherence
- Seek psychiatric consultation
- (SSRI or SNRI) + quetiapine (tolerability concerns)
- (SSRI or SNRI) + (lithium or T3)
- (SSRI or SNRI) + (L-Methylfolate or S-adenosylomethionine)
- Tricyclic antidepressant (TCA)
- Monoamine oxidase inhibitor (MAOI)
- Electroconvulsive therapy (ECT)
- Transcranial magnetic stimulation (TMS)*

**Note: Most evidence for TMS is in the acute treatment.*

Level 4 If Levels 1 – 3 are ineffective and/or not well tolerated:

- Re-evaluate diagnosis if patient has failed to respond to 2 or more treatments
- Monoamine oxidase inhibitor (MAOI) augmentation (AVOID CONTRAINDICATED COMBINATIONS)
- Triple drug combination (little evidence exists supporting or refuting this strategy)
  - (SSRI or SNRI) + mirtazapine + bupropion
  - (SSRI or SNRI) + mirtazapine + lithium*
  - (SSRI or SNRI) + bupropion + second generation antipsychotic (SGA)
- Other neuromodulatory approaches [e.g., vagus nerve stimulation (VNS)]

**Note: Caution should be used when prescribing lithium due to increased risk to the fetus with use during pregnancy (i.e., Ebstein's anomaly).*

Box 6. Assessment Scales for Adult Major Depressive Disorder with Mixed Features

- Beck Depression Inventory
- Clinical Global Impression (CGI) Scale
- Montgomery-Asberg Depression Rating Scale (MADRS)
- Patient Health Questionairre-9 (PHQ-9)
- Quick Inventory of Depression Symptomatology (QIDS)
- Young Mania Rating Scale (YMRS)

Note: Treatment recommendations are based on levels of evidence and expert opinion. For a description of the criteria for each level, see pages 2-3.

Conduct comprehensive assessment and use measurement-based care. Refer to Principles of Practice on pages 4-9.

Mixed features are subsyndromal hypomanic features defined according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition Text Revision (DSM-5TR).

Strongly recommend psychiatric consultation prior to initiation of therapy + psychotherapeutic medication using a multi-disciplinary approach if treated by a non-psychiatrist.

Assess for:

- Prior history of hypomania/mania
- Psychiatric and medical comorbidities (e.g., substance use disorders, anxiety disorders, obesity, diabetes)

Level 1 Initial Treatment:

- Minimal evidence for treating major depressive order (MDD) with mixed features specifier
- Discuss treatment option, including evidence-based psychotherapy [Cognitive Behavioral Therapy (CBT), Interpersonal Psychotherapy (IPT), Behavioral Activation]
- Consider FDA-approved second-generation antipsychotic (SGA; lurasidone, lumateperone, cariprazine)** for augmentation in MDD or mood stabilizer (e.g., lithium*)
- Antidepressant monotherapy 4 to 8-week trial at adequate dose and evaluate
  - Selective serotonin reuptake inhibitor (SSRI), serotonin-norepinephrine reuptake inhibitor (SNRI), or vortioxetine
  - Bupropion (if tolerability concerns) or mirtazapine

Note: Antidepressant monotherapy in MDD with subsyndromal hypomania may be associated with a higher rate of suboptimal therapeutic outcomes when compared to MDD without subsyndromal hypomania.

- For all Level 1 treatments, if partial response at 4 weeks, may continue for another 2 to 4 weeks or go to Level 2.
- For all Level 1 treatments, if no response at 4 weeks, ensure dose optimization and go to Level 2.

Level 2 If multiple Level 1 trials are ineffective and/or not well tolerated:

- Reassess for hypomania/mania
- Ensure dose optimization of medication used in Level 1
- Switch to lurasidone or lumeteperone monotherapy or adjunct

Level 3 If Levels 1 and 2 are ineffective and/or not well tolerated:

- Alternative adjunctive SGA or lithium or lamotrigine
- Consider electroconvulsive therapy (ECT) or transcranial magnetic stimulation (TMS; consider accelerated TMS protocol)
- Alternative antidepressants, including tricyclic antidepressant (TCA), monoamine oxidase inhibitor (MAOI), or first-generation antipsychotic (FGA)**

Notes:

**Caution should be used when prescribing lithium, lamotrigine, divalproex or carbamazepine to women of reproductive age due to increased risks to the fetus with use during pregnancy, including neural tube and other birth defects. Please see Florida Best Practice Recommendations for Women of Reproductive Age with Serious Mental Illness and Comorbid Substance Use Disorders and online guideline on the Pharmacological Treatment of Mood Disorders During Pregnancy available at https://floridabhcenter.org.*

***Side-effect concerns with these agents include weight gain, metabolic syndrome, and extrapyramidal symptoms (EPS). Side-effects warrant vigilance and close monitoring on the part of the clinician.*

Treatment of Major Depressive Disorder with Psychotic Features

Box 7. Assessment Scales for Adult Major Depressive Disorder with Psychotic Features

- Beck Depression Inventory
- Brief Psychiatric Rating Scale
- Clinician-Rated Dimensions of Psychosis Symptom Severity (CRDPSS)
- Hamilton Rating scale for Depression (HAM-D)
- Montgomery-Asberg Depression Rating Scale (MADRS)
- Positive and Negative Syndrome Scale (PANSS)

Note: Treatment recommendations are based on levels of evidence and expert opinion. For a description of the criteria for each level, see pages 2-3.

Conduct comprehensive assessment and use measurement-based care. Refer to Principles of Practice on pages 4-9.

Psychotic features are the presence of delusions and/or hallucinations as defined by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition Text Revision (DSM-5TR). Psychotic features may be mood-congruent, where the content of all delusions and/or hallucinations are consistent with typical depressive themes of personal inadequacy, guilt, disease, death, nihilism, or deserved punishment, or mood-incongruent, where the content of the delusions and/or hallucinations either does not involve these typical depressive themes or is a mixture of mood-congruent and mood-incongruent themes.

Strongly recommend psychiatric consultation prior to initiation of therapy + psychotherapeutic medication using a multi-disciplinary approach if treated by a non-psychiatrist.

Assess for:

- Prior history of hypomania/mania
- If MDD with psychosis presents post-partum, evaluate for bipolar disorder.
- Psychiatric and medical comorbidities (e.g., substance use disorders, anxiety disorders, obesity, diabetes)

Level 1 Options for initial treatment:

- Treatment with Level 1 antidepressant for major depressive disorder without psychotic features. Selective serotonin reuptake inhibitor (SSRI) or serotonin-norepinephrine reuptake inhibitor (SNRI) or vortioxetine + second generation antipsychotic (SGA)*
- Electroconvulsive therapy (ECT) (if patient safety is an immediate concern)
- Cognitive-behavioral therapy (CBT) and interpersonal psychotherapy (IPT) are not recommended as a first-line modality.

**Consider extrapyramidal symptoms (EPS) risk and metabolic concerns, including weight gain.*

Level 2 If multiple Level 1 trials are ineffective and/or not well tolerated:

- Alternative antidepressant + SGA combination
- ECT

Level 3 If Levels 1 and 2 are ineffective and/or not well tolerated:

- Re-evaluate diagnosis
- Other antidepressant combinations with SGA
- Other antidepressant combinations with first generation antipsychotic (FGA)
- ECT (if not attempted earlier)

Summary: Treatment of Major Depressive Disorder

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Introduction

It is amply documented that major depressive disorder (MDD) is a prevalent, early age at onset, severe disorder with high rates of non-recovery, recurrence and chronicity. The COVID-19 pandemic has resulted in an increase in the number of persons across the USA and globally affected by MDD and related disorders (e.g., anxiety disorders). The foregoing composite of MDD alongside the national opioid epidemic and increased reporting of suicidality, especially amongst younger populations, has resulted in a consensus position that the USA and many other countries around the world are experiencing a mental health crisis.

Busy practitioners are highly familiar with the overlap of MDD with other mental disorders as well as disparate medical conditions. The vulnerability to medical conditions amongst persons living with mood disorders was further instantiated by observations of persons living with MDD are at greater risk of contracting COVID-19, experiencing complications due to COVID-19 requiring hospitalization as well as mortality. Moreover, the morbidity of MDD is amplified further by the existence of comorbid conditions and results in an increase in health service utilization and costs.

Accumulated research results during the past decade indicates that the majority of adults with MDD are either undiagnosed or delayed in receiving the diagnosis. For persons with access to healthcare settings the majority are not prescribed evidence-based strategies, and for those who are, discontinuation occurs for most persons within a few months. The foregoing "knowledge-implementation" gap represents a robust modifiable deficiency in managing adults with MDD. In addition, most persons with MDD are not receiving "next-step" treatments if the first-line treatment proves to be inadequate resulting in a sizable proportion of persons with MDD impaired by the illness unnecessarily.

The diagnosis of MDD remains a clinical endeavor and the selection of antidepressant treatment is informed by "deep in vivo" clinical characterization of the patient. Digital psychiatry holds tremendous promise for the future from the point of view of ecological momentary assessment (EMA), passive ambient digital fingerprinting of the illness, illness self-management as well as multidisciplinary case management and evaluation for suicide risk. Moreover, virtual healthcare across different media skyrocketed during the pandemic and is undoubtedly remaining a significant access point for persons living with MDD as well as a framework to provide protocolized psychotherapies. As with pharmacogenomics, however, the digital revolution (with the exception of telehealth) at point-of-care implementation remains a future aspiration rather than routine practice today.

During the past four years, the FDA has approved for MDD several new treatment approaches including by not limited to intranasal esketamine (for treatment-resistant depression and depression with suicidality), combination dextromethorphan-bupropion, the first rapid-acting oral NMDA antagonist and sigma 1 agonist, the dopamine D2/D3 partial agonist atypical antipsychotic cariprazine as well as cleared MRI-guided accelerated transcranial stimulation (the first time the FDA has cleared and/or approved radiology as a component of the treatment of a persons with a mental disorder). These developments along with refinement of protocolized psychotherapies that are accessible via telehealth provides hope for persons living with MDD that genuinely innovative strategies are appearing.

Moreover, later in 2023 it is anticipated that the FDA will decide whether it will approve the first ever GABA-ergic antidepressant that is taken "when needed" for a brief duration (i.e., two weeks) representing a tectonic plate shift in the management of this chronic disorder.

As we anticipate approval of innovative new approaches narrowing the implementation gap, fidelity to evidence-based approaches, measurement-based care and guideline-informed treatments remain accessible and powerful approaches. Clinicians are encouraged to be sensitive to inequities in the healthcare system as a function of race, ethnicity, gender identification, sexual orientation and/or economic position when assessing and providing care as an additional area for improvement in managing persons living MDD.

Principles of Treatment

Similar to the 2019-2020 Florida Best Practice Psychotherapeutic Medication Guidelines for Adults, the emphasis for the 2023 guidelines is the emphasis on full functional recovery and integration as a priority therapeutic objective in MDD. Towards this overarching and patient-desired aim, it is essential that clinicians consider self-rating instruments when screening for MDD. It is also essential that once the clinical diagnosis of MDD has been established that therapeutic objectives include full symptom mitigation and consensually agreed upon therapeutic objectives in collaboration with patients. Available evidence also indicates that individuals with MDD who function at a higher level, despite being depressed, are more likely to respond and remit with antidepressant therapy. Along with underscoring the complex interrelationship between symptoms and function in MDD, the improved symptomatic outcomes in higher functioning adults with MDD provides the impetus for simultaneously targeting symptoms and functioning in patients with MDD.

Along with careful attention to the presence of depressive symptoms, the relatively high rates of medical and mental disorder comorbidity in the MDD population provides the basis for careful attention to preventing and, when present, treating comorbidity in MDD populations. Commonly encountered comorbidities (e.g., anxiety disorder, substance use disorders, attention deficit hyperactivity disorder, eating disorders), as well as medical disorders (e.g., cardiovascular disease, obesity, diabetes mellitus) should be part of routine assessment of any adult with MDD. Moreover, as with all patients, assessing for imminent risk of suicide is critical. Unfortunately, psychiatry is unable to predict suicide in ways that are robust, evidence-based and clinically applicable. The hope is that the future, perhaps through artificial intelligence machine-learning, we position clinicians to better predict lethal self-harm.

For many individuals presenting with depression of mild severity, manual-based psychotherapy may be a preferred option. Moreover, exercise therapy has also demonstrated symptom mitigating effects in individuals with depressive episodes of milder severity. For others presenting with depression of moderate to severe depressive episodes as part of MDD, pharmacotherapy should certainly be considered. In many cases, manual-based psychotherapy can also be an alternative and/or adjunctive treatment. The current evidence base indicates that for adults with treatment-resistant MDD, manual-based psychotherapy is most effective when combined with pharmacotherapy. Moreover, combination pharmacotherapy-manual based psychotherapy approaches are recommended for persons with persistent depressive disorder, MDD with select comorbidities (e.g., obsessive compulsive disorder) and situations where patients report histories of childhood trauma and/or manifest maladaptive personality traits.

Practitioners very frequently encounter persons living with MDD who exhibit inadequate response to first-line antidepressant treatments. Treatment-resistant depression (TRD) does not have a consensus definition and/or been externally validated by a biomarker. The absence of a validated biomarker has resulted in a range of prevalence estimates from approximately

30-60%. For adults presenting with inadequate response to first-line treatments, FDA-approved second-generation atypical antipsychotics should be considered ahead of adjunctive antidepressants. Available evidence does suggest that although combining antidepressants together can be effective and well-tolerated, the rigor of that data is inferior to data with atypical antipsychotics. For persons not tolerating the first-line treatment, switching is recommended; if the first-line treatment is sufficiently tolerated there are advantages to adjunctive strategies if patients prefer that approach with some suggestion of superiority with adjunctive atypical agents when compared to switching to antidepressant monotherapy. For persons with TRD, ECT, rTMS and esketamine co-initiated with an antidepressant can be considered as well as off-label intravenous racemic ketamine. Available evidence suggests that esketamine may be relatively more efficacious than some second-generation antipsychotics in adults with TRD.

Major Depressive Disorder Without Mixed Features

The DSM-5 introduced mixed features specifier in the manual published in 2013. Mixed features refers to subthreshold hypomanic symptoms occurring during a depressive episode in an individual with MDD. The panel was of the view that the hazards posed by mixed features (e.g., a more complex illness presentation, higher rates of comorbidity, suicidality) as well as diminished response to conventional antidepressants warrants assessment as to the presence or absence of mixed features. In an adult who is presenting MDD without mixed features, clinicians are encouraged to select and sequence treatments according to the ***2023–2024 Florida Best Practice Psychotherapeutic Medication Guidelines for Adults***.

Major Depressive Disorder with Mixed Features

For patients presenting with MDD and mixed features, the panel was of the view that it is important to consider the possibility that the identified patient may possibly have bipolar disorder. Longitudinal studies indicate that the majority of individuals with MDD and mixed features exhibit phenotypic stability across time (i.e., they retain the diagnosis of MDD). Notwithstanding, the relative risk for bipolar disorder in adults with MDD and mixed features is increased relative to the general population. Conventional antidepressants can and should be considered with careful attention for any amplification and/or new onset hypomanic symptoms. Symptom intensification manifests in many ways including, but not limited to, anxiety, agitation, irritability, dysphoria and sleep disruption. Preliminary evidence suggests that for some adults with MDD with mixed features, second-generation antipsychotics may not only be efficacious but may also be better tolerated in this particular population. As per the Florida Best Practice Psychotherapeutic Medication Guidelines for Adults, the panel agreed that despite the lack of rigorous evidence, other agents with mood stabilizing properties (e.g., lithium, lamotrigine) may also be considered in MDD with mixed features as an adjunct to antidepressants or perhaps in some cases, as a treatment alternative.

Major Depressive Disorder with Psychosis

There was no substantive change in the panel's recommendation in treatment for MDD with psychosis. MDD with psychosis affects at least 20% of individuals with MDD. Results from a recently completed randomized control trial provide results that comport with clinical impression that the combination of a conventional antidepressant and antipsychotic is the preferred, acute, and recurrence-prevention treatment option when compared to conventional antidepressant monotherapy. Indeed, electroconvulsive therapy is an alternative treatment option for MDD with psychosis; antidepressant monotherapy as well as manual-based psychotherapy as stand-alone treatment are not recommended.

Maintenance Treatment in Major Depressive Disorder

Evidence indicates that the majority of individuals with MDD are at risk of recurrence. Furthermore, episode frequency is a powerful predictor of future episodes. Delineating which patients should be considered for longer-term therapy is informed by identifying recurrence vulnerability factors (e.g., number of prior episodes, residual symptoms, cognitive symptoms, comorbidity, and stressors). Clinicians are encouraged to consider long-tern tolerability and safety concerns (e.g., weight gain, glucose homeostatic disturbances) when selecting antidepressants acutely. Evidence also indicates that manual-based psychotherapy as well as mindfulness-based psychotherapeutic approaches can be helpful adjunctive and/or alternative treatment strategies during the maintenance treatment of MDD in individuals who have acutely responded to antidepressant monotherapy. The overarching therapeutic objective of maintenance treatment in MDD is to assist patients in full functional recovery in achieving consensually agreed upon PROs. A point of emphasis is that psychosocial treatments, including protocolized psychotherapies, should be considered as maintenance treatments in persons with MDD.

References:

1. Ceban F, Nogo D, Carvalho IP, et al. Association Between Mood Disorders and Risk of COVID-19 Infection, Hospitalization, and Death: A Systematic Review and Meta-analysis. JAMA Psychiatry 2021;78(10):1079–91.
2. Maj M, Stein DJ, Parker G, et al. The clinical characterization of the adult patient with depression aimed at personalization of management. World Psychiatry 2020;19(3):269–93.
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4. McIntyre RS, Rosenblat JD, Nemeroff CB, et al. Synthesizing the Evidence for Ketamine and Esketamine in Treatment-Resistant Depression: An International Expert Opinion on the Available Evidence and Implementation. Am J Psychiatry 2021;178(5):383–99.

Box 8. Assessment Scales for Adult Schizophrenia

- Brief Psychiatric Rating Scale (BPRS)
- Clinical Global Impression (CGI) Scale
- Clinician-Rated Dimensions of Psychosis Symptoms Severity (CRDPSS)
- Positive and Negative Syndrome Scale (PANSS)

Note: Treatment recommendations are based on levels of evidence and expert opinion. For a description of the criteria for each level, see pages 2-3.

Conduct comprehensive assessment and use measurement-based care. Preferred tools recommended. Refer to Principles of Practice on pages 4-9.

Most importantly, assess social support system (housing, family, other caregivers) and evaluate threats to continuity of care (access to medication, adherence, etc.).

Strongly recommend psychiatric consultation prior to initiation of therapy + psychotherapeutic medication using a multi-disciplinary approach if treated by a non-psychiatrist.

Proper antipsychotic trial sequence:

- Begin with systematic 6 to 10-week trial of one antipsychotic with optimal dosing.
- If inadequate response, follow with systematic trial of monotherapy with one or more antipsychotics at adequate dose and duration.
- If inadequate response, follow with a trial of clozapine or a long-acting antipsychotic.
- Follow with a trial of clozapine, if not tried before.

Note: Recent evidence suggests that long-acting injectable antipsychotic medications should be offered early as a treatment option for all individuals diagnosed with schizophrenia to reduce the risk of non-adherence, prevent future relapse/deterioration, and improve treatment outcomes.

- If insufficient response with the previously listed therapies, consider other strategies (e.g. antipsychotic polypharmacy).

Level 1 Initial Treatment:

- Monotherapy with an antipsychotic (SGA) other than clozapine*—either oral, or oral antipsychotic followed by the same SGA-LAI (if tolerable and sufficiently efficacious).
- If initial trial of antipsychotic monotherapy unsuccessful, try monotherapy with another SGA antipsychotic (either oral or LAI) with low metabolic adverse effects.

**Note: Balance efficacy, side-effects, individual vulnerabilities and preferences. Select a medication with lower metabolic risk, lower risk of extrapyramidal symptoms (EPS), sedation, and sexual side-effects. For more detail on LAIs, refer to page 42.*

Level 2A If non-adherent or refractory to Level 1:

- Long-acting injectable antipsychotic medication (LAI)

Level 2B If Level 1 is ineffective in at least two antipsychotic trials:

- Clozapine

Note: Clozapine requires monitoring through the United States Food and Drug Administration Risk Evaluation and Mitigation Strategies (REMS) program. The clozapine REMS program can be found at: https://www.newclozapinerems.com/home.

Level 3 If Levels 1 and 2 are ineffective and/or not well tolerated:

- Diagnostic review to include substance use, other psychiatric comorbidities, social determinants (e.g., housing) and/or consultation
- Clozapine if not tried earlier
- Antipsychotic, including clozapine + electroconvulsive therapy (ECT)
- Augmentation of clozapine with aripiprazole, lamotrigine, topiramate or if partial or incomplete response to clozapine

Level 4 If Levels 1, 2, and 3 are ineffective and/or not well tolerated:

- Two antipsychotics, ideally with different pharmacological mechanisms* and side-effect profiles (evidence is weak). Avoid additive side effects.
- First generation antipsychotic use

**Full antagonist with partial agonist; loose binding with tight binding*

Table 5. Recommended Medications for the Treatment of Schizophrenia: Oral Antipsychotics

Medication	Chlorpromazine Equivalents[1]	Acute Therapy	Maintenance Therapy[2]
First Generation Antipsychotics (FGAs)			
Chlorpromazine	100	300–1,000 mg/day	300–800 mg/day
Fluphenazine HCl	2	5–20 mg/day	5–15 mg/day
Haloperidol	2	5–20 mg/day	6–12 mg/day
Loxapine	10	30–200 mg/day	30–100 mg/day
Molindone	10	30–200 mg/day	30–100 mg/day
Perphenazine	8	16–80 mg/day	16–64 mg/day
Thiothixene	5	15–50 mg/day	15–30 mg/day
Trifluoperazine	5	15–50 mg/day	15–30 mg/day
Second Generation Antipsychotics (SGAs)			
Aripiprazole	N/A	10-30 mg/day	10–30 mg/day
Asenapine	N/A	10–20 mg/day	10–20 mg/day
Brexpiprazole	N/A	2–4 mg/day	2–4 mg/day
Cariprazine	N/A	1.5–6 mg/day	3–6 mg/day
Clozapine	N/A	150–800 mg/day	150–800 mg/day
Iloperidone	N/A	12–24 mg/day	12–24 mg/day
Lumateperone	N/A	42 mg/day	42 mg/day
Lurasidone	N/A	40–160 mg/day	40–160 mg/day
Olanzapine	N/A	10–30 mg/day	10–20 mg/day
Olanzapine/Samidorphan*	N/A	5mg/10mg or 10mg/10mg once per day	10mg/10mg, 15mg/10mg, or 20mg/10mg once per day
Paliperidone	N/A	3–12 mg/day	3–12 mg/day
Quetiapine	N/A	300–800 mg/day	300–800 mg/day
Risperidone	N/A	2–8 mg/day	2–8 mg/day
Ziprasidone	N/A	80–240 mg/day	80–160 mg/day

Notes:

Recommendations may be below FDA maximum approved doses but are based on current evidence and expert consensus.

Samidorphan is an opioid receptor antagonist approved for use in combination with olanzapine to mitigate olanzapine-associated metabolic side effects.

Consider lower doses for first episode due to better response and higher side effects to medications in pharmaceutically naïve patients. Use atypical antipsychotics and avoid haloperidol completely due to well-documented neuronal cell death caused by haloperidol (and also fluphenazine and perphenazine). Thioridazine is not recommended due to concerns about ventricular arrhythmias (Torsades de Pointes).

1 Approximate dose equivalent to 100 mg of chlorpromazine (relative potency); it may not be the same at lower versus higher doses. Chlorpromazine equivalent doses are not relevant to the second-generation antipsychotics and therefore are not provided for these agents.

2 Drug-drug interactions (DDIs) can impact dosing. Maintenance dose should generally be no less than half of the initial clinically effective dose, as that can result in reduced effectiveness of relapse prevention.

Treatment of Schizophrenia with Long-Acting Injectable Antipsychotic Medications (LAIs)

Note: Treatment recommendations are based on levels of evidence and expert opinion. For a description of the criteria for each level, see pages 2-3.

Conduct a comprehensive assessment and use measurement-based care as found in the Principles of Practice on pages 4-9.

Assess social determinants (housing, family, other caregivers) and evaluate threats to continuity of care (access to medication, adherence, etc.).

Strongly recommend psychiatric consultation prior to initiation of therapy + psychotherapeutic medication using a multi-disciplinary approach if treated by a non-psychiatrist.

Level 1 Initial Treatment:

- After stabilization or obtaining sufficient evidence for efficacy and tolerability, offer any of the following long-acting injectable antipsychotics (LAI). Base the selection on past efficacy and tolerability patterns to specific oral or LAI, expected tolerability advantages*, desired injection intervals, and procedural (oral overlap needed – yes versus no)/logistic/access/cost considerations:
  - Aripiprazole monohydrate
  - Aripiprazole lauroxil
  - Paliperidone palmitate
  - Risperidone microspheres
  - Risperidone extended release subcutaneous injectable.
- If initial, adequate trial (minimum 3 to 4 months) of LAI is unsuccessful, try monotherapy with another LAI from the above group or address potential reasons for efficacy difficulty on the LAI. Refer to Figure 1: Management of Breakthrough Psychosis with LAI for options to consider if psychotic symptoms persist despite adequate medication trial.

**Note: Balance efficacy, side-effects, individual vulnerabilities and preferences. Select medication with lower propensity for metabolic and extrapyramidal side-effects.*

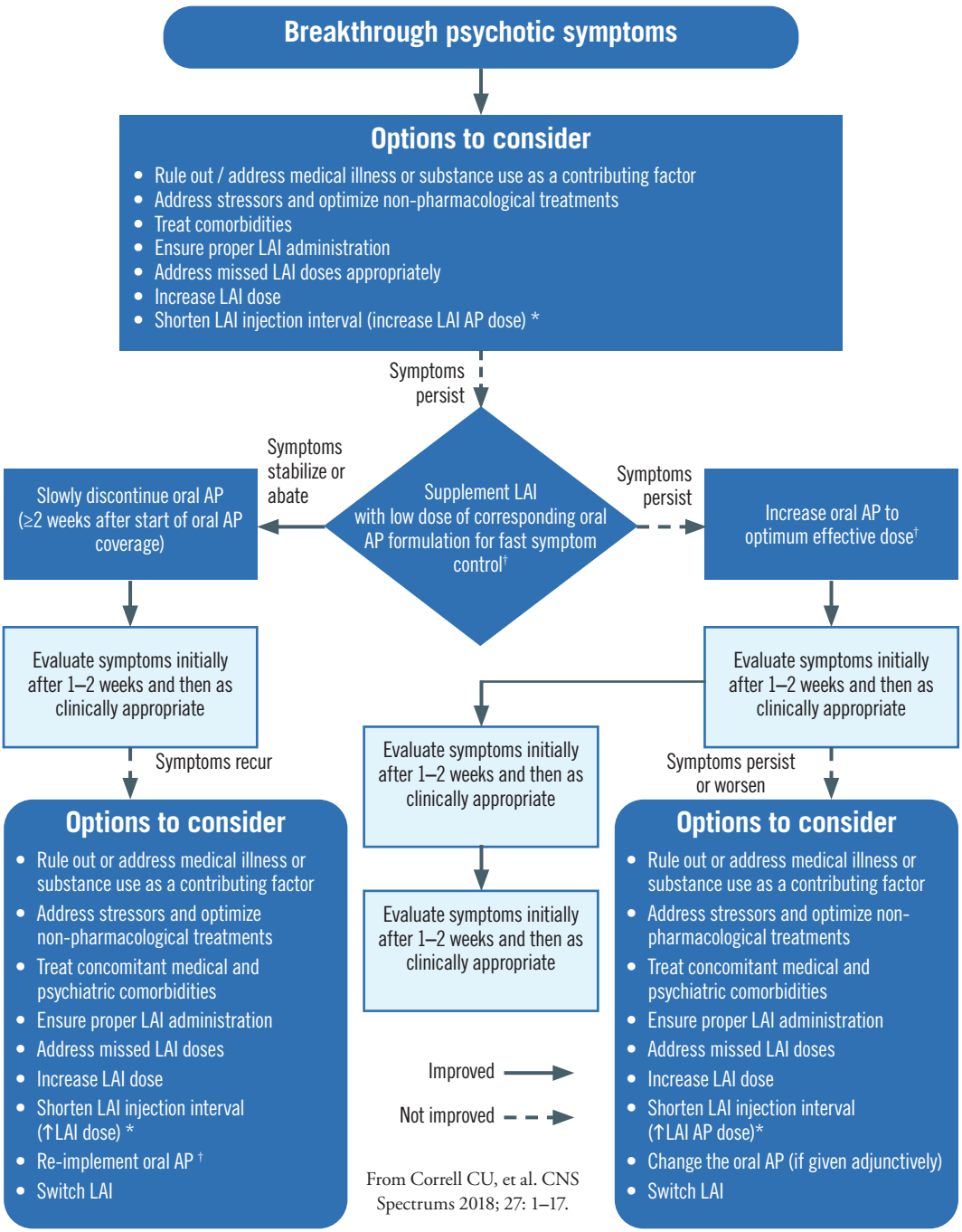
Level 2 If multiple Level 1 trials are ineffective and/or not well tolerated:

- Consider LAI with greater adverse effect risk [olanzapine: post-injection delirium/sedation syndrome (PDSS); FGA-LAIs: EPS, TD]
  - Olanzapine pamoate
  - Fluphenazine decanoate
  - Haloperidol decanoate

Level 3 If Levels 1 and 2 are ineffective and/or not well tolerated:

- Diagnostic review and/or consultation
- Consider switch to an oral antipsychotic not available as an LAI (if adherence can be assured)
- Clozapine if not tried earlier
- LAI + electroconvulsive therapy (ECT) or oral antipsychotic
- Clozapine + ECT

Figure 1. Management of Breakthrough Psychosis with Long-Acting Injectable Antipsychotics (LAIs)



From Correll CU, et al. CNS Spectrums 2018; 27: 1–17.

**Off-label strategy; based on expert opinion.*

†Caution should be exercised with this strategy, because data on the safety of concomitant use of LAI and oral APs are limited, especially over extended periods of time.

Table 6. Recommended Medications for the Treatment of Schizophrenia: Long-Acting Injectable Antipsychotics

Medication	Dose Interval	Dosage Strengths/ Forms	Starting Dose	Maintenance Dose	Oral Supplementation	Time to Peak	Steady State
First-Generation Long-Acting Injectable Antipsychotics*							
Fluphenazine decanoate	Varies	25 and 100 mg/mL ampoules/vials/ syringes	Varies, 12.5 mg	Varies, 12.5 to 100 mg	No	2 to 4 days	2 to 3 months
Haloperidol decanoate	4 weeks	50 and 100 mg/mL ampoules	Varies, 50 mg	Varies, 300 mg	No	6 to 7 days	2 to 3 months
Second-Generation Long-Acting Injectable Antipsychotics*							
Aripiprazole monohydrate (Abilify Maintena®)	Monthly	300, 400 mg vial kits and dual-chamber syringe	400 mg	400 mg (300 to 400 mg)	2 weeks	5 to 7 days	400 mg: 4 to 8 months 300 mg: 3 to 4 months
(Aripiprazole lauroxil (Aristada®)	Monthly for 441 mg dose; monthly to every 6 weeks for 882 mg dose; bimonthly for 1,064 mg dose	441; 662; 882; 1,064 mg prefilled syringes	Varies 441 mg to 1,064 mg**	Varies, 441 to 882 mg	3 weeks if Aristada Initio® is not administered at the beginning of treatment. If initiating treatment with Aristada Initio®, 1 day oral supplementation with aripiprazole 30 mg tablet is required.	4 days	4 to 6 months
Aripiprazole lauroxil (Aristada Initio®)	Once at the beginning to initiate aripiprazole lauroxil (Aristada®) treatment	675 mg	675 mg	Not applicable (N/A)	1 day (aripiprazole 30 mg tablet) —therapeutic levels in 4 days	27 days	With single IM injection of Aristada initio® and 30 mg oral aripiprazole at time of first Aristada® dose, aripiprazole concentration reaches therapeutic levels within 4 days

Table 6 (continued). Recommended Medications for the Treatment of Schizophrenia: Long-Acting Injectable Antipsychotics

Medication	Dose Interval	Dosage Strengths/ Forms	Starting Dose	Maintenance Dose	Oral Supplementation	Time to Peak	Steady State
Olanzapine pamoate‡ (Zyprexa Relprevv®)	2 to 4 weeks	210, 300, 405 mg vial kits	Varies, up to 300 mg every 2 weeks	Varies, up to 300 mg every 2 weeks	No	4 days	3 months
Paliperidone palmitate (Invega Sustenna®)	Monthly	38, 117, 156, 234 mg prefilled syringes	234 mg (day 1) + 156 mg (day 8)	117 mg (38 to 234 mg)	No	13 days	7 to 11 months
Paliperidone palmitate (Invega Trinza®)	Once every 3 months	273, 410, 546, 819 mg prefilled syringes	Depends on once-monthly paliperidone palmitate (Invega Sustenna®) dose	Varies, 273 to 819 mg	No	30 to 33 days	Continues steady state at equivalent dose
Paliperidone palmitate (Invega Hafyera™)	Once every 6 months	1,092 mg and 1,560 mg prefilled syringes	Depends on last dose of one-month (Invega Sustenna®) or three-month (Invega Trinza®) formulation of paliperidone palmitate	Varies; 1,092 mg or 1,560 mg	No	29-32 days	Continues steady state at equivalent dose of one-month or 3-month formulation of paliperidone palmitate
Risperidone microspheres (Risperdal Consta®)	Once every 2 weeks	25, 37.5, 50 mg vial kits	Varies, 12.5 mg to 25 mg	Varies, 12.5 mg to 50 mg	3 weeks	4-6 weeks	Steady state reached after 4 injections and maintained for 4-6 weeks after last injection
Risperidone extended release subcutaneous injectable (Perseris®)	Monthly	90 mg, 120 mg powder and liquid filled syringes	90 mg, 120 mg	90 mg, 120 mg	No	4-48 hours	4-6 weeks

Adapted and updated from: Correll CU, Kane JM, Citrome LL. Epidemiology, Prevention, and Assessment of Tardive Dyskinesia and Advances in Treatment. J Clin Psychiatry. 2017 Sep/Oct;78(8):1136-1147.

Notes: For the most updated Florida Medicaid Preferred Drug List, visit https://ahca.myflorida.com/medicaid/Prescribed_Drug/pharm_thera/fmpdl.shtml.

**First-generation long-acting injectable antipsychotic medications (fluphenazine decanoate and haloperidol decanoate) have an oil base. Second-generation long-acting injectable antipsychotic medications (aripiprazole monohydrate, aripiprazole lauroxil, olanzapine pamoate, 1-month and 3-month paliperidone palmitate, and risperidone microspheres) have a water base.*

*** Initial Aristada® dose is based on current oral aripiprazole dose as follows: If oral aripiprazole dose is 10 mg/day, initial Aristada® dose is 441 mg once monthly. If oral aripiprazole dose is 15 mg/day, initial Aristada® dose is either 882 mg once monthly, 882 mg Aristada every 6 weeks, or 1,064 mg Aristada® every 2 months. If oral aripiprazole dose is ≥20 mg/day, initial Aristada® dose is 882 mg once monthly.*

‡Olanzapine pamoate (Zyprexa Relprevv) requires prescriber certification and patient enrollment with the Risk Evaluation and Mitigation Strategy (REMS) program. Administration of olanzapine pamoate requires at least 3-hours of post-injection monitoring for post-injection delirium/sedation syndrome (PDSS). Olanzapine has been found to cause more weight gain and related metabolic side effects than other SGAs

Summary: Treatment of Schizophrenia

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Introduction

The primary objectives in the treatment of schizophrenia are to reduce frequency and severity of psychotic exacerbation, ameliorate a broad range of symptoms, prevent relapses, and improve functional capacity and quality of life. Treatment includes medication and a range of psychosocial interventions. Antipsychotics are the cornerstone of pharmacological treatment for schizophrenia. The twenty-three antipsychotics available in our country have traditionally been classified into two major groups: 10 first-generation (conventional) agents (FGAs) and 13 second-generation (atypical) agents (SGAs), although this dichotomization can be misleading. Since the last iteration of the Florida Center for Behavioral Health Improvements and Solutions (FCBHIS) guidelines in 2019, one new antipsychotic agent (lumateperone [®Caplyta]) and a new combination (olanzapine-samidorphan [®Lybalvi]) have been introduced into clinical practice along with some new long-acting injectable formulations of existing antipsychotic agents. Basic principles of the Florida FCBHIS guidelines for the treatment of schizophrenia are summarized.

Pharmacological Treatment of Schizophrenia: What Do Antipsychotics Do?

Schizophrenia is characterized by positive (reality distortion and disorganization), negative, cognitive, and mood symptoms, with the types and severity of symptoms differing among patients and over the course of the illness. With its typical onset in early adulthood, schizophrenia tends to be a chronic illness with a relapsing and remitting course. Antipsychotic medications are the mainstay in the pharmacological treatment of schizophrenia. In addition to reducing symptoms in the acute psychotic phase of the illness, antipsychotic medications are very effective in reducing the likelihood of psychotic relapses in stable patients. Antipsychotics are most effective in ameliorating positive and disorganization symptoms, but ineffective in treating negative and cognitive symptoms. They can help but can also worsen mood symptoms (eg., neuroleptic dysphoria) and motor symptoms (eg., neuroleptic malignant syndrome). In DSM-5TR, the distinction between the different psychopathological dimensions of schizophrenia is explicitly catalogued and a simple scale for measurement of each dimension over the course of treatment (SCoRS) is provided.

Comparative Efficacy

Although it was formerly believed that FGAs are less effective than SGAs, recent trials have not confirmed this belief. Clozapine is the only antipsychotic agent that is found to be more effective than other antipsychotic agents in treating positive symptoms in otherwise refractory patients and in reducing suicidality. All other agents are found to be about equally effective, although different degrees of ease-of-use lead to minor differences in efficacy being observed in routine clinical practice. Antipsychotic medications substantially decrease likelihood of relapse in schizophrenia, without any consistent differences among agents. Since medication non-adherence is common in schizophrenia, long-acting injectable antipsychotics may have an advantage over oral treatment in reducing relapse rates.

Safety and Tolerability

Antipsychotic medications cause a range of neurological, metabolic, cardiovascular, gastrointestinal, hematological, genitourinary, musculoskeletal, endocrine, and other side-effects. In contrast to their broadly similar efficacy, antipsychotics differ markedly in adverse-effect profiles. Compared with the FGAs, SGAs generally have a lower risk of EPS. However, due to differences in pharmacological profiles within the FGA and SGA classes, there is substantial variation within both classes in their propensity to cause EPS and metabolic adverse effects. Thus, no categorical distinction can be made between so-called FGAs and SGAs with regard to these risks. Antipsychotic medications also differ in their propensity to cause other side effects, such as sedation, hypotension, cardiac arrhythmias, prolactin elevation and related sexual dysfunction, and anticholinergic effects, with substantial variation within both the FGAs and the SGAs for each of these effects, without any definitive categorical separation between the two classes. Patients with schizophrenia also vary in their vulnerability to develop various adverse effects with different agents. The likelihood that a patient will develop a particular side effect thus depends on the agent selected, how that agent is used (e.g., dose, titration method, in combination with what other agents), and the patient's vulnerability.

Optimizing Individual Outcomes

Given the significant variability in drug pharmacokinetics and treatment responsivity in individual patients, it should be emphasized that broadly equivalent efficacy across patient groups does not translate into equal efficacy in individual patients. It is not currently possible to predict which antipsychotic may be optimal for a given patient. There is no best agent or best dose for all patients, although dose ranges for optimal effectiveness do appear to exist. Decisions about antipsychotic therapy therefore often entail a trial-and-error process involving careful monitoring of response and adverse effects, an ongoing risk-benefit assessment, and judicious switching if necessary. To achieve optimal therapy for schizophrenia, clinicians must balance efficacy benefits and side-effect costs of treatments in a way that is customized for the needs and vulnerabilities of the individual patient. The meticulous application of this approach can reduce the significant gap between what we know about best practices and the therapy that is actually provided for patients with schizophrenia.

The Florida Center for Behavioral Health Improvements and Solutions (FCBHIS) guidelines for the pharmacological treatment of schizophrenia were developed on the basis of our current understanding of what they do and how they compare and a clinician-friendly elaboration of key principles.

Clinical Guidance

Schizophrenia is characterized by positive, negative, cognitive, disorganization, and mood symptoms. Antipsychotics are the mainstay of the pharmacological treatment of schizophrenia. Findings concerning efficacy for positive symptoms and disorganization suggest no consistent differences among available antipsychotics, with the exception of clozapine's superior efficacy for treatment-resistant schizophrenia. Efficacy for negative, depressive, and cognitive symptoms appears to be determined by: (i) the extent to which reduction in positive symptoms brings about improvement in these other domains and (ii) the extent to which extrapyramidal side effects (EPS) and anticholinergic effects (of the antipsychotic and of agents used to treat EPS) exacerbate them. Thus, the ability of antipsychotics to produce a potent antipsychotic effect without EPS and need for concomitant anticholinergic therapy yields multiple therapeutic benefits. In contrast to their broadly similar efficacy, antipsychotics differ markedly in their propensity to cause various adverse effects. Choice of antipsychotic medication should be

based on individual preference, prior treatment response and side-effect experience, medical history and risk factors, and adherence history, with side-effect profile a major determinant of antipsychotic choice [Box 9].

Summary

Whereas the efficacy of these antipsychotic agents in the treatment of schizophrenia is broadly similar (with the exception of clozapine's greater efficacy in otherwise treatment-refractory patients), there are significant differences in their side-effect profiles. Optimal individualized pharmacological treatment of schizophrenia requires an understanding of the nature of schizophrenia (multiple pathological dimensions, remitting and relapsing course), knowledge about the similarities and differences between available antipsychotic treatments, and awareness of how to use these treatments most effectively (targeted, measurement-based, individualized). Targeted use of a range of non-antipsychotic medications can be useful in reducing comorbid symptoms. Antipsychotic polypharmacy may be reasonable after dose optimization and consideration of clozapine and long-acting injectable antipsychotic agents.

Box 9. Steps to achieve optimum outcomes with currently available antipsychotics

1. Considerations in selecting the best antipsychotic for a particular patient

- Equivalent efficacy across agents
- Individual variability in response
- No good predictor of individual response to different agents
- Different agents have different side effects
- Different patients have different vulnerabilities and preferences

2. Proper antipsychotic trial sequence

- Begin with systematic 6-10 week trial of one antipsychotic with optimal dosing
- If inadequate response, follow with systematic trial of monotherapy with one or more other antipsychotics at adequate dose and duration
- If inadequate response, follow with a trial of clozapine or a long-acting antipsychotic
- Follow with a trial of clozapine, if not tried before
- Only then consider other strategies (e.g., antipsychotic polypharmacy)

3. Good practice guidelines for ongoing antipsychotic treatment

- Measurement-based individualized care
- Repeated assessment of efficacy using reliably defined treatment targets (facilitated by use of standard rating scales)
- Careful assessment of adverse effects
- Care consistent with health monitoring protocols
- Standard protocols customized to individual vulnerabilities/needs and specific agent
- Ongoing collaboration with patient in decision-making

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Summary: Navigating Insurance

The 2023 Florida Expert Panel offers these tips to optimize accessibility and/or reimbursement for a proposed plan of medication treatment. These tips represent the expert opinion of the diverse stakeholders of the Panel, although not "evidence based" in the traditional sense of the term as used elsewhere in these guidelines.

Tips for Ensuring Successful Medications Approval:

1. Make sure the medicine you prescribe has an FDA indication for the condition and age group you are treating.
2. Consider generic formulations wherever possible.
3. For behavioral health conditions: Specify the severity of illness. Note if the patient was just released from a hospital, if patient was suicidal or homicidal, disabled, had violent behavior, demonstrated self-injurious behavior, or was under court-ordered treatment.
4. For LAI antipsychotics: A history of repeated non-adherence to oral medications, multiple admissions, and no side effects from a trial of the oral equivalent of the LAI antipsychotic are key to approval.
5. If quantity limits are an issue, note if you are prescribing the effective dose needed for symptom management or are cross-tapering medications.
6. Provide a list of past medications tried and failed and specific reasons why those medication trials failed.
7. Document non-medication interventions being used in addition to prescribed medications.
8. Familiarize yourself with the Preferred Drug List of the health plans you work with. Consider medications that do not require a prior authorization for the conditions you most commonly see in your practice.
9. For children: Provide parental informed consent as well as the child's diagnosis, severity of illness, metabolic profile/labs, BMI, treatment plan and goals, and baseline AIMS.
10. For Tardive Dyskinesia, include the Abnormal Involuntary Movement Scale (AIMS) test scores. A score of 3 or 4 on any AIMS subscale is a criteria for approval by some plans.
11. You can always ask for a doctor to doctor review.
12. You always have the right to appeal if you feel the managed care company does not have all the information.

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