Next-Step Treatment Options for Treatment-Resistant Depression:

Insights From the Mayo Clinic Depression Center Panel

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Abstract

Objective: Treatment-resistant depression (TRD) affects one-third of patients with major depressive disorder, leading to increased morbidity, health care costs, and suicide risk. TRD lacks a standardized definition, complicating treatment selection. Current guidelines often group treatments broadly without clear prioritization, and evidence gaps persist, particularly regarding newer interventions and real-world clinical complexity. A simulated case-based discussion, modeling a modified Delphi consensus, was conducted to offer a clinical perspective to this gap.

Participants: A panel of 10 psychiatrists, directly engaged in the treatment of TRD at the Mayo Clinic Depression Center, participated in the surveys.

Evidence: Results represent expert opinion from participants. The process included an initial group review of TRD, where participants reviewed and presented a summary on each TRD treatment option, followed by discussion.

Process: Using a structured clinical vignette of a patient with TRD after 3 antidepressant trials, statements regarding next-step treatments were created through iterative ranking of options. Six vignette variations reflecting common clinical considerations (eg, metabolic disease, age) were included. Agreement was measured in 3 anonymous survey rounds, with group discussions in between.

Conclusions: Strong consensus emerged recommending augmentation with second-generation antipsychotics, transcranial magnetic stimulation, and ketamine/esketamine as next-step treatments in the base vignette. Treatment preferences shifted to include nonaugmentative antidepressants and electroconvulsive therapy based on changes in patient characteristics. This study highlights the importance of tailoring treatment strategies for TRD to patient factors that extend beyond conventional guideline tiers. Integrating multidisciplinary perspectives and patient preferences holds promise for enhancing therapeutic selection and advancing personalized care in TRD.

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Depression is a leading cause of increased morbidity, work absenteeism, and health care costs worldwide. Patients who fail to achieve remission after multiple treatment attempts are often diagnosed with treatment-resistant depression (TRD). These individuals face a particularly high burden of illness, with prolonged depressive episodes, greater career disruption, and an elevated risk of suicide compared to other depressed patients.[1–3] From a public health perspective, TRD accounts for a substantial share of depression-related treatment and disability costs.[4]

Efforts to improve TRD treatment face fundamental challenges, beginning with the lack of diagnostic consensus. A systematic review by Brown et al[5] identified 155 definitions of TRD. Regulatory agencies such as the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) also partially differ in their description. There are also attempts for staging TRD such as the Thase and Rush staging model[6] and the Maudsley Staging Model.[7] Such variability in TRD definitions culminates in significant obstacles for the development of research, public policies, and clinical guidelines.[8] A common contemporary TRD definition, including the FDA and the EMA, is the failure of at least 2 trials of antidepressant treatments with adequate dose and duration.[5,9] Still, treatment trials investigating TRD treatment at times have defined it as failure of only 1 antidepressant trial.[10]

Treatment of TRD is further complicated by important gaps in the evidence concerning interventions

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Clinical Points

- Caring for individuals with treatment-resistant depression (TRD) presents several challenges, including inconsistencies in its definition, uncertainty about how to integrate newer interventions into stepwise treatment algorithms, and the need to tailor recommendations to individual patient characteristics.
- Expert consensus supports second-generation antipsychotic augmentation, transcranial magnetic stimulation, and ketamine/esketamine as preferred next-step options following multiple treatment failures. Treatment preferences varied based on patient characteristics, highlighting the importance of individualizing care.
- This simulated case-based discussion, modeling a modified Delphi consensus process and grounded in real-world clinical experience, underscores the value of incorporating clinician judgment and patient-specific factors to guide treatment selection in TRD.

in this population. The landmark Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial[11] remains one of the most important references available in the sequential treatment of depression. However, the study was conducted 2 decades ago, and many now established interventions were not included, such as augmentation with second-generation antipsychotics (SGA), ketamine/esketamine (for the purposes of this paper, ketamine will be used to refer to both agents), combination of dextromethorphan and bupropion, and transcranial magnetic stimulation (TMS); electroconvulsive therapy (ECT) was also not part of the STAR*D. Data are also limited on direct comparisons between available treatments and how previous treatment failures might predict response to subsequent interventions.

Such limitations of evidence become even more important when considering the complexity of real-world TRD patients. Randomized controlled trials often exclude patients with TRD. Higher suicidality, hospitalizations, and longer duration of depressive episodes in individuals with TRD can also lead to exclusion of these patients from studies. Beyond such exclusions, patients with TRD commonly present somatic and psychiatric comorbidities that substantially influence treatment selection.[8,12] For instance, metabolic conditions may preclude antipsychotic augmentation, cardiovascular disease limits options like tricyclic antidepressants (TCAs) and raises concerns about hemodynamic effects of other agents, and substance use disorders create dilemmas around potentially addictive medications. Finally, sensitivity to interventions limiting adherence is also present in practice. Given this disconnect between available evidence and clinical reality, treatment decisions often rely heavily on clinical judgment. To systematically capture how expertise may bridge this disconnect between available evidence and clinical reality, we conducted a simulated case-based discussion/consensus study among board-certified psychiatrists from the Mayo Clinic Depression Center (MCDC), using clinical vignettes. Treatment recommendations from these discussions may be adapted to specific patient characteristics.

METHODS

The simulated case-based discussion process involved a panel with 10 Mayo Clinic Mood psychiatrists who are directly engaged in the treatment of TRD at the MCDC. The panel's objective was to identify 1 to 3 most recommended next-step treatment options for TRD through consensus. A clinical vignette (presented in Box 1) served as the basis for discussion and consensus-building, reflecting a case of no remission after treatment with 3 different agents present in steps 1 and 2 of the STAR*D trial.[11] In addition to the primary vignette, the group aimed to reach consensus on 6 variations in which *one aspect* of the clinical presentation was modified (as outlined in Table 1). Direct recommendations for TRD treatment considering each variation in these 6 additional scenarios are not provided in several important guidelines for treatment of depression.[13–16] For the purposes of this study, the vignette assumed that the patient had completed an adequate course of psychotherapy and regular exercise, so these were not included as treatment options. The consensus process was facilitated by a psychiatrist completing an additional year of training as a Mood Fellow (M.G.M.), who did not participate in the surveys. Two other Mayo Clinic psychiatrists (B.P. and S.C.) were also part of the creation of the questionnaire and did not participate in the consensus survey.

A modified Delphi method was employed to facilitate consensus among participants. The traditional Delphi approach involves a structured, iterative process in which

Box 1.

The Clinical Vignette

"Ms X is a 30-year-old woman who presents to our service for consultation regarding the management of her depression. Her symptoms are consistent with a depressive episode of Major Depressive Disorder, single episode, with an approximate duration of 12 months. She endorses passive suicidal ideation but denies active intent or plan. There are no psychotic features. PHQ-9 today is 24. The interview does not indicate a history of prior depressive episodes, substance use, manic/hypomanic episodes, anxiety disorder, OCD, or characteristics suggestive of an underlying personality disorder. She has no prior psychiatric hospitalizations or suicide attempts. She has been consistently engaged in weekly psychotherapy for the last 6 months and exercises 30 minutes 3–4 times a week. She had 3 prior adequate antidepressant trials (1 SSRI, followed by combination with bupropion, later switching to venlafaxine XR). She has been taking venlafaxine XR 300 mg for the last eight weeks. Her past medical history is negative for hypothyroidism, anemia, vitamin deficiency, diabetes, seizures, TBI, or coronary artery disease. Her Body Mass Index is 24 kg/m^2. She has never been pregnant."

Table 1.
Vignette Variations

Vignette	Variations
1	Base clinical vignette
2	Base clinical vignette with comorbid substance use disorder
3	Base clinical vignette, but the patient is 70 years old
4	Base clinical vignette with comorbid diabetes and body mass index greater than 40 kg/m^2
5	Base clinical vignette with comorbid coronary artery disease of moderate severity
6	Base clinical vignette with a history of seizures (no longer on anticonvulsant per neurologist recommendations)
7	Base clinical vignette with a history of sensitivity to medications affecting adherence

participants respond anonymously to a specific question or statement, with opportunities to revise their responses after reviewing the group's aggregated feedback.[17] The process continues until consensus is reached—ideally based on a predetermined definition—or until a set number of iterations have been completed.[18] This method is often the recommended strategy for consensus studies in health research.[19] The modified approach used in this study allowed for open discussion among participants between survey rounds, while maintaining the anonymity of individual responses, and therefore cannot be considered a traditional Delphi study.

Creating the Consensus Questionnaire

The consensus questionnaire was developed through open group discussions, interspersed with anonymous surveys designed to capture treatment recommendation statements for formal appraisal. Prior to the initial discussion, each participant was assigned a TRD treatment option to review and present in a 10-minute summary. Microsoft Forms was used to administer surveys. The first survey included the original clinical vignette and its 6 variations. Participants were asked to rate each treatment option as "definitely recommend," "likely to recommend," "likely not to recommend," or "will not recommend." They also ranked treatments from most to least appropriate and were prompted to revise or maintain their responses based on the vignette variations. This step additionally allowed participants to suggest changes to the list of treatment options or propose modifications to the vignette for clarity.

In the subsequent 2 surveys, participants were asked: "What would be your top 1–3 treatment choices (equally recommended) as the next step for the patient described in the vignette and its variations?" They were also invited to identify the options that they would not recommend in each scenario. Additionally, participants had the opportunity to provide anonymous comments explaining their reasoning and to highlight other factors they believed should inform treatment decisions but were not included in the vignette. After each survey round, the group reviewed and discussed the aggregated results. The final consensus questionnaire was developed based on the data gathered through this iterative process. A complete list of treatment options considered is presented in Table 2.

Consensus Definition and Process

Each item in the consensus questionnaire was phrased as: "...would be my main choice(s) as the next treatment recommendation for this patient." Agreement was assessed using a 9-point Likert scale, where 1 indicated complete disagreement, 9 indicated complete agreement, and 5 represented a neutral stance. Full consensus was defined as all members rating the statement above neutral (ie, >5), with a mean agreement score exceeding 7. There was no predetermined number of rounds required to reach consensus. Responses remained anonymous, and the group reviewed and discussed the results following each round.

RESULTS

The consensus process occurred between May and October 2024. The consensus survey was answered by 10 psychiatrists (50% female) involved in the MCDC. The process included 3 meetings—2 in-person sessions lasting 3 hours each and 1 virtual meeting lasting 1 hour—along with 3 surveys used to develop the consensus questionnaire. Agreement on treatment recommendations was assessed through 3 rounds of responses to the final questionnaire. The results after the third and final round of voting are represented in Table 3. Across all scenarios, treatment recommendations achieved strong consensus (mean rating >8.0 in all cases). In addition to the consensus questionnaire, participants also selected treatment options that they would recommend against in each scenario. Table 4 lists the treatment options that 50% of the group or more would not recommend in each scenario.

Throughout the discussions, several adjustments were made to the clinical vignette and treatment options based on participant feedback. It was clarified that, in the presented case, bupropion was combined with the first SSRI tried, rather than with a second SSRI. Initially, a seventh vignette variation addressing postpartum depression was included in the first survey; however, the group agreed to remove it in subsequent rounds, as there was clear consensus that brexanolone or zuranolone would be the preferred treatments if no prescribing

Table 2.
Treatment Options Present in the Surveys

Add	Switch
FDA-approved SGA	SRI not yet tried
Lithium	Mirtazapine
Thyroid hormone	TCA
Ketamine or esketamine	MAO-I
TMS	Dextromethorphan-bupropion
ECT	

Abbreviations: ECT = electroconvulsive therapy, FDA = US Food and Drug Administration, MAO-I = monoamine oxidase inhibitor, SGA = second-generation antipsychotic, SRI = serotonin reuptake inhibitor, TCA = tricyclic antidepressant, TMS = transcranial magnetic stimulation.

barriers existed. Vortioxetine and vilazodone were originally listed as separate options, but following discussion, they were combined with the "SSRI/SNRI not yet tried" category (now termed "SRI not yet tried"), reflecting members' view that these agents would be considered similarly to other SSRIs in the clinical scenarios presented.

DISCUSSION

This study describes a consensus-building effort among psychiatrists at the MCDC to identify preferred next-step treatment options for a patient with TRD, using a structured clinical vignette of a patient without remission after 3 treatment trials. The clinical discussions and consensus process, modeling a modified Delphi approach, allowed for both anonymous input and open discussion, fostering thoughtful engagement and minimizing individual bias. The patient described in the vignette met commonly accepted definitions of TRD, having not achieved remission after multiple evidence-based interventions. By narrowing the focus to 1 to 3 next-step recommendations and examining how these choices shift in response to variations in clinical presentation, this study provides practical insights into the clinical decision-making process in TRD. Importantly, the group achieved consensus on several treatment pathways and demonstrated how specific patient characteristics—such as comorbidities, history of response, or contextual factors—may influence treatment prioritization. The findings, along with the discussions that informed them, provide a clinical perspective on the management of TRD and highlight the challenges clinicians face in navigating the gap between available evidence and real-world decision-making.

In the original vignette, following nonresponse to an SSRI, an SNRI, and augmentation with bupropion, the most recommended next-step treatment options were TMS, ketamine, and augmentation with an SGA. Notably, none of these options were included as part of the STAR*D trial, reflecting the evolving landscape of pharmacotherapy and neuromodulation, as well as the growing influence of real-world clinical experience in guiding treatment decisions. These recommendations reflect overall clinical experience rather than a formal review of the literature. The selection of TMS and ketamine highlights their growing role in TRD treatment, with both modalities being listed as possible recommendations in clinical guidelines such as the Canadian Network for Mood and Anxiety Treatments and the Department of Veterans Affairs.[13,14] Two recent clinical trials[20,21] comparing TMS to pharmacotherapy in patients with TRD reported findings favorable to TMS, supporting its earlier consideration in the treatment algorithm for TRD.[22] While IV ketamine is not FDA-approved for TRD, it has a strong evidence base for TRD[23,24] and will likely continue to be an option for the off-label treatment of TRD. Esketamine, which was FDA-approved for TRD augmentation in 2019, was recently approved as monotherapy treatment for TRD.[25] Augmentation with an SGA has also consistently demonstrated efficacy in patients who have not responded to previous trials.[26,27]

Scenario-Specific Considerations

Older adults. In older adults, the top 3 recommended treatment options were ECT, TMS, and augmentation with an SGA. Participants emphasized the robust evidence base for ECT and potentially greater efficacy in older adults.[28] Data also support the efficacy of SGA augmentation, in particular aripiprazole, when compared to placebo[29] and bupropion.[30] Ketamine was not among the main recommendations in this scenario. Although esketamine is FDA-approved for MDD without age-specific restrictions and available data suggest reasonable safety and acceptability in older adults,[31] participants expressed concerns regarding the limited amount of age-specific data, potential drug interactions, and the presence of medical comorbidities common in this population.[23,32]

Substance use disorder. In the vignette involving comorbid substance use disorder, participants emphasized the importance of addressing addiction with a primary focus on achieving abstinence. Main recommendations were TMS, augmentation with an SGA, or trial of SRI not yet tried by the patient. There was hesitation to recommend ketamine in this context, due to it being a controlled substance and concerns about its potential for misuse and its mechanism of action, which may promote positive reinforcement in a patient already vulnerable to addiction.[33]

Metabolic disease. Participants' main recommendations for the vignette involving a patient with a body mass index over 40 kg/m^2 and diabetes were TMS, SRI not yet tried by the patient, or a combination of dextromethorphan and bupropion. A key part of the discussion emphasized prioritizing treatments that are weight-neutral or that may contribute to weight loss.

Table 3.

Consensus Recommendations

If the patient in the vignette…	Main recommendations	All ratings 6 or higher?	Average recommendation rating (1–9)
Base vignette	Augmentation with SGA, TMS, or ketamine/esketamine	Yes	8.40
Had a comorbid substance use disorder	Augmentation with SGA, TMS, or SRI not yet tried	Yes	8.30
Was 70 years old	Augmentation with SGA, TMS, or ECT	Yes	8.30
Had diabetes and body mass index greater than 40 kg/m²	TMS, SRI not yet tried, or dextromethorphan-bupropion	Yes	8.44
Had comorbid coronary artery disease of moderate severity	TMS or SRI not yet tried	Yes	8.50
Had a history of seizures (no longer on anticonvulsant per neurologist recommendations)	Augmentation with SGA or SRI not yet tried	Yes	8.40
Had a history of sensitivity to medications affecting compliance	TMS	Yes	8.70

Abbreviations: ECT = electroconvulsive therapy, SGA = second-generation antipsychotic, SRI = serotonin reuptake inhibitor, TMS = transcranial magnetic stimulation.

Table 4.

Not Recommended by at Least 50% of Participants as the Next Step

If the patient in the vignette…	At least 50% of members would not recommend:
Base vignette	ECT (60%) and MAO-I (70%)
Had a comorbid substance use disorder	Ketamine (100%) and dextromethorphan-bupropion (90%)
Was 70 years old	Ketamine (80%)
Had diabetes and body mass index greater than 40 kg/m²	Augmentation with SGA (90%) and mirtazapine (80%)
Had comorbid coronary artery disease of moderate severity	Augmentation with SGA (90%) and ketamine (50%)
Had a history of seizures (no longer on anticonvulsant per neurologist recommendations)	TMS (90%)
Had a history of sensitivity to medications affecting compliance	Augmentation with lithium (80%), MAO-I (70%) and TCA (70%)

Abbreviations: ECT = electroconvulsive therapy, MAO-I = monoamine oxidase inhibitor, SGA = second-generation antipsychotic, TCA = tricyclic antidepressant, TMS = transcranial magnetic stimulation.

SGAs are known to contribute to metabolic disorders and cardiovascular disease, which represent leading causes of morbidity and mortality in patients with mood disorders. The well-established risks of weight gain, dyslipidemia, and poor glycemic control associated with many SGAs[34] make minimizing exposure in patients with existing metabolic conditions a prudent approach. Still, it is important to note that metabolic risk varies among SGAs, with agents such as aripiprazole and cariprazine demonstrating a lower propensity for metabolic side effects.[35] Ketamine was not among the main recommendations for this patient; some participants mentioned concerns that, should rare adverse effect such as respiratory depression occur, management such as intubation would be complicated in an outpatient setting. Additionally, the preference for treatments with a lower risk of weight gain contributed to the decision to recommend against mirtazapine.

Coronary artery disease. The group chose TMS or SRI not yet tried as the main treatment recommendations in the scenario of moderate coronary artery disease. Similar to the vignette involving metabolic disease, the group recommended against augmentation with an SGA. This recommendation reflects the known adverse metabolic effects of SGAs, which are independent risk factors that may exacerbate coronary artery disease.[36] Ketamine was also not recommended due to its association with transient increases in blood pressure. Although these increases are typically of low magnitude, cases of hypertensive urgency have been reported, underscoring the need to carefully consider cardiovascular risks when selecting treatment.[37–39]

History of seizures. In the vignette featuring a patient with a past history of seizures no longer requiring anticonvulsant treatment, SRI not yet tried or augmentation with SGA were the main recommendations. This was the only scenario in which TMS was not recommended as the next treatment step. Although an increased risk of seizures with TMS has been reported, the implications for patients with a remote seizure history remain unclear, as does how this risk compares to that associated with other antidepressants. Additionally, insurance coverage for TMS in patients with a

seizure history is often challenging, as some insurers list seizure history as an exclusion criterion.

History of sensitivity to medications. TMS was the only primary recommendation for the vignette involving sensitivity to medications that may limit treatment adherence, with participants emphasizing its relatively low side-effect burden. Augmentation with an SGA was not among the main recommendations in this scenario, reflecting concerns that side effects could further reduce tolerability in this population—although side-effect profiles do vary across different agents.[40] Participants also chose not to recommend ketamine as a main option due to concerns about its side effects, despite evidence indicating that discontinuation rates for ketamine are not higher than those for other antidepressants. Additionally, the use of monoamine oxidase inhibitors, TCAs, and lithium augmentation was discouraged in this scenario because of concerns about lower tolerability. Although pharmacogenomic testing was considered as a potential option for this subgroup, the group ultimately decided not to include it among the treatment recommendations.

Clinical Implications and Real-World Applications

Based on the group's discussion, changes in treatment recommendations across vignettes were largely driven by increased risk, potential contraindications, or limited available data for specific subgroups. Ketamine was the clearest example of this trend, with the group demonstrating a low threshold for removing it from the main recommendations in scenarios where added clinical complexity highlighted the need for more robust evidence. This cautious approach may also reflect the fact that none of the added variables were strongly predictive of improved outcomes with an alternative treatment—except for ECT in older adults, where evidence supports greater efficacy. It is important to interpret these recommendations within the context of the vignette's treatment stage: The patient had failed only 3 interventions, leaving several evidence-based options still available. As treatment resistance progresses, the balance of risks and benefits may shift, potentially altering the group's willingness to consider certain options.

While patient comorbidities may have steered members away from certain treatments in this exercise, in clinical practice such impediments are not always immutable. For example, not only are options now available to mitigate weight gain associated with SGAs (eg, metformin[41,42]), but also treatment options for obesity have increased, including the use of glucagon-like peptide-1 receptor agonists.[43,44] Coronary artery disease of moderate severity, while requiring cautious consideration, may not be prohibitive for certain treatments such as ketamine with proper multidisciplinary discussion and adequate illness control in place.[45] Finally, this consensus did not explore certain nuances that could have affected recommendations, such as the type of substance in the vignette addressing substance use disorder.

In addition to the clinical variations addressed in each vignette, participants identified several sociodemographic factors relevant to treatment decisions. Accessibility was frequently noted, including the cost of interventions and the distance to facilities offering specific treatments such as ECT, TMS, and ketamine. Participants also emphasized the importance of considering particular symptom profiles—such as sleep disturbances, low energy, anhedonia, and anxiety—when selecting a treatment. The group discussed how clinical response might guide the choice to switch medications rather than adding another agent. Additionally, a family history of positive response to a specific treatment was recognized as a potentially influential factor in decision-making.

A commonly expressed challenge among participants was the contrast between the vignette patient and the typical clinical experience of treating individuals with TRD. While TRD encompasses a heterogeneous population, it is uncommon to encounter patients who present without somatic or psychiatric comorbidities, who are physically active, fully adherent to medications, and have received adequate psychotherapy—all features assumed in the vignette. In real-world practice, these complicating factors are common and should be addressed alongside decisions about the next pharmacologic or neuromodulation intervention. Another point raised was the absence of detailed information about the patient's degree of response to prior treatments. Participants interpreted the case as one of nonresponse based on the PHQ-9 score of 24. As such, the consensus findings may not apply to cases where partial response has been observed, where preferences may shift toward augmentation strategies or antidepressant combinations.[27]

Interestingly, in most vignette scenarios, only a small number of treatments were consistently rated as "not recommended." Participants acknowledged that aside from treatments with clear contraindications or disproportionate risks, many available options could still offer some benefit, even if they were not included among the top recommendations. Given the limitations of the current evidence base, it was felt that few treatments could be categorically ruled out in the scenarios presented.

The consensus findings are informative but should be interpreted within the context of several limitations. First, the study was conducted at a single institution with a relatively small sample of psychiatrists, which may limit its generalizability. Furthermore, participants'

area of research and clinical expertise with certain interventions may influence their appraisal, and we sought to mitigate this by inviting participants from multiple settings of practice and requiring a high threshold for consensus. Second, although the modified Delphi method supports rigorous qualitative input with anonymous surveys, it is possible that the open discussion phase between survey iterations may have influenced participants in unintended ways. The absence of patient perspectives is also a notable limitation, particularly with the importance of shared decision-making. Finally, the treatment options discussed were based on the collective clinical expertise and their interpretation of literature; as the evidence base evolves, so may these recommendations.

Despite its limitations, this survey meaningfully contributes to the literature on TRD management by complementing existing guidelines, which often group treatment options in broad tiers without providing clear hierarchical rankings within each tier.[13–16] When patient-specific factors are considered[13,15] to refine these options further, the focus is typically on *DSM-5* specifiers (eg, melancholic features, anxious distress) or symptom profiles (eg, insomnia, cognitive dysfunction). Our consensus offers an additional perspective by highlighting how other clinically relevant variables—commonly encountered in clinical practice but not explicitly addressed in current guidelines—may inform treatment prioritization. Future efforts could build on this approach by incorporating multidisciplinary perspectives and integrating patient preferences, further advancing the goal of individualized TRD care.

CONCLUSIONS

With a wide range of treatment options available, individualized care remains essential. Treatment selection must account for each patient's unique clinical profile, comorbidities, and preferences. Factors such as the urgency of symptom relief, tolerance for potential side effects, treatment duration, cost, and logistical barriers all play a role. Importantly, the risks and benefits of treatment are weighed differently by each individual, and any recommendation should be framed within the context of shared decision-making.

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