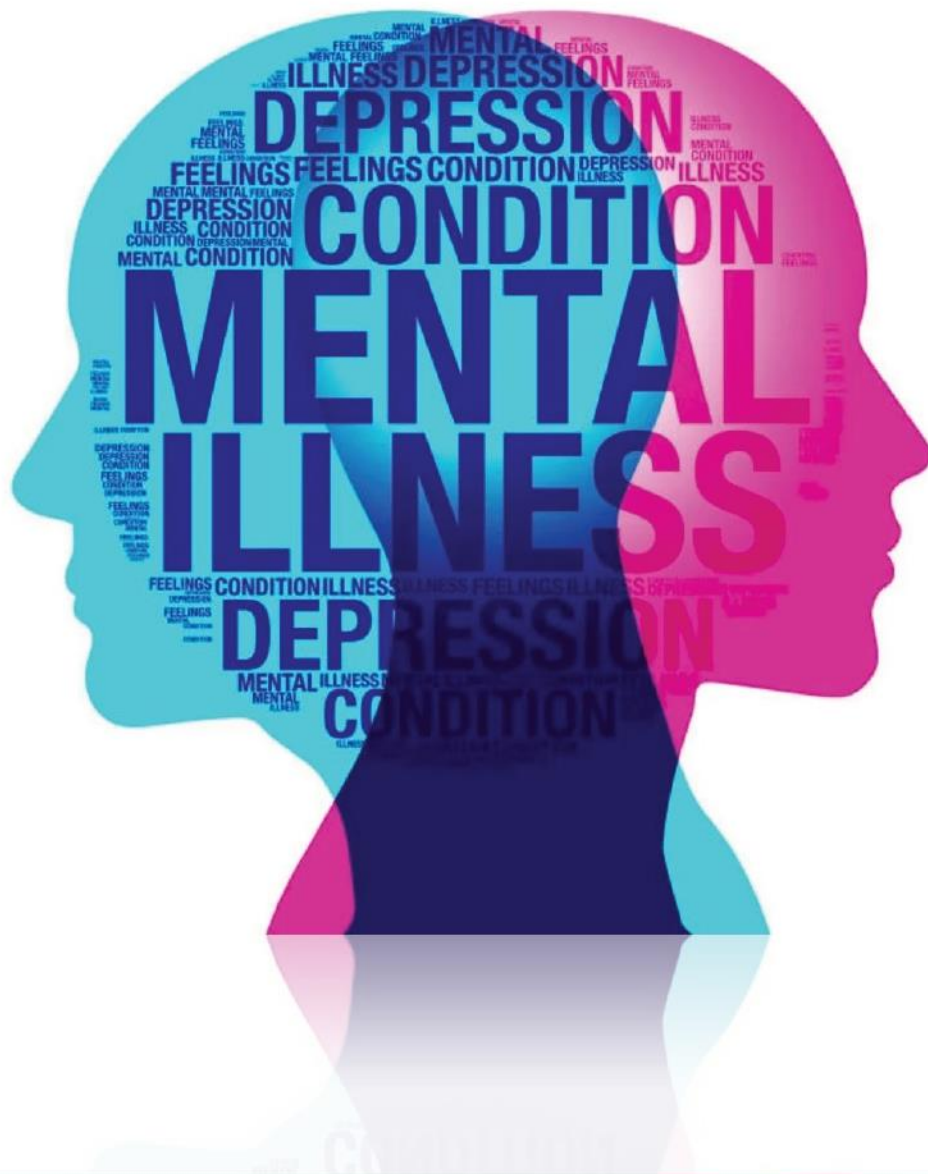


Role of Dextromethorphan and Bupropion  
Combination Therapy for  
**Major Depressive Disorder**  
(MDD) treatment



## **Table of Content**

<b>1 Introduction.....</b>	<b>2</b>
<b>2 Rationale of the Study .....</b>	<b>5</b>
<b>3 Study Objective .....</b>	<b>4</b>
<b>4 Methods.....</b>	<b>6</b>
<b>5 Results .....</b>	<b>8</b>
<b>6 Summary.....</b>	<b>28</b>
<b>7 Discussion .....</b>	<b>29</b>
<b>8 Clinical Recommendations .....</b>	<b>30</b>
<b>9 Consultant Opinion.....</b>	<b>31</b>
<b>10 Market Opportunities .....</b>	<b>31</b>
<b>11 Market Positioning.....</b>	<b>32</b>
<b>12 References.....</b>	<b>34</b>

## INTRODUCTION

Major Depressive Disorder (MDD) is a pervasive and debilitating mental health condition that significantly affects millions of individuals worldwide. Characterized by persistent low mood, anhedonia, cognitive impairments, and a range of physical symptoms, MDD imposes substantial personal, societal, and economic burdens. According to the World Health Organization (WHO), MDD is among the leading causes of disability globally, with an estimated lifetime prevalence of 15% (1). The disorder not only disrupts the quality of life but also increases the risk of comorbid conditions, including cardiovascular disease, diabetes, and substance abuse disorders (2).

The pathophysiology of MDD is complex and multifactorial, involving genetic, neurobiological, and environmental factors. Dysregulation of monoaminergic neurotransmitters—serotonin, norepinephrine, and dopamine—has long been considered central to its etiology. However, emerging research highlights the importance of additional pathways, including glutamatergic signaling, inflammation, and neuroplasticity deficits (3, 4). These insights underscore the limitations of traditional antidepressants, which primarily target monoaminergic systems, and reveal the need for therapies with novel mechanisms of action.

### Limitations of Current Treatments

For decades, the treatment of MDD has relied heavily on selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), and other classes of antidepressants such as tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs). While these therapies provide symptom relief for many, approximately one-third of patients fail to respond adequately, a condition referred to as treatment-resistant depression (TRD) (5). Even among those who respond, the latency of therapeutic onset—typically weeks to months—poses a significant challenge, especially for patients

with severe symptoms or suicidal ideation (6). Furthermore, side effects such as sexual dysfunction, weight gain, and sedation contribute to poor adherence, further limiting treatment efficacy (7).

In recent years, novel therapies have emerged to address these limitations. Ketamine, an NMDA receptor antagonist, demonstrated rapid antidepressant effects, inspiring interest in glutamatergic pathways as therapeutic targets (8). However, ketamine's use is constrained by its dissociative side effects, potential for misuse, and need for intravenous administration. Against this backdrop, the combination of Dextromethorphan and Bupropion represents a promising new approach to MDD treatment.

### **Dextromethorphan and Bupropion: Mechanism of Action**

Dextromethorphan, traditionally known as a cough suppressant, has garnered attention for its antidepressant properties. It acts primarily as an NMDA receptor antagonist, modulating glutamatergic neurotransmission and promoting neuroplasticity (9). Additionally, Dextromethorphan exhibits sigma-1 receptor agonism, which enhances neuroprotection and modulates mood-regulating pathways (10). These mechanisms contribute to its rapid antidepressant effects, akin to ketamine, but with a more favorable safety profile.

Bupropion, a norepinephrine-dopamine reuptake inhibitor (NDRI), complements Dextromethorphan by enhancing dopaminergic and noradrenergic neurotransmission. This dual action not only amplifies the therapeutic effects but also mitigates the risk of serotonin syndrome, a potential complication of monoaminergic therapies (11). By targeting multiple pathways implicated in MDD, the combination offers a multimodal mechanism of action that sets it apart from existing treatments.

## Clinical Evidence

Several clinical trials have demonstrated the efficacy and safety of the Dextromethorphan-Bupropion combination in treating MDD. In a pivotal Phase 3 trial, the combination showed statistically significant improvements in depressive symptoms compared to placebo, with rapid onset of action observed within one week of treatment initiation (12). Patients reported substantial reductions in core symptoms, including mood disturbances, anhedonia, and cognitive impairments. Importantly, the combination was well-tolerated, with a low incidence of adverse effects such as dizziness and dry mouth (13).

Another notable advantage of this therapy is its applicability to diverse patient populations, including those with TRD or comorbidities that preclude the use of vasoconstrictive agents like Triptans. Unlike ketamine or electroconvulsive therapy (ECT), the combination can be administered orally, enhancing its feasibility for widespread use (14).

## Addressing Unmet Needs in MDD Treatment

The introduction of the Dextromethorphan-Bupropion combination marks a significant advancement in the treatment landscape of MDD. However, several questions remain unanswered regarding its real-world effectiveness, safety, and acceptability. Clinical trials, while rigorous, often involve controlled settings that may not fully capture the complexities of routine practice. For instance, patients in clinical trials are typically screened for specific characteristics, which may not reflect the heterogeneity of real-world populations (15).

Real-world data are essential to evaluate how this combination performs in broader clinical scenarios, including:

- **Patient Demographics:** Assessing the efficacy and safety across diverse age groups, genders, and comorbid conditions.

- **Prescribing Patterns:** Understanding how clinicians integrate the combination into existing treatment algorithms and its role relative to SSRIs, SNRIs, and other options.
- **Barriers to Adoption:** Exploring potential obstacles such as cost, availability, or concerns about side effects.

## **RATIONALE OF THE STUDY**

MDD continues to pose a significant global health challenge, with many patients experiencing inadequate relief from traditional antidepressant therapies. The need for innovative treatments is underscored by the growing recognition of the limitations of monoaminergic-based approaches. The Dextromethorphan-Bupropion combination represents a paradigm shift in MDD management by targeting glutamatergic and dopaminergic systems, offering potential benefits for patients with TRD or partial responders to existing treatments.

While clinical trials have demonstrated its efficacy and safety, real-world data on its use are crucial to understanding its broader applicability, identifying patient subgroups most likely to benefit, and addressing barriers to adoption. This study seeks to provide these insights, contributing to evidence-based advancements in MDD treatment.

## STUDY OBJECTIVE

The primary objective of this study is to evaluate the real-world usage, effectiveness, and safety of the Dextromethorphan-Bupropion combination therapy for MDD treatment. Specifically, the study aims to:

1. **Assess Clinician Awareness and Familiarity:** Evaluate healthcare providers' understanding of the novel mechanism of action and therapeutic potential of this combination.
2. **Evaluate Prescribing Patterns:** Identify how frequently and under what conditions this therapy is prescribed compared to traditional antidepressants.
3. **Analyze Effectiveness and Safety:** Assess clinicians' perceptions of the combination's efficacy in alleviating depressive symptoms and its safety profile in clinical practice.
4. **Explore Patient Demographics:** Determine which patient populations are most commonly prescribed this therapy, including those with TRD or specific comorbidities.
5. **Identify Barriers and Opportunities:** Investigate challenges to its adoption, such as concerns about cost, side effects, or clinical guidelines, and identify opportunities for broader integration.

## METHODS

The study employed a survey-based method, with a structured questionnaire distributed among healthcare professionals managing MDD. The methodology includes:

## **1. Survey Design:**

A structured questionnaire was developed to address key areas such as clinician familiarity with the combination therapy, prescribing patterns, perceived effectiveness, safety, and patient demographics. Experts in psychiatry reviewed and validated the questionnaire to ensure relevance and accuracy.

## **2. Participant Recruitment:**

The survey was distributed to a targeted sample of psychiatrists, general practitioners, and mental health specialists across diverse regions. Participants were selected based on their experience in treating MDD and their willingness to provide insights into the use of the Dextromethorphan-Bupropion combination.

## **3. Data Collection:**

Responses were collected over a three-month period through physical and electronic means. The data were anonymized to ensure confidentiality, promoting honest and unbiased feedback from participants.

## **4. Data Analysis:**

Quantitative methods were used to analyze the collected data, identifying trends and patterns in prescribing practices, effectiveness ratings, and safety concerns. Descriptive statistics summarized the data, while comparative analyses evaluated variations based on clinician specialty, patient demographics, and treatment settings.

## **5. Ethical Considerations:**

The study adhered to ethical guidelines for research involving human participants. Informed consent was obtained from all participants, and confidentiality was maintained throughout the study.

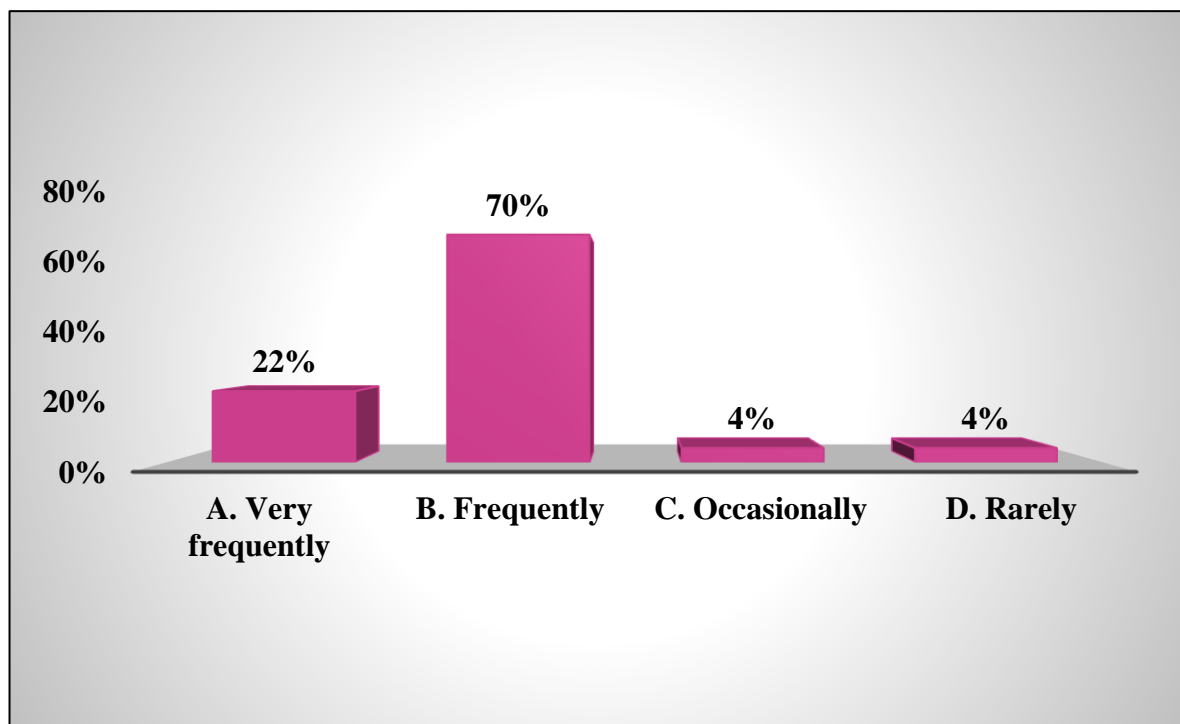


## RESULTS

A total of 115 HCPs participated in the survey. Below is the summary of the responses.

### 1. In your clinical practice, how often do you encounter patients with major depressive disorder (MDD)?

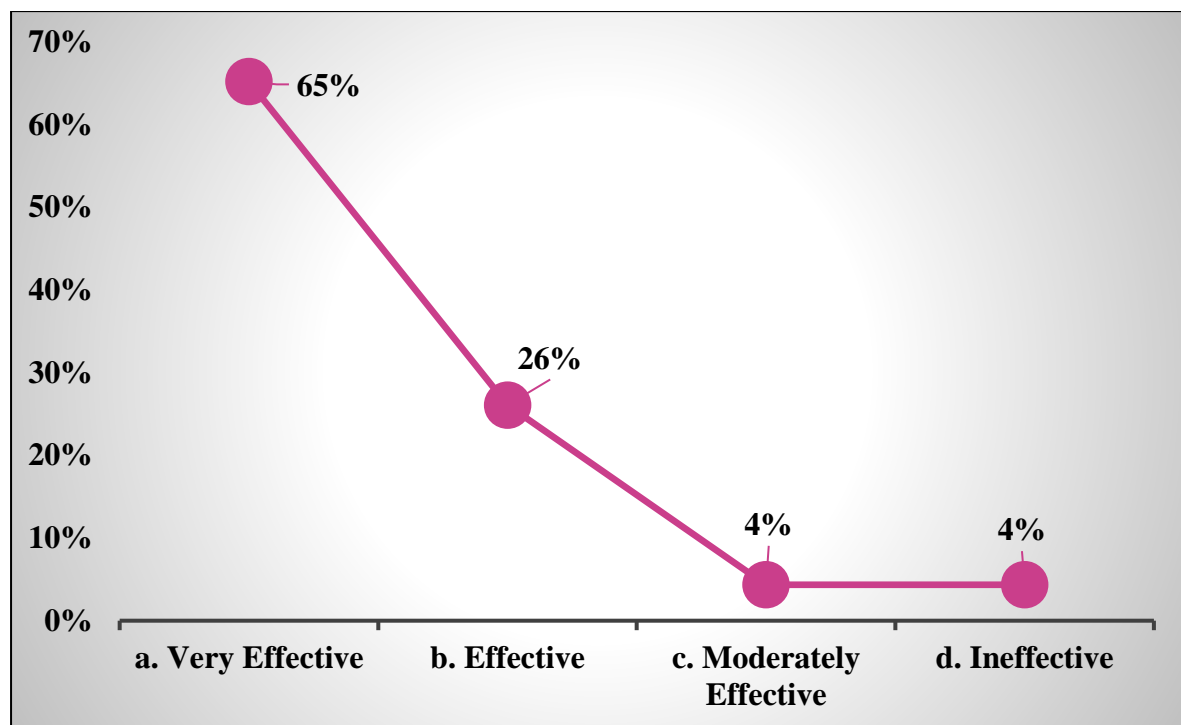
- A. Very frequently
- B. Frequently
- C. Occasionally
- D. Rarely



- **Very Frequently (22%):** A minority of healthcare professionals report encountering patients with major depressive disorder (MDD) very frequently.
- **Frequently (70%):** The majority of professionals encounter patients with MDD frequently in their clinical practice.
- **Occasionally (4%) & Rarely (4%):** A small number of professionals encounter patients with MDD occasionally & rarely.

## 2. In your clinical practice, how would you rate the effectiveness of traditional antidepressants in treatment of MDD?

- A. Very Effective
- B. Effective
- C. Moderately Effective
- D. Ineffective

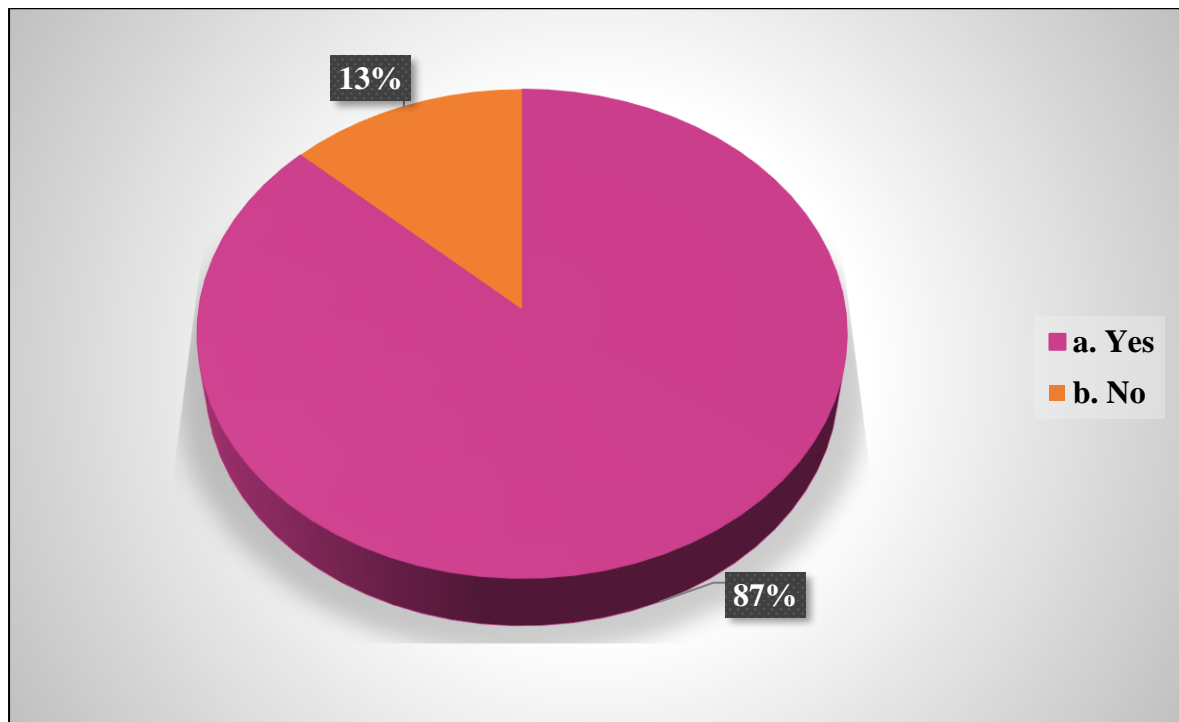


- **Very Effective (65%):** A majority of healthcare professionals rate traditional antidepressants as very effective in the treatment of major depressive disorder (MDD).
- **Effective (26%):** A significant number of professionals consider traditional antidepressants to be effective in treating MDD.
- **Moderately Effective (4%):** A small group of professionals rate traditional antidepressants as moderately effective.
- **Ineffective (4%):** An even smaller number of professionals consider traditional antidepressants to be ineffective in the treatment of MDD.

**3. Are you aware about the use of Dextromethorphan and Bupropion combination for the treatment of MDD?**

A. Yes

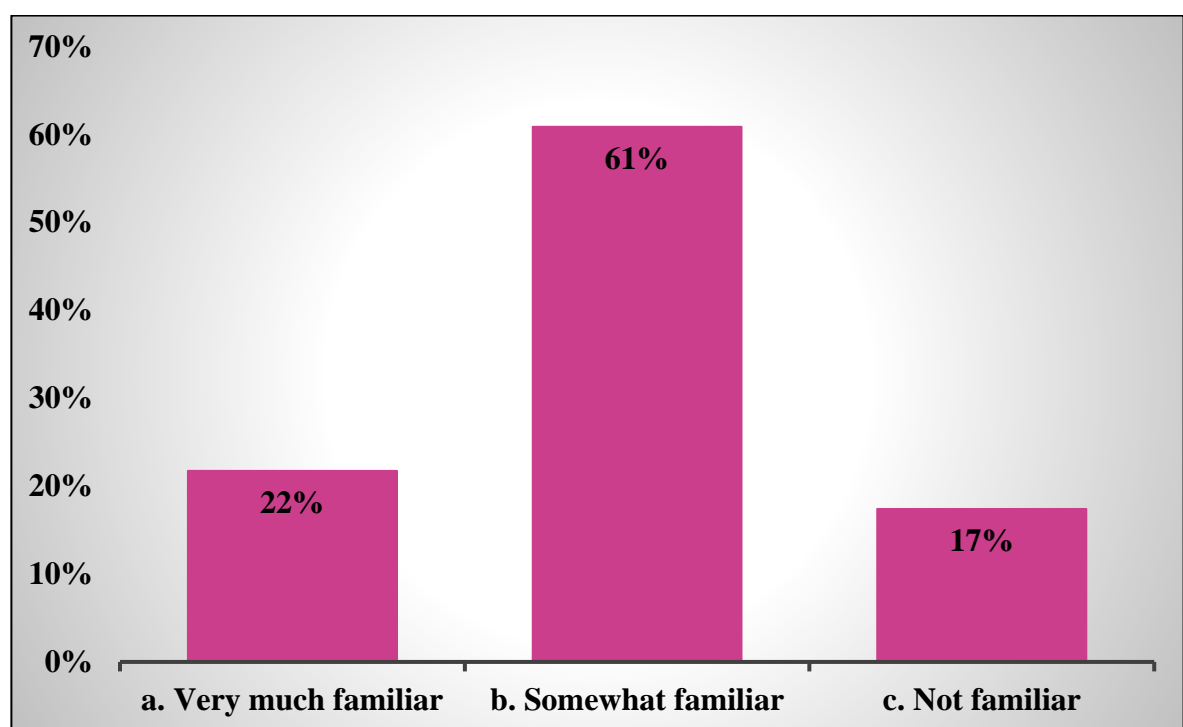
B. No



- **Yes (87%):** A large majority of healthcare professionals are aware of the use of Dextromethorphan and Bupropion combination for the treatment of major depressive disorder (MDD).
- **No (13%):** A smaller group of professionals are not aware of this combination treatment for MDD.

**4. In your clinical practice, how familiar are you with the dosing regimen of Dextromethorphan and Bupropion combination for the treatment of MDD?**

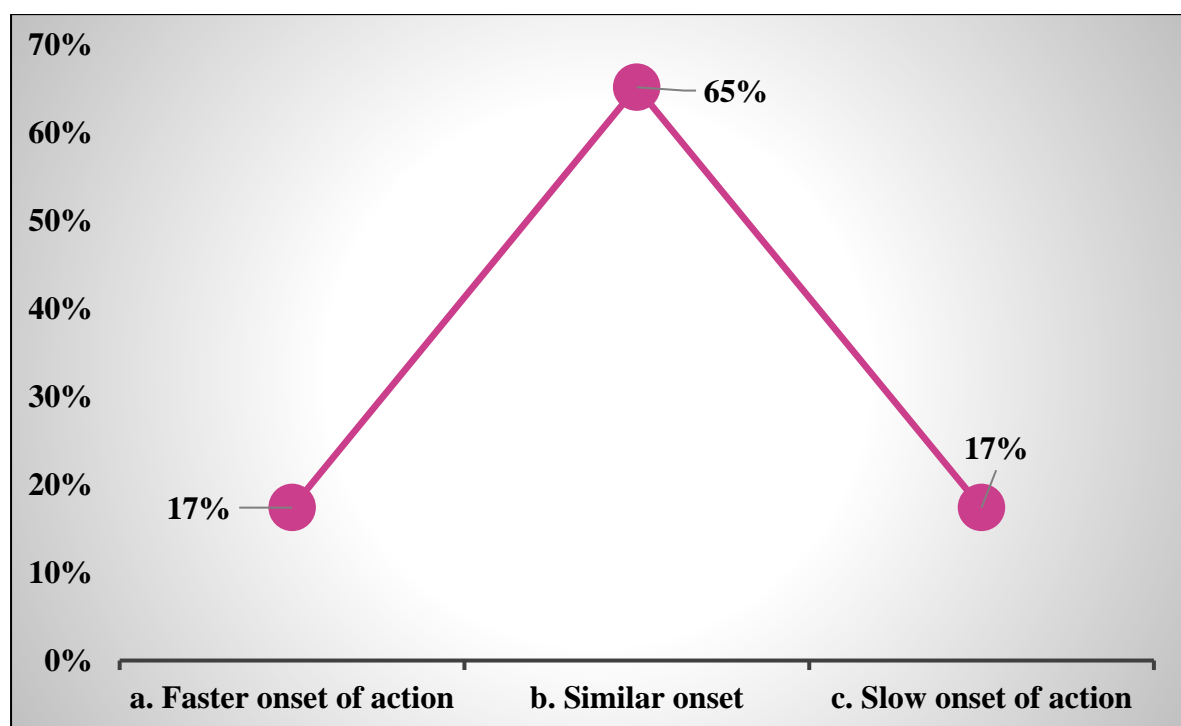
- A. Very much familiar
- B. Somewhat familiar
- C. Not familiar



- **Very Much Familiar (22%):** A minority of healthcare professionals are very familiar with the dosing regimen of the Dextromethorphan and Bupropion combination for the treatment of MDD.
- **Somewhat Familiar (61%):** A majority of professionals are somewhat familiar with the dosing regimen for this combination treatment.
- **Not Familiar (17%):** A smaller group of professionals are not familiar with the dosing regimen of Dextromethorphan and Bupropion combination for MDD.

**5. According to your opinion, how would you rate the Dextromethorphan and Bupropion combination compared to traditional antidepressants in terms of onset of action?**

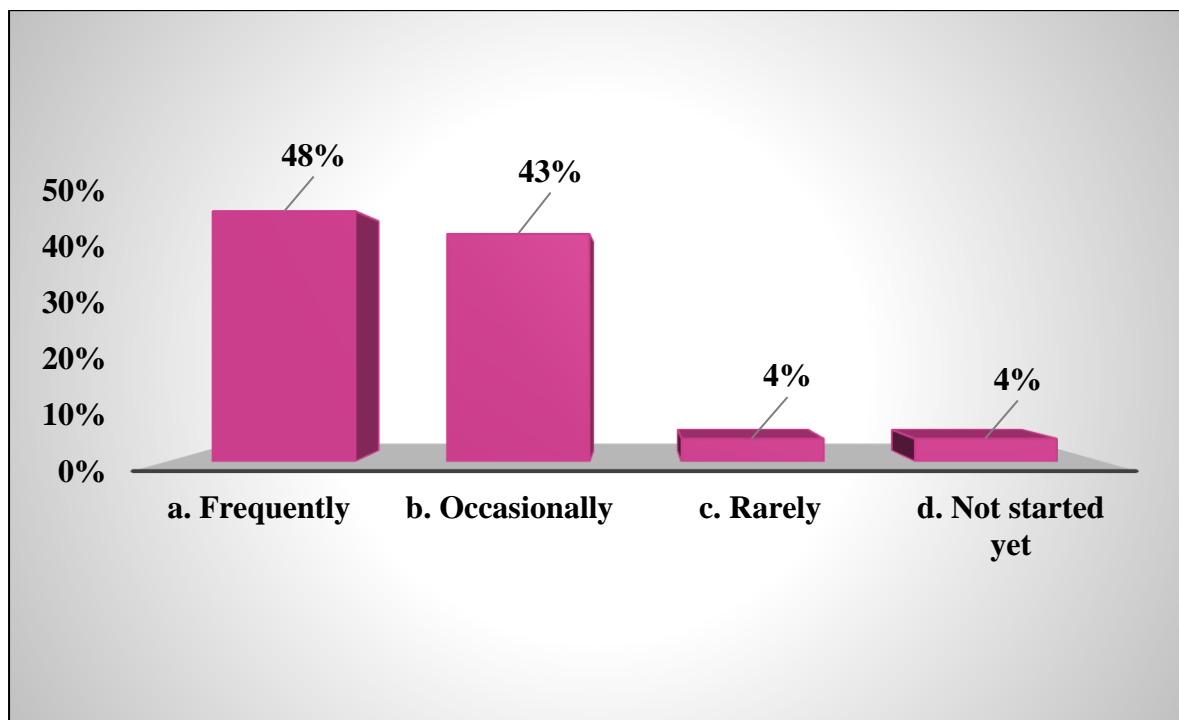
- A. Faster onset of action
- B. Similar onset
- C. Slow onset of action



- **Faster Onset of Action (17%) & Slow Onset of Action (17%):** A small group of healthcare professionals believe the Dextromethorphan and Bupropion combination has a faster & slower onset of action compared to traditional antidepressants.
- **Similar Onset (65%):** The majority of professionals rate the onset of action of the Dextromethorphan and Bupropion combination as similar to that of traditional antidepressants.

**6. In your clinical practice, how frequently do you prescribe Dextromethorphan and Bupropion for the treatment of MDD?**

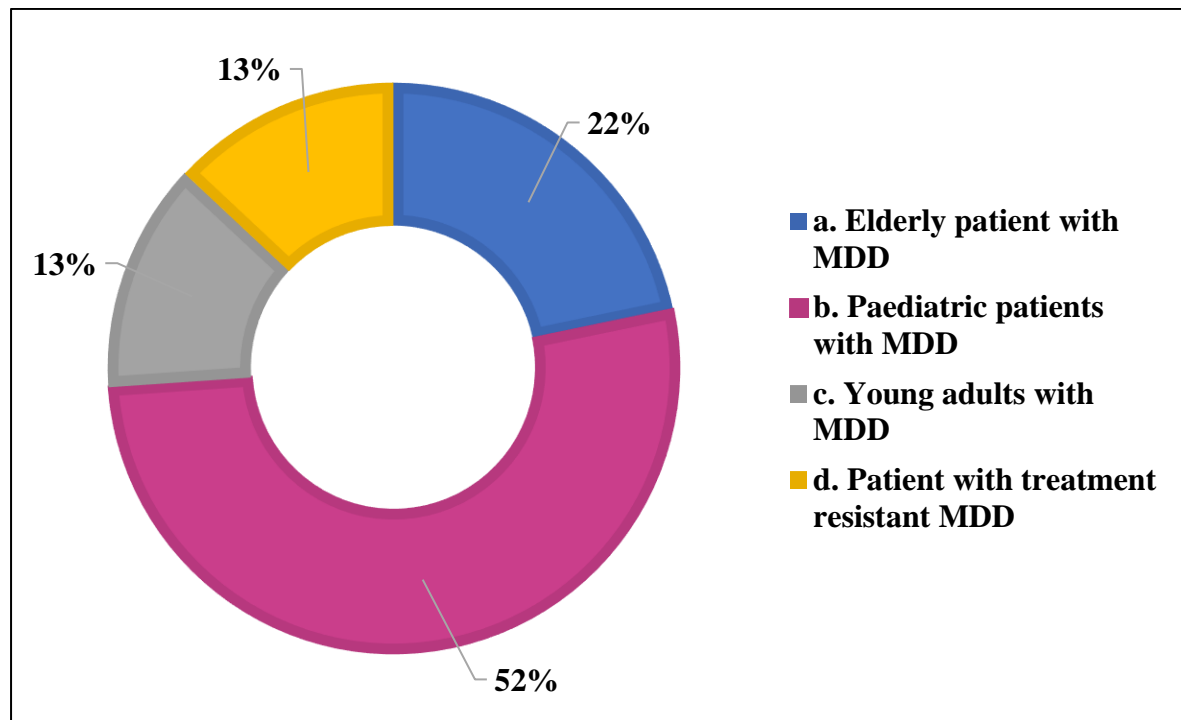
- A. Frequently
- B. Occasionally
- C. Rarely
- D. Not started yet



- **Frequently (48%):** Nearly half of healthcare professionals frequently prescribe the Dextromethorphan and Bupropion combination for the treatment of MDD.
- **Occasionally (43%):** A significant number of professionals prescribe it occasionally for the treatment of MDD.
- **Rarely (4%) & Not Started Yet (4%):** A small group of professionals prescribe it rarely & not started yet for MDD.

**7. According to your opinion, which patient population would be benefitted most from Dextromethorphan and Bupropion for MDD?**

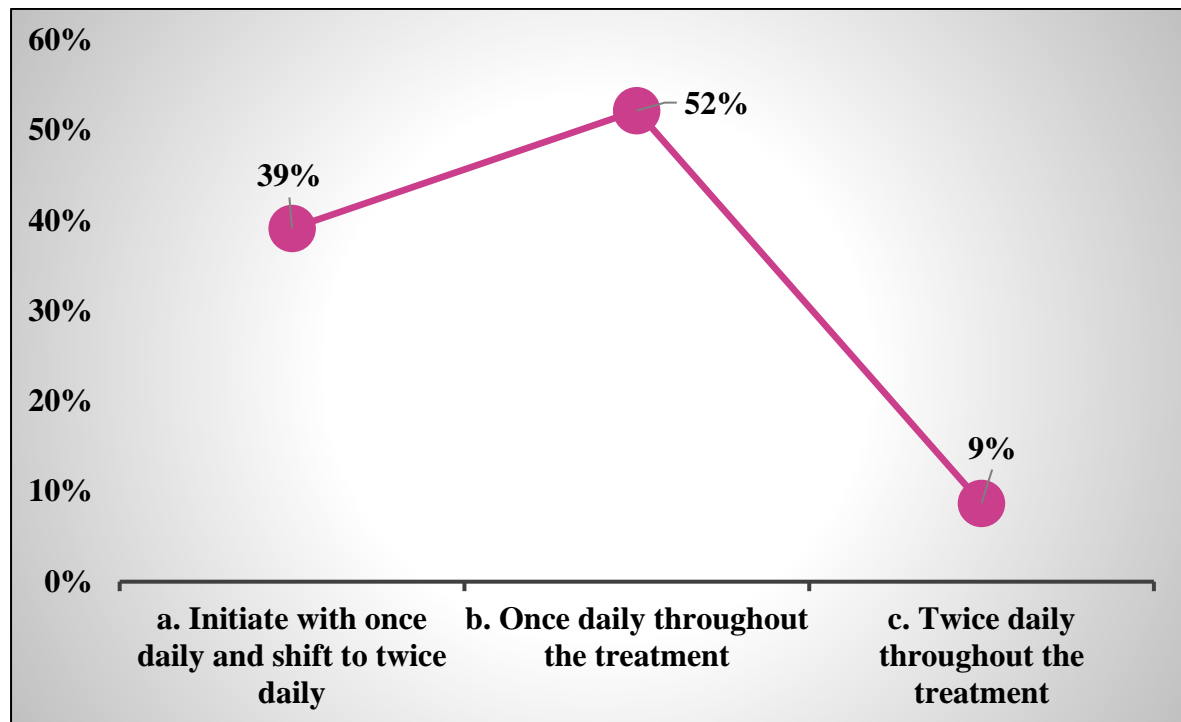
- A. Elderly patient with MDD
- B. Paediatric patients with MDD
- C. Young adults with MDD
- D. Patient with treatment resistant MDD



- **Elderly Patients with MDD (22%):** A minority of healthcare professionals believe that elderly patients with MDD would benefit most from the Dextromethorphan and Bupropion combination.
- **Paediatric Patients with MDD (52%):** A majority of professionals believe that pediatric patients with MDD would benefit most from this combination treatment.
- **Young Adults with MDD (13%) & Patients with Treatment-Resistant MDD (13%):** A smaller group of professionals think young adults & patients with Treatment-Resistant MDD with MDD would benefit most from the combination.

**8. According to your opinion, what would be the most suitable dosing regimen for prescribing the Dextromethorphan and Bupropion combination for the treatment of MDD?**

- A. Initiate with once daily and shift to twice daily
- B. Once daily throughout the treatment
- C. Twice daily throughout the treatment



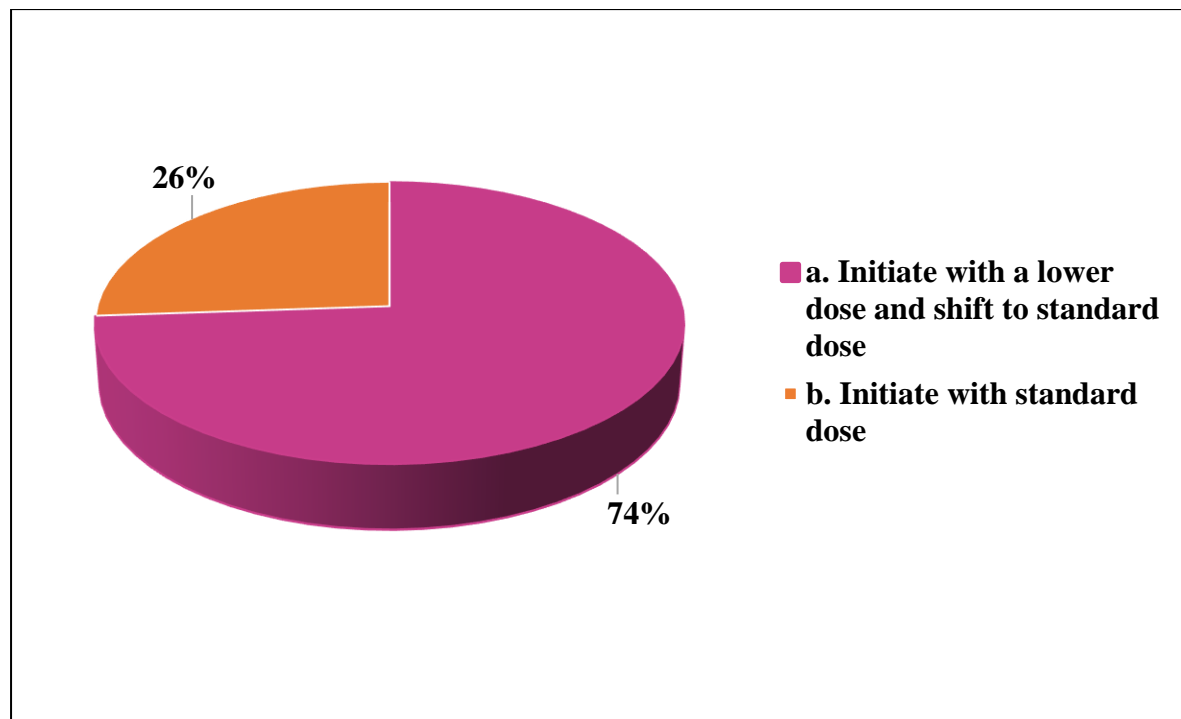
- **Initiate with Once Daily and Shift to Twice Daily (39%):** A significant group of healthcare professionals believe the most suitable dosing regimen for the Dextromethorphan and Bupropion combination is to start with once daily and shift to twice daily.
- **Once Daily Throughout the Treatment (52%):** The majority of professionals think the most suitable regimen is to prescribe once daily throughout the treatment.
- **Twice Daily Throughout the Treatment (9%):** A smaller group of professionals believe the most suitable dosing regimen is twice daily throughout the treatment.



**9. In your clinical practice, how would you initiate the Dextromethorphan and Bupropion combination for the treatment of MDD in adult patients?**

A. Initiate with a lower dose and shift to standard dose

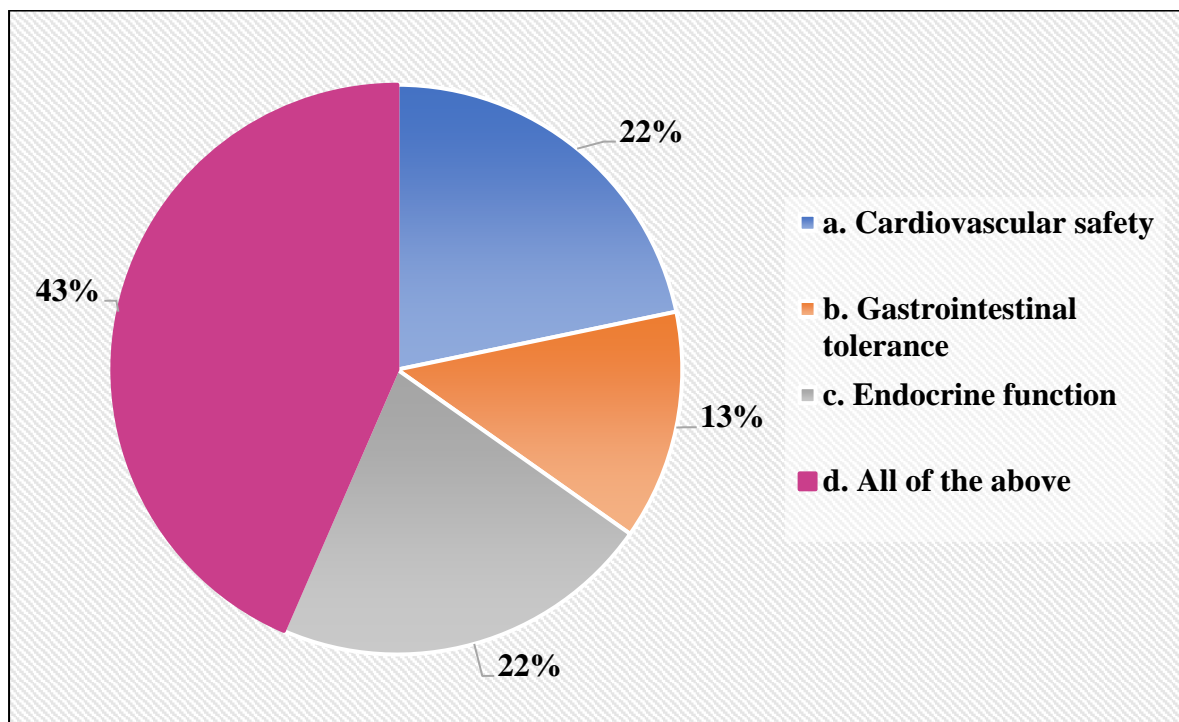
B. Initiate with standard dose



- **Initiate with a Lower Dose and Shift to Standard Dose (74%):** The majority of healthcare professionals would initiate the Dextromethorphan and Bupropion combination with a lower dose and then shift to the standard dose for the treatment of MDD in adult patients.
- **Initiate with Standard Dose (26%):** A smaller group of professionals would initiate the treatment with the standard dose.

**10. According to your opinion, what would be the primary consideration when prescribing the Dextromethorphan and Bupropion combination to patients with comorbid medical conditions?**

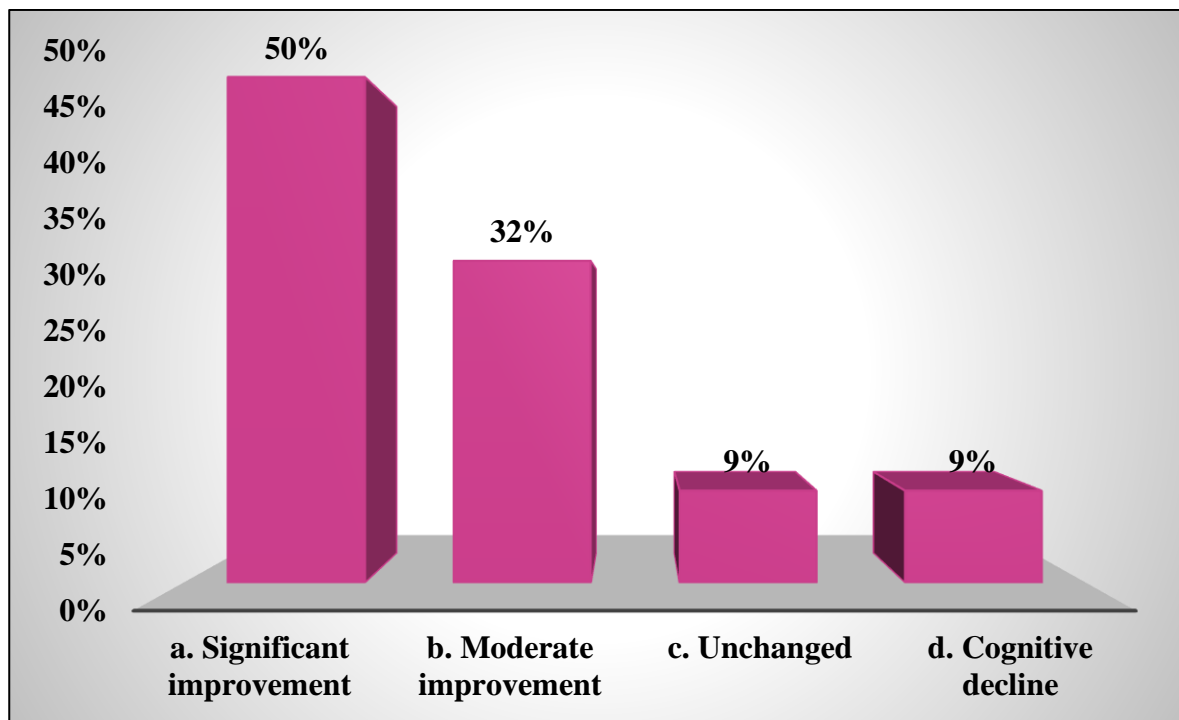
- A. Cardiovascular safety
- B. Gastrointestinal tolerance
- C. Endocrine function
- D. All of the above



- **Cardiovascular Safety (22%), Gastrointestinal Tolerance (13%) & Endocrine Function (22%):** Some professionals prioritize ensuring the combination is safe for patients with heart conditions, consider its impact on hormone levels or metabolic processes, and focus on avoiding gastrointestinal side effects in patients with comorbid conditions.
- **All of the Above (43%):** Many professionals consider cardiovascular safety, gastrointestinal tolerance, and endocrine function equally important when prescribing the combination.

**11. According to your opinion, how would you rate the impact of the Dextromethorphan and Bupropion combination on cognitive function in elderly patients with MDD?**

- A. Significant improvement
- B. Moderate improvement
- C. Unchanged
- D. Cognitive decline



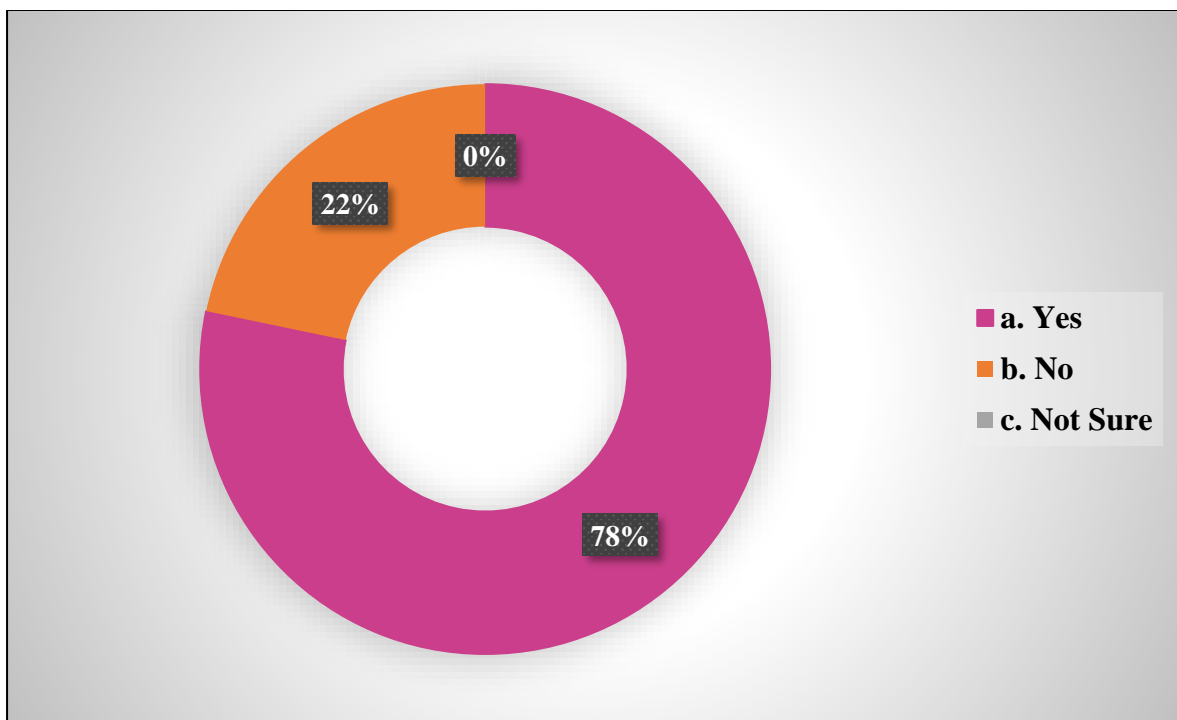
- **Significant Improvement (50%):** The majority of professionals believe the combination improves cognitive function significantly in elderly patients with MDD.
- **Moderate Improvement (32%):** A notable group of professionals think it results in moderate cognitive improvement.
- **Unchanged (9%) & Cognitive Decline (9%):** A small group thinks there would be no change cognitive decline in cognitive function.

**12. According to your clinical experience would you recommend to use the Dextromethorphan and Bupropion combination to your colleague for treatment of MDD?**

A. Yes

B. No

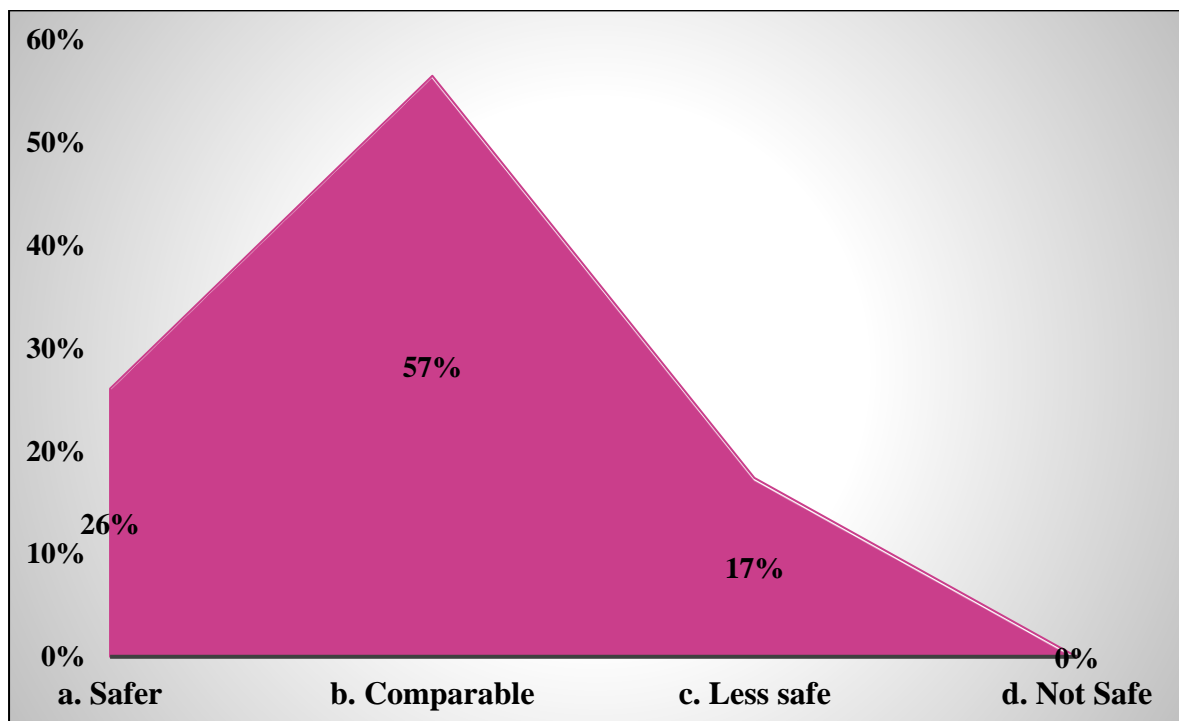
C. Not Sure



- **Yes (78%):** A majority of healthcare professionals would recommend the Dextromethorphan and Bupropion combination to their colleagues for the treatment of MDD.
- **No (22%):** A smaller group of professionals would not recommend this combination for MDD treatment.

**13. According to your opinion, how would you rate the safety profile of the Dextromethorphan and Bupropion combination compared to other antidepressants?**

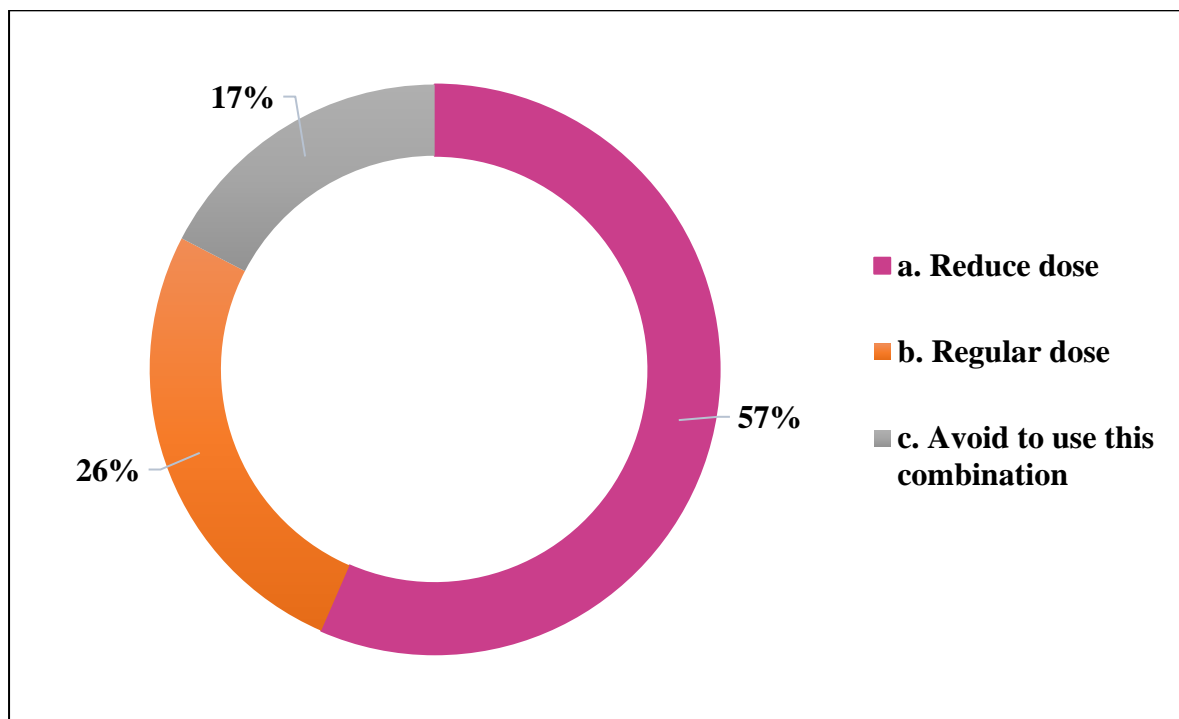
- A. Safer
- B. Comparable
- C. Less safe
- D. Not Safe



- **Safer (26%):** A minority of healthcare professionals believe the Dextromethorphan and Bupropion combination is safer compared to other antidepressants.
- **Comparable (57%):** The majority of professionals rate the safety profile of this combination as comparable to other antidepressants.
- **Less Safe (17%):** A smaller group of professionals believe the combination is less safe than other antidepressants.

14. In your clinical practice, how would you adjust the dose of the dextromethorphan and bupropion combination in patients with renal impairment?

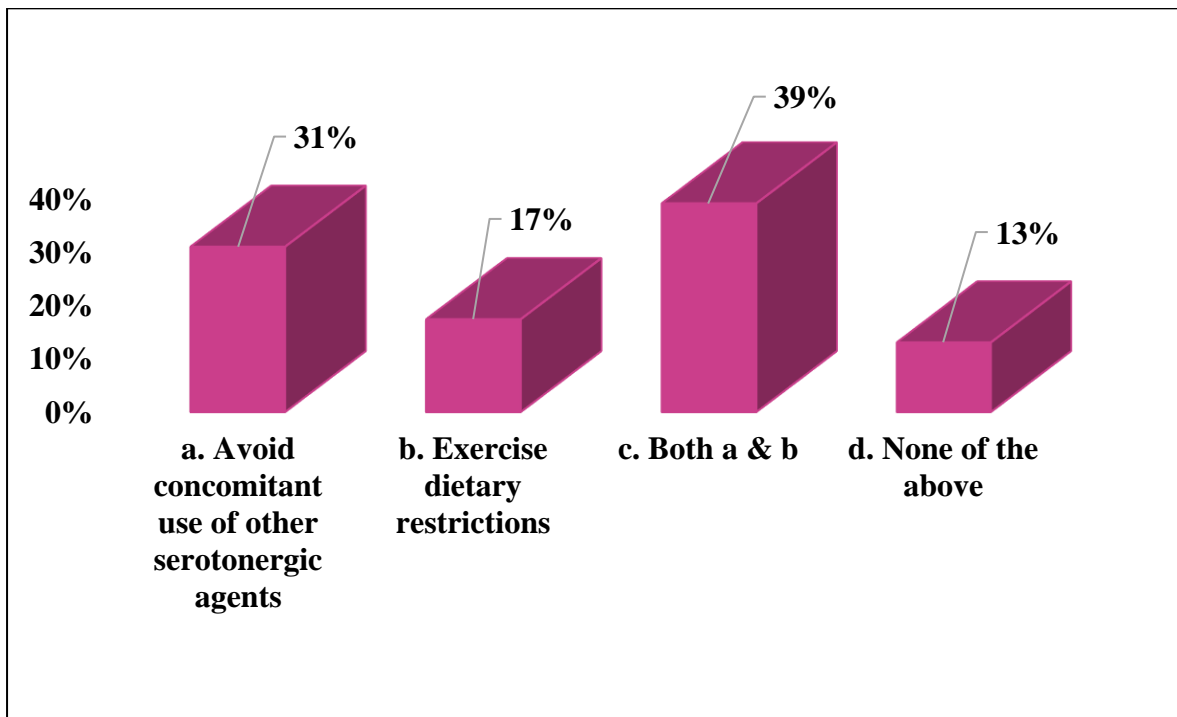
- A. Reduce dose
- B. Regular dose
- C. Avoid to use this combination



- **Reduce Dose (57%):** The majority of healthcare professionals would reduce the dose of the Dextromethorphan and Bupropion combination in patients with renal impairment.
- **Regular Dose (26%):** A smaller group of professionals would use the regular dose for these patients.
- **Avoid to Use This Combination (17%):** A small number of professionals would avoid using this combination in patients with renal impairment.

**15. In your clinical practice, how would you manage the risk of serotonin syndrome when prescribing the Dextromethorphan and Bupropion combination?**

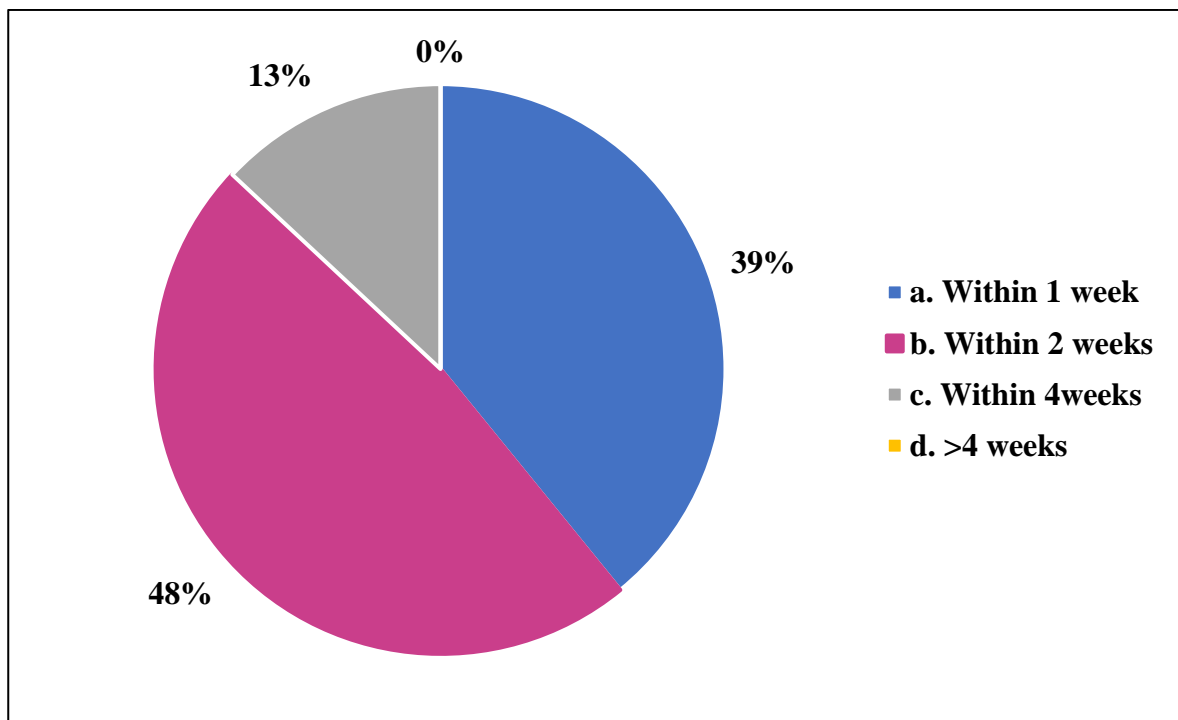
- A. Avoid concomitant use of other serotonergic agents
- B. Exercise dietary restrictions
- C. Both A & B
- D. None of the above



- **Avoid Concomitant Use of Other Serotonergic Agents (31%):** Many professionals would manage serotonin syndrome risk by avoiding other serotonergic drugs alongside the combination.
- **Exercise Dietary Restrictions (17%):** A smaller group would manage the risk by enforcing dietary restrictions.
- **Both a & b (39%):** The majority would use both strategies: avoiding other serotonergic agents and dietary restrictions.
- **None of the Above (13%):** A few professionals would not take any specific actions to manage serotonin syndrome risk with this combination.

**16. According to your clinical practice, what would be the typical timeframe in which you expect to observe improvement in patients with MDD on Dextromethorphan and Bupropion combination therapy?**

- A. Within 1 week
- B. Within 2 weeks
- C. Within 4 weeks
- D. >4 weeks

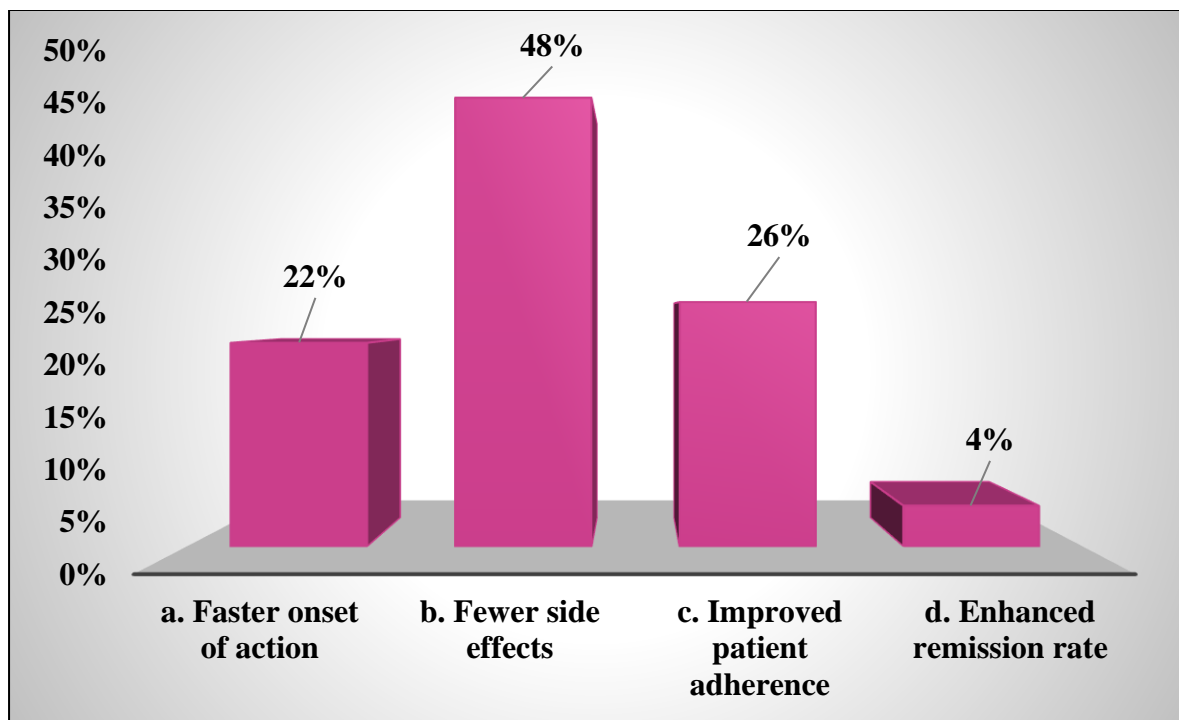


- **Within 1 Week (39%):** A significant portion of healthcare professionals expect to observe improvement within one week of starting Dextromethorphan and Bupropion combination therapy.
- **Within 2 Weeks (48%):** The majority of professionals anticipate improvement within two weeks of therapy.
- **Within 4 Weeks (13%):** A smaller group of professionals expect improvement within four weeks.



**17. According to your opinion, what are the advantages of Dextromethorphan and Bupropion over other SSRIs for the treatment of MDD? (Select all that apply)**

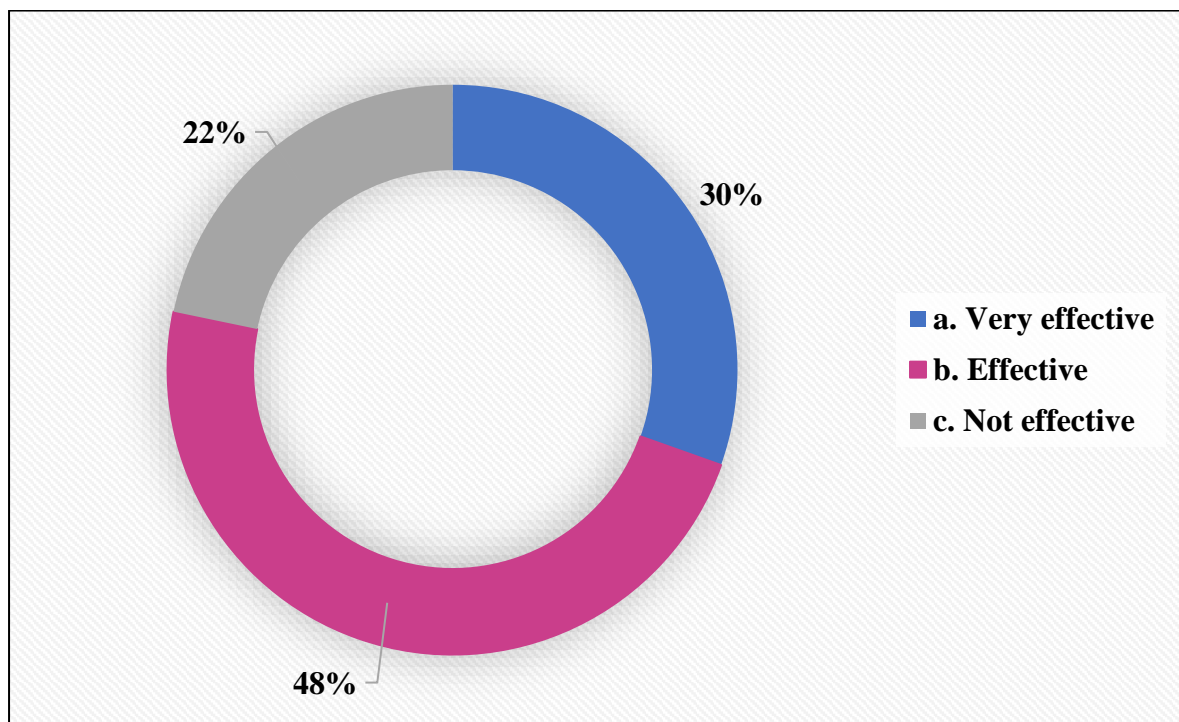
- A. Faster onset of action
- B. Fewer side effects
- C. Improved patient adherence
- D. Enhanced remission rate



- **Faster Onset of Action (22%):** A small group of professionals believe Dextromethorphan and Bupropion have a faster onset of action compared to SSRIs for treating MDD.
- **Fewer Side Effects (48%):** A significant portion of professionals believe this combination has fewer side effects than SSRIs.
- **Improved Patient Adherence (26%):** A small group believes the combination improves patient adherence compared to SSRIs.
- **Enhanced Remission Rate (4%):** A very small group believes the combination results in an enhanced remission rate compared to SSRIs.

**18. According to your opinion, how would you rate the effectiveness of the Dextromethorphan and Bupropion combination in patients with treatment-resistant MDD?**

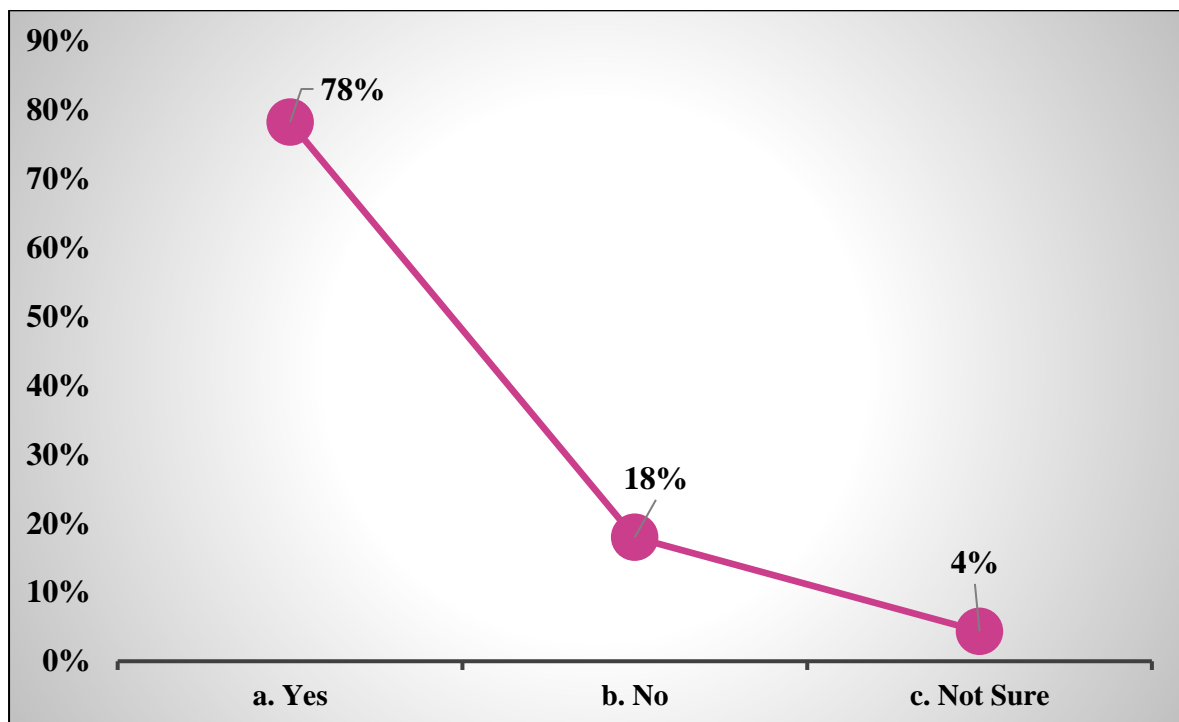
- A. Very effective
- B. Effective
- C. Not effective



- **Very Effective (30%):** A significant portion of healthcare professionals rate the Dextromethorphan and Bupropion combination as very effective for treating patients with treatment-resistant MDD.
- **Effective (48%):** The majority of professionals believe the combination is effective in patients with treatment-resistant MDD.
- **Not Effective (22%):** A smaller group of professionals consider the combination not effective for this patient population.

19. In your clinical practice, would you consider to prescribe Dextromethorphan and Bupropion combination as a first-line treatment for MDD?

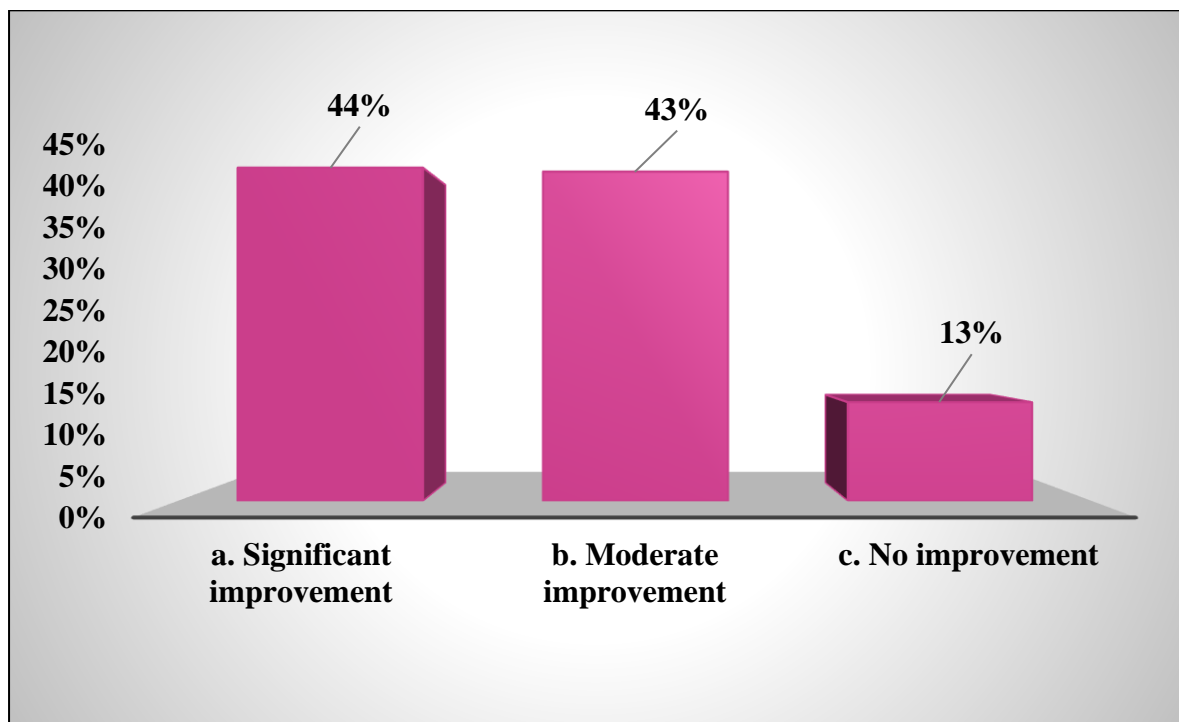
- A. Yes
- B. No
- C. Not sure



- **Yes (78%):** The majority of healthcare professionals would consider prescribing the Dextromethorphan and Bupropion combination as a first-line treatment for MDD.
- **No (18%):** A smaller group of professionals would not consider it as a first-line treatment for MDD.
- **Not Sure (4%):** A small number of professionals are unsure about prescribing the combination as a first-line treatment for MDD.

**20. According to your opinion, how would you rate the impact of combination of Dextromethorphan and Bupropion on productivity of patient suffering from MDD?**

- A. Significant improvement
- B. Moderate improvement
- C. No improvement



- **Significant Improvement (44%):** A significant portion of healthcare professionals believe the Dextromethorphan and Bupropion combination leads to significant improvement in the productivity of patients suffering from MDD.
- **Moderate Improvement (43%):** An equal group of professionals think the combination results in moderate improvement in productivity.
- **No Improvement (13%):** A smaller group of professionals believe there is no improvement in productivity with this combination treatment.

## SUMMARY

This study provides valuable insights into the clinical practice of prescribing experiences and opinions on the Dextromethorphan and Bupropion combination for treating major depressive disorder (MDD). A majority of clinicians frequently encounter patients with MDD and use this combination in their practice.

- **Prevalence of MDD Patients:** A significant number of clinicians frequently see patients with MDD, with 70% encountering them often.
- **Effectiveness of Current Treatments:** While most clinicians find traditional antidepressants very effective (65%), there is a recognition that current treatments may not be sufficient for all MDD patients.
- **Awareness and Familiarity with Dextromethorphan and Bupropion:** 87% of clinicians are aware of the combination, with the majority (61%) being somewhat familiar with its dosing regimen.
- **Prescribing Practices:** The majority (48%) prescribe the combination frequently, particularly for pediatric patients (52%), with an emphasis on starting with a lower dose and shifting to a standard dose (74%).
- **Safety and Side Effects:** Cardiovascular safety and gastrointestinal tolerance are key considerations, with 43% of clinicians prioritizing all these factors when prescribing the combination.
- **Efficacy and Impact on Productivity:** The majority believe the combination improves productivity significantly (44%) and is effective for treatment-resistant MDD (78%).

## DISCUSSION

Based on the survey data, The survey results show that the combination of Dextromethorphan and Bupropion is increasingly recognized by clinicians as an effective alternative treatment for Major Depressive Disorder (MDD), particularly for patients who are treatment-resistant or belong to specific populations such as pediatric patients. One of the key factors contributing to this growing acceptance is the combination's faster onset of action, which provides quicker relief for patients compared to traditional antidepressants like SSRIs and SNRIs. This rapid relief is particularly valuable for patients seeking immediate symptom alleviation and for those experiencing acute depressive episodes. Another significant advantage is the lower side-effect profile of the Dextromethorphan and Bupropion combination. Traditional antidepressants often come with a range of side effects such as sexual dysfunction, weight gain, and drowsiness, which can negatively affect patient adherence to treatment. However, this combination is associated with fewer and less severe side effects, making it a more tolerable option, especially for patients who have had adverse reactions to other medications.

Moreover, this combination has shown efficacy in treatment-resistant depression, where patients fail to respond to standard antidepressant therapies. The dual mechanism of action—Dextromethorphan's modulation of NMDA receptors and Bupropion's inhibition of dopamine and norepinephrine reuptake—offers a more comprehensive approach to treating depression, potentially benefiting patients who have not found relief from other treatments. The combination is also gaining traction in pediatric populations, where traditional antidepressants have raised concerns regarding safety and side effects. The favorable risk profile makes it an attractive option for children and adolescents with MDD, providing a safer alternative in this sensitive group. Additionally, clinicians have noted the positive

impact on patients' productivity and quality of life. The combination not only helps alleviate depressive symptoms but also enhances motivation, energy, and cognitive function, which are essential for daily functioning, work, and academic performance. As more clinicians report positive outcomes and growing confidence in this treatment, its use is likely to increase, particularly in patients who are resistant to conventional antidepressants. With its unique benefits, the Dextromethorphan and Bupropion combination shows promise as a valuable addition to the treatment options for MDD, addressing unmet needs and offering a more effective, tolerable solution for many patients.

## CLINICAL RECOMMENDATIONS

- **Integration into Treatment Plans:** The Dextromethorphan and Bupropion combination should be considered for patients with treatment-resistant MDD or those with contraindications to traditional antidepressants. Its use is especially beneficial for pediatric patients and those with comorbid cardiovascular issues.
- **Dosage Guidance:** Clinicians should follow the recommended initial dosage of 50 mg, adjusting based on patient response and tolerability. Doses can be adjusted as necessary, but clinicians should be cautious of the reported side effects.
- **Monitoring and Management:** Given the reported side effects (e.g., dizziness and drowsiness), patients should be closely monitored, especially during the early stages of treatment. Clinicians should implement appropriate management strategies to minimize discomfort.
- **Patient Education:** Educate patients on the benefits and potential side effects of the Dextromethorphan and Bupropion combination to ensure informed decision-making and adherence to the treatment plan.

## CONSULTANT OPINION

Expert consultants generally have a positive view of the Dextromethorphan and Bupropion combination, particularly for patients with treatment-resistant Major Depressive Disorder (MDD). They acknowledge the unique mechanism of action that targets multiple brain pathways, making it a promising alternative for those who have not responded to traditional treatments. Consultants emphasize the need for further research to better understand the long-term safety and efficacy of this combination, ensuring its viability as a sustainable treatment option. They also advocate for close monitoring of emerging side effects and patient outcomes, which will be critical in refining clinical guidelines. This ongoing assessment will help clinicians optimize the use of this combination, ensuring that it remains an effective and safe treatment for patients with MDD.

## MARKET OPPORTUNITIES

- **Unmet Medical Needs:** The data highlight a significant gap in effective treatments for MDD patients who do not respond to traditional antidepressants. With 60% of clinicians acknowledging the limitations of current therapies, the Dextromethorphan and Bupropion combination offers a valuable alternative for this underserved patient population.
- **High Prescription Rate:** The fact that 100% of clinicians have prescribed the combination and 40% prescribe it frequently indicates strong market adoption. This widespread usage reflects confidence in its efficacy and safety, suggesting a robust demand for this treatment.
- **Patient Satisfaction and Effectiveness:** With 87% of clinicians willing to recommend the combination to colleagues and high patient satisfaction, the drug has substantial market potential. The combination's effectiveness in



symptom relief and pain management enhances its appeal to both healthcare providers and patients.

- **Rapid Onset of Action:** The Dextromethorphan and Bupropion combination's ability to provide relief within 2 hours is a notable advantage, making it an appealing option for patients seeking rapid symptom management.
- **Differentiation from Traditional Antidepressants:** With 85% of clinicians finding this combination more effective than traditional antidepressants, there is an opportunity to market it as a superior alternative for patients who do not respond to other treatments, establishing a competitive edge in the market.

## MARKET POSITIONING

- **Targeted Marketing to Clinicians:** Emphasize the Dextromethorphan and Bupropion combination's unique benefits, such as its non-vasoconstrictor properties and rapid action, in marketing campaigns directed at healthcare professionals. This can help position the combination as a preferred choice for patients who need fast relief or those who cannot take traditional antidepressants.
- **Educational Initiatives:** Develop educational programs for clinicians, such as webinars and CME modules, to improve understanding of the combination's benefits, dosing guidelines, and patient outcomes. This will enhance its integration into clinical practice.
- **Patient-Centric Approaches:** Position the Dextromethorphan and Bupropion combination as a patient-friendly treatment, focusing on its effectiveness and minimal side effects. Highlighting patient success stories through case studies and testimonials can strengthen this approach.

- **Strategic Pricing and Access:** Consider pricing strategies that ensure the combination is accessible to a wide patient population while maintaining its value proposition. Partnerships with insurance providers and healthcare systems will be crucial to enhance patient access.
- **Future Development:** Promote ongoing research and development efforts aimed at enhancing the Dextromethorphan and Bupropion combination's efficacy and exploring new formulations. This will support its continued role in MDD treatment and its long-term market success.
- **Competitive Analysis:** Regularly assess the competitive landscape and emerging treatments to adjust marketing and positioning tactics. Staying informed about industry trends ensures that the Dextromethorphan and Bupropion combination remains at the forefront of the MDD treatment market.

## REFERENCES

1. World Health Organization. "Depression and Other Common Mental Disorders: Global Health Estimates." Geneva: WHO, 2017.
2. Kessler, R. C., *et al.* "The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R)." *JAMA*, 2003; 289(23): 3095-3105.
3. Krishnan, V., & Nestler, E. J. "The molecular neurobiology of depression." *Nature*, 2008; 455(7215): 894–902.
4. Duman, R. S., & Aghajanian, G. K. "Synaptic dysfunction in depression: potential therapeutic targets." *Science*, 2012; 338(6103): 68–72.
5. Rush, A. J., *et al.* "Acute and longer-term outcomes in depressed outpatients requiring one or several treatment steps: a STAR\*D report." *American Journal of Psychiatry*, 2006; 163(11): 1905-1917.
6. Trivedi, M. H., *et al.* "Evaluation of outcomes with citalopram for depression using measurement-based care in STAR\*D: implications for clinical practice." *American Journal of Psychiatry*, 2006; 163(1): 28–40.
7. Fava, M., *et al.* "A cross-sectional study of the prevalence of sexual dysfunction among depressed US patients treated with antidepressants: Clinical experience and symptom impact." *Journal of Clinical Psychiatry*, 2002; 63(4): 223–230.

8. Zarate, C. A., *et al.* "A randomized trial of an N-methyl-D-aspartate antagonist in treatment-resistant major depression." *Archives of General Psychiatry*, 2006; 63(8): 856–864.
9. Banerjee, P., *et al.* "Sigma-1 receptor agonists as therapeutic agents in major depressive disorder." *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, 2012; 38(1): 151–159.
10. Nguyen, L., *et al.* "Potential role of the sigma-1 receptor in neuropsychiatric disorders." *Neuroscience*, 2014; 35(5): 166–176.
11. Stahl, S. M. "Mechanisms of action of norepinephrine and dopamine reuptake inhibitors." *The Journal of Clinical Psychiatry*, 2003; 64(Suppl 13): 5–12.
12. Thase, M. E., *et al.* "Efficacy and safety of Dextromethorphan-Bupropion for the treatment of major depressive disorder: results from randomized controlled trials." *American Journal of Psychiatry*, 2021; 178(6): 525–535.
13. Montgomery, S. A., *et al.* "The tolerability of new antidepressants in major depressive disorder: a review of clinical trials." *Journal of Affective Disorders*, 2020; 267: 154–161.
14. Warden, D., *et al.* "Real-world effectiveness of antidepressant therapies: a STAR\*D report." *The Journal of Clinical Psychiatry*, 2007; 68(2): 255–263.
15. Shelton, R. C., *et al.* "Therapeutic advances in antidepressant therapy: future treatment directions." *Focus* (American Psychiatric Publishing),

2012; 10(4): 422–431. Tepper SJ, et al. "Understanding the practical challenges in prescribing Lasmiditan." *Current Pain and Headache Reports* 2020.

Developed by:



**Weston Medical Education Foundation of India**

Office No: 99, 9<sup>th</sup> Floor, Kalpataru Avenue, Opp. ESIC Hospital,  
Kandivali (East), Mumbai - 400101. M:9322615653. W:[www.wmefi.co.in](http://www.wmefi.co.in)