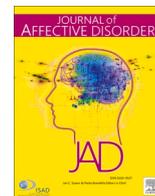


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Treatment patterns and decision drivers to discharge patients with depression hospitalised for acute suicidal ideation in Europe

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ABSTRACT

Background: There is limited published information about the management of patients with major depressive disorder (MDD) hospitalised for acute suicidal ideation (SI). This study aimed to identify treatment patterns and unmet needs in the management of these patients and the decision drivers for hospital discharge.

Methods: Cross-sectional survey-based study enrolling hospital-based European psychiatrists. The study had a qualitative and a quantitative stage, including a conjoint exercise.

Results: Each respondent ($N = 413$) managed, on average, 62 MDD patients with acute SI per typical three-month period; 76% of these patients required hospitalisation. Severity of SI and severity of MDD were considered the most important factors for hospital admission and discharge. In the conjoint analysis, these attributes accounted for 54% of the discharge decision. Key treatment goals included improving depressive symptoms and achieving MDD remission. Antidepressants were a standard treatment for 98% of respondents but 63% defined rapid onset of action as a critical unmet need, followed by a good tolerability profile (34%).

Limitations: The study has a cross-sectional design representing respondents' behaviour and attitudes at a particular point in time. In the conjoint analysis, the results represent stated behaviour and not observed clinical behaviour.

Conclusions: Physicians' decisions to admit and discharge patients with MDD hospitalised for acute SI are mostly driven by the severity of SI and depression. Antidepressants with rapid onset of action, which can quickly improve depressive symptoms, represent a key unmet need for these patients and may contribute to a higher likelihood of early discharge.

1. Introduction

More than half of the people who die by suicide have a psychiatric disorder at the time of their death (Brieger et al., 2020; Kim et al., 2021). The psychiatric condition most often associated with suicidal behaviour is major depressive disorder (MDD) (Fu et al., 2021; Moitra et al., 2021).

For many patients with MDD, an acute event of suicidal ideation (SI) constitutes a psychiatric emergency (Vuorilehto et al., 2014). Clinical guidelines provide some guidance for the management of these patients, but there is currently no standardised approach to care. Implementing

an effective treatment strategy during the early hours and days of the acute event is critical for patients. Antidepressants and anxiolytics are typically administered as a first treatment option but, although available antidepressants seem effective in treating depressive symptoms, may take up to 4 weeks to reach optimal efficacy, which constitutes a limitation for patients requiring urgent treatment (Machado-Vieira et al., 2010).

Hospitalisation is often required to quickly address the psychiatric emergency. Though hospitalisation itself may not be perceived as a treatment, it can provide an immediate sense of secure environment and

Abbreviations: A&L, attributes and levels; SI, suicidal ideation.

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facilitate continuous monitoring and care to help ensure patient safety (Wasserman et al., 2012). However, hospitalisation is temporary and does not always lead to stable improvement, and, during treatment, suicidal thoughts can be reactivated, especially at the time or immediately after discharge while patients may experience a worsening of symptoms. A national clinical survey based on a 10-year sample of people in England and Wales who had died by suicide from 1997 to 2006 showed that 14% of all deaths by suicide were enacted by psychiatric inpatients (Hunt et al., 2010). Further, there is a rise in the risk of suicide immediately after the patient is discharged (Britton et al., 2021; De Leo and Svetcic, 2011; Olfson et al., 2016).

The decision of admitting or discharging a patient with MDD and acute SI constitutes a critical and complex process for psychiatrists (Bolton et al., 2015; Vuorilehto et al., 2014). The patient's vulnerable clinical condition and the absence of robust predictive tools to assess suicidal risk represent major challenges (Fehling and Selby, 2021). But, there are also aspects associated with the acuity of the psychiatric emergency (e.g., lack of knowledge of a patient's medical history and what are the best treatments for that patient) and socio-economic and environmental factors (e.g., a patient's will to be hospitalised, access to a support network at home or to community care, availability of beds in the hospital) playing an important role in the process (Jaffe et al., 2019).

It is not rare for psychiatrists to discharge patients who are not in full remission as there is a constant need to prioritise the admission of higher risk patients, due to the limited availability of hospital beds and resources. This might be one of the reasons contributing to the increased risk of readmission, attempting suicide, or even completing suicide observed after patients are discharged (Britton et al., 2021; Chung et al., 2017; Olfson et al., 2016).

As there is limited published information available on this field, this study was conducted to identify treatment patterns and key unmet needs in patients with MDD hospitalised for acute SI as well as the key attributes considered by psychiatrists when making decisions about the patient's readiness to be discharged from the hospital.

2. Methods

2.1. Key inclusion criteria

Inclusion criteria were defined to ensure psychiatrists enrolled in the study were heavily involved in admission and discharge decisions and in the overall management of patients with MDD who have been hospitalised for acute SI. Respondents were included if they met the following inclusion criteria: had 3 to 35 years of clinical practice, dedicated 75% or more of their time (60% in the UK) to direct patient care, and managed at least 30 adult patients with a moderate-to-severe episode of MDD in a typical 3-month period, of whom at least 10% (i.e., 3 patients) had a diagnosis of acute SI (the target population in scope for this study). Full inclusion criteria detailed in Supplementary Table 1.

2.2. Target patient population

Respondents were asked to refer to the target patient population when responding to the survey. The target population consisted of adult patients (i.e., age ≥ 18 years) with a diagnosis of MDD who were hospitalised for acute SI. MDD diagnosis criteria were defined according to the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) of the American Psychiatric Association or to the International Classification of Disease, 10th revision (ICD-10) (World Health Organization, 1992; American Psychiatric Association, 2013). Acute SI was defined as current thoughts of suicide or plans, wishes, or intent to complete suicide, regardless of having made an active attempt. For this study, psychiatrists were asked to not consider patients with a diagnosis of bipolar disorder, schizophrenia and other non-mood psychotic disorders, moderate-to-severe substance use disorder (except nicotine-use disorder), intellectual disability, or cluster B personality disorder.

2.3. Study development and structure

The study was conducted in two sequential phases in France, Germany, Italy, Spain, and the UK. Psychiatrists were recruited by an independent third-party through a mix of email and telephone recruitment. All psychiatrists interested in participating in the study were provided with a screener to determine their eligibility. Quotas were applied to ensure sample representativity across the practice settings in the countries in scope.

In Phase I (qualitative phase), 30 psychiatrists (6 per country) participated in a 45-minute web-assisted telephone depth interview, which aimed to understand how patients with MDD who have been hospitalised for acute SI are assessed and treated while in the hospital, including the admission and discharge process and the key variables influencing the likelihood of discharge, and to test the attributes and level (A&L) grid to be used in the conjoint analysis. In this phase, an A&L grid used in an identical study conducted in the United States (US) (Voelker et al., 2020) was shown to respondents, who reviewed and validated the grid to reflect the European context, according to their practice and experience. All inputs collected from these interviews and subsequent pilot interviews were used to develop the survey administered in the quantitative phase. Seven attributes, each with three to four levels, were selected for the conjoint analysis (Table 1).

In Phase II (quantitative stage), 413 psychiatrists were recruited to answer a two-part 45-minute online survey. Part I was a survey collecting data on practice background, treatment patterns, unmet needs, and the criteria and tools used to inform the decisions to admit and discharge patients with MDD hospitalised for acute SI. Part II was the conjoint analysis.

A choice-based conjoint methodology, also known as a discrete choice experiment, was used to assess hospital discharge decisions across a range of potential patient profiles. Respondents were provided with three hypothetical profiles of patients with MDD hospitalised for acute SI, developed based on the A&L grid (Table 1), and were asked to determine which profile they believed was most appropriate to discharge. Each respondent was given a total of 14 tasks to complete.

Respondents were compensated for time spent answering the questionnaire based on fair market value, determined using independently acquired third party data reflecting market rates in the healthcare industry by country.

The elementary derivative output from the conjoint analysis is the relative importance of the attributes. The range of values across the levels within each attribute were re-proportioned to calculate the relative importance of each attribute, i.e., its importance in the decision to discharge a patient. "Relative importance" is a measure of the difference in appeal between the most severe and least severe level of each attribute and allows calculation of the extent to which each attribute influences the total utility of a decision to discharge a patient. Relative importance values are comparable across attributes (e.g., an attribute valued at 20% is twice as important as one valued at 10%). The relative importance of each attribute was reported as a percentage summing to 100% and the values were specific to this project, i.e., they cannot be compared with values from other studies.

When completing the conjoint exercise, physicians were asked to make the following assumptions about the patient profiles they were assessing: (1) patients met the definition of the target population; (2) the patient was being considered for discharge from the hospital; and (3) the patient's condition was considered stable. Any patient information not shown (age, gender, etc.) was assumed to be the same across the different profiles.

2.4. Statistical analysis

Descriptive statistics associated with analyses of the quantitative survey covering demographics and clinical characteristics were conducted according to the type of variable being described. For numeric

Table 1
Definition of attributes and attribute levels (A&L grid) used in the conjoint exercise.

Attribute	Level 1	Level 2	Level 3	Level 4
Clinician assessment of suicidal ideation at admission	Intermittent or regular ideation with intent Passive intention with no immediate plan	Frequent or constant ideation with intent Passive intention with no immediate plan	Frequent or constant ideation with intent Active or uncontrollable with immediate plan or preparations	
Clinician assessment of suicidal ideation when making discharge decision	No suicidal ideation	Minimal or occasional ideation with no intent	Intermittent or regular ideation with intent Passive intention, no immediate plan	Frequent or constant ideation with intent Active or uncontrollable with immediate plan or preparations
Previous history of suicide attempts	No previous attempts	Suicide attempted >1 month ago	Suicide attempted within the last 4 weeks	
MDD severity when making discharge decision (MADRS score)	Remission (0–12)	Mild MDD (13–19)	Moderate MDD (20–34)	Severe MDD (≥35)
Psychosocial support at discharge	Stable living situation, support network present	Stable living situation but no support network	Unstable living situation but support network present	Unstable living situation and no support network
Follow-up visits with psychiatrists in hospital ^a	3 or more visits in the month after discharge	2 visits in the month after discharge	1 visit in the month after discharge	
Patient engagement in the follow-up plan	Patient is engaged in the follow-up plan; compliance is felt to be likely	Patient is relatively engaged in follow-up plan but will need support to ensure compliance	Patient is not engaged in the follow-up plan; compliance is doubted	

Abbreviations: MADRS, Montgomery-Asberg Depression Rating Scale; MDD, major depressive disorder.

^a Assume this follow-up is in addition to any community support required.

values, mean values of country aggregated data are reported, unless otherwise noted; for categorical values, number and/or percentage of subjects are reported in each category.

Descriptive analyses were performed using Q Professional Research Software. Where significance tests were used, the threshold for statistical significance was $p < 0.05$ and each test was two-tailed. The conjoint exercise used Lighthouse Studio 9.6.1 (by Sawtooth Software).

Hierarchical Bayesian estimation was performed on the conjoint data to robustly estimate the relative value each respondent placed on each level of every attribute from the A&L grid. The values from this hierarchical Bayesian estimation are the preference scores (mean part worth utilities) and indicate the value or desirability of a level in the decision to discharge. A low utility score indicates less value; a high desirability or utility indicates greater value. A negative value for the level of an attribute means that level was less preferred than the other levels of the attribute. The greater the range of utilities within an attribute, the more important that attribute.

The selections made by physicians in the conjoint exercise were used to: estimate the relative value of each feature (attribute level) tested; calculate the conditional relative importance of clinical characteristics and impact of attributes; and simulate preference share, referred to as relative likelihood to discharge, between alternative patient profiles.

2.5. Sample size

Sample sizes in qualitative research are typically determined based on the concept of saturation, commonly defined as the point at which no new relevant concepts are identified (i.e., all concepts of importance to patients have been elicited), and in consideration of the heterogeneity of the population of respondents (Glaser and Strauss, 1967). Past experiences and evidence in the literature suggest that conceptual saturation can be achieved in as few as 12 individual interviews among a relatively homogeneous population (Francis et al., 2010; Guest et al., 2006; Lamoureux et al., 2015). For the quantitative research, sample sizes were calculated based on the A&L grid size and number of tasks. With a 7×3 A&L grid and 14 tasks, two of which were hold-out tasks, the minimum sample to achieve a significance level of 0.05 is 130.

Variations in sample size across countries were due to population feasibility and the respective size of the physician groups. Sampling quotas were used to track demographic and behavioural characteristics of the population of respondents.

3. Results

3.1. Respondent demographics

Respondents ($N = 413$: 101 from Spain, 94 from Germany, 83 from France, 71 from the UK, and 64 from Italy) had, on average, 17.4 years of clinical practice and a high level of seniority (72% consultant, 21% head of department). Primary practice setting was well distributed among university/teaching hospitals (38%), specialist psychiatric hospitals (35%), and general hospitals (26%). Eighty-nine percent of their time was spent in direct patient care, mostly in hospitals (inpatient care) or at outpatient clinics attached to the hospitals (day hospital). Each respondent managed, on average, 130 MDD patients in a typical 3-month period; almost half (62/130) of these patients had a diagnosis of MDD and acute SI, of whom 76% (47/62) required hospitalisation.

All respondents were responsible for admission and discharge decisions, either as the sole or the main decision-maker.

3.2. Patient presentation, criteria for admission, and average length of stay

Respondents estimated that, before being admitted to the hospital, 46% of patients with MDD and acute SI are likely to present at the emergency department, 23% at an outpatient visit, 15% at a primary care facility, and 12% in the community setting. Patient presentation at the emergency department appeared to be more common in Spain (59%), Italy (54%), and France (51%), as compared to the UK (40%) or Germany (26%). UK respondents estimated that 24% of patients present in the community setting, while in Germany it was estimated that 31% of patients present in primary care.

Severity of SI and MDD were considered the key drivers of psychiatrists' decisions to hospitalise a patient (Supplementary Fig. 1), with 92% and 83% of respondents rating severity of suicidal ideation and severity of MDD, respectively, as "very important". Also considered "very important" were prior history of suicide attempts (65%), patient's degree of distress or inability to cope (65%), and presence of a support network (57%). Availability of beds and hospital resources and the patient's economic situation were considered the least important factors but were still rated as very important/somewhat important by 73% and 63% of respondents, respectively.

According to psychiatrists' experiences, at the time of admission,

most patients are likely to have prior history of suicide attempt (30% with 1 previous attempt and 26% with ≥ 2 previous attempts) and these patients are predicted to require a longer hospital stay. Overall, respondents estimated an average length of stay of 5.2 weeks in patients without prior history of suicide attempt and 6.9 weeks in patients with repeated suicide attempts (Supplementary Table 2). Average length of stay appears to be identical in all countries, except Germany, where psychiatrists reported the longest length of stay. Mean estimates ranged from 4.4 weeks in Italy to 4.8 weeks in France vs. 7.1 weeks in Germany. In patients with prior history of suicide attempt, the average length of stay increased by 1.9 weeks in Germany and by about 1.5 weeks in the remaining countries. The estimated ranges were, however, very broad, from a minimum of 3 days to a maximum of 16.3 weeks in patients with no prior history of suicide attempt and 1 to 26 weeks in patients with repeated suicide attempts (Supplementary Table 2).

3.3. Treatment patterns and key unmet needs

Almost all respondents (98%) considered antidepressants as standard treatment for patients with MDD and acute SI (Fig. 1). When asked to distinguish treatments used for the broad range of patients or for specific patients only, 85% of respondents considered antidepressants a standard treatment for the broad range of patients, followed by psychotherapy (51%) and anxiolytics (43%). Only 10% of respondents selected electroconvulsive therapy (ECT) as standard therapy for broader use, with this treatment being mostly limited to specific patients. Thirty-eight percent reported having limited or no experience with this treatment or did not consider it standard of care. Use of intravenous (IV) ketamine also appeared limited among respondents: only 13% considered it a standard treatment, 13% reported having experience with it but did not consider it a standard treatment, 29% were still gaining experience or use it occasionally, and 45% reported never using it and/or were not familiar with it (Fig. 1).

Across countries, and as compared to the European average, use of psychotherapy appeared more common in Germany, where all respondents considered it standard treatment for the broad range (84%) or specific (16%) patients, and which is aligned with German guidelines. Mood stabilisers seemed to be more commonly used in Italy, with 48% and 45% of respondents considering them as standard treatment for either broad use or for specific patients, respectively. ECT use is likely to be lower in Italy and Germany, with 55% of Italian and 39% of German respondents reporting being not familiar or having had limited experience with this treatment.

Psychiatrists' perceptions were well reflected in the type of treatments commonly administered to patients during hospitalisation. Overall, it was estimated that 77% of patients receive antidepressants while hospitalised and fewer than 10% are expected to receive ECT (7%) or IV ketamine (3%). Estimated use of anxiolytics and psychotherapy was 54% and 48%, respectively (Supplementary Table 3).

Cross-country comparisons showed that antidepressants are reported by psychiatrists as the most used therapy in all countries, with their use ranging from 69% of patients in France and Italy to 84% in Germany. The use of anxiolytics appeared less common in the UK, being reported in only 36% of patients (vs. 52%–62% in the other countries), and psychotherapy seems to be commonly prescribed in Germany, with respondents estimating to use it in 79% of patients, but less common in Italy and the UK (25% and 29% of patients, respectively). Respondents in Italy reported the highest use of mood stabilisers (47% of patients vs. 21%–26% in the other countries) (Supplementary Table 3).

When asked about the timing of administration of different treatments during hospitalisation, >80% of respondents stated initiation of anxiolytics and antidepressants within the first 48 hours after admission, while psychotherapy and mood stabilisers were reported to be used more often within the first 2 weeks or later. If used, respondents also reserved ECT for later usage (2 weeks or after post admission).

Improving depressive symptoms and achieving remission of MDD were classified as the major treatment goals by 80% of respondents, and 77% agreed that antidepressants with a rapid onset of action constitute a key unmet need for treating patients with MDD and acute SI. When asked to list the top 3 unmet needs of current treatments, 63% of respondents mentioned rapid onset of action, with 50% of respondents ranking this as the top unmet need (Fig. 2). This perception of the unmet needs was consistent across countries, with the percentage of respondents mentioning rapid onset of action varying from 45% in Italy to 73% in Spain and France.

3.4. Conjoint analysis

The A&L grid validated during the qualitative phase retained most of the attributes and levels used in the study conducted in the US (Voelker et al., 2020). Apart from small changes in wording, and addition of new levels to more accurately reflect the variables considered in the decision, the respondents suggested the removal of one attribute related with current length of stay in the hospital, which was considered irrelevant, as the length of stay is impacted by the condition of the patient and not a decision factor on its own, and the addition of a new attribute related to

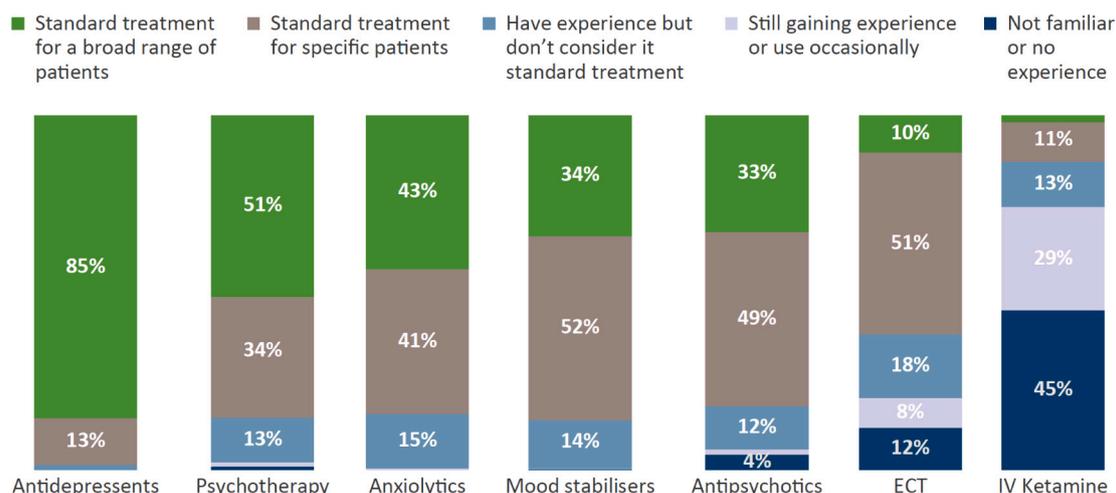


Fig. 1. Treatment patterns for available therapies. Abbreviations: ECT, electroconvulsive therapy; IV, intravenous. N = 413 physicians. Data labels $\leq 2\%$ not shown.

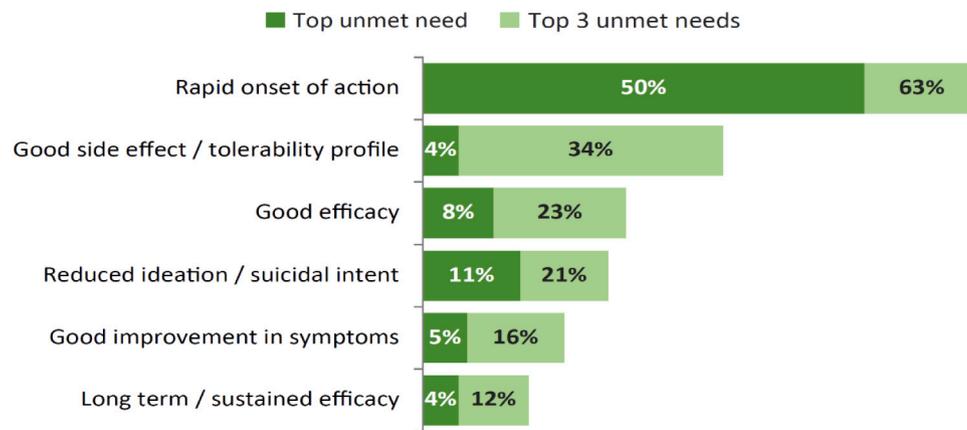


Fig. 2. Top unmet needs of current treatments. Based on spontaneous reporting of top 3 unmet needs by each respondent. N = 413 physicians.

the extent of patient engagement in the follow-up plan.

After quality checks, which included review of the time taken to complete the exercise and repeat patterns of response, 392 responses were considered valid and included in the analysis.

The conjoint analysis showed that among respondents, the most influential drivers of discharge in patients with MDD hospitalised for acute SI are the clinician's assessment of the severity of SI and the severity of MDD at the time of discharge. These two attributes accounted for more than half of the importance values in the discharge decision (54.1%) (Fig. 3).

According to the outcomes of the conjoint exercise, the factors potentially associated with a higher likelihood of discharge include having no or minimal suicidal ideation and being at remission or having mild MDD, assessed at the time of discharge, no history of suicide attempts, and patient engagement in a follow-up plan. Conversely, the factors associated with a lower likelihood of discharge include having frequent/constant suicidal ideation, severe or moderate MDD, assessed at the time of discharge, history of suicide attempt within the past month, unstable living conditions, and lack of patient engagement in the follow-up plan (Fig. 4).

The root likelihood of the data was examined to check the agreement between each respondent's utility estimates and actual choices made. The higher the value of the root likelihood score (in a range 0–1), the

greater the consistency between utility estimates and actual choices. Respondents' root likelihood scores were between 0.37 and 0.91, with an average of 0.72, thus indicating good consistency between their utility estimates and actual choices and supporting the validity of the conjoint model.

4. Discussion

This is, to our knowledge, the first European study providing insights on treatment patterns, unmet needs, and key drivers of hospital admission and discharge in patients with MDD hospitalised for acute SI. In this study, severity of SI and severity of MDD were the factors with the largest influence on the decision to hospitalise a patient with MDD and acute SI.

Psychiatrists estimated that patients stay, on average, 5.2 weeks in the hospital, with the longest length of stay reported by German respondents (7.1 weeks). This might be linked to the high-level of resource availability in Germany (Zipfel et al., 2016).

Severity of SI and severity of MDD at the time of discharge were also considered the key drivers of psychiatrists' decisions when assessing the readiness to discharge, accounting for more than half of the importance of the attributes considered in the conjoint analysis. Other attributes impacting this decision were patient engagement in the follow-up plan,

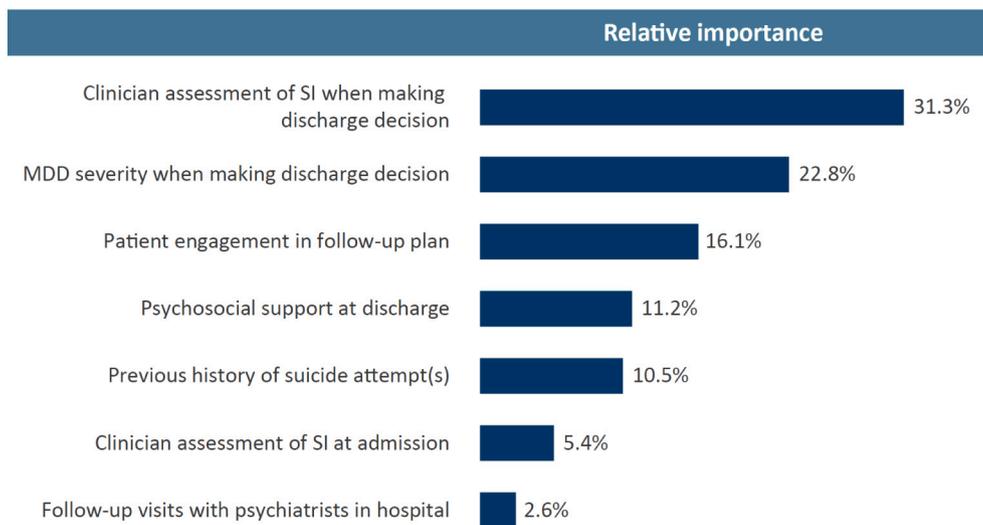


Fig. 3. Conjoint analysis: relative importance of the seven attributes in discharge decision. Abbreviations: MDD, major depressive disorder; SI, suicidal ideation. N = 392 physicians.

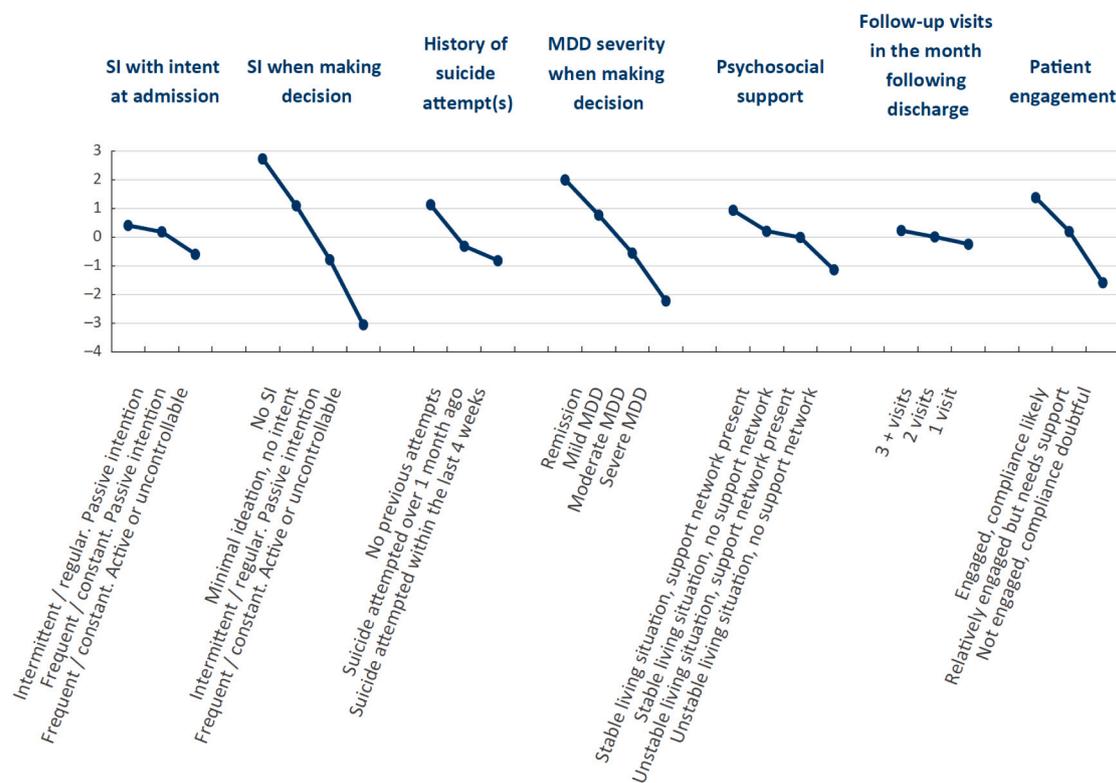


Fig. 4. Conjoint analysis: preference scores across attributes and levels. Abbreviations: MDD, major depressive disorder; SI, suicidal ideation. N = 392 physicians.

psychosocial support at discharge, and previous history of suicide attempts.

While there are factors that cannot be modified by treatment, such as prior history of suicide attempt, others can be improved by selecting the optimal treatment approach. Too often, the complex interaction between life stressors and patient vulnerability on the specific reasons that triggered the SI cannot be easily identified. Therapeutic intervention and patient coping strategies, as well as interventions aimed at understanding patient suffering together with the improvement of depression, are unquestionably an important part of a comprehensive treatment approach.

While ameliorating suicidal ideation severity is critical, with no medicines currently available with proven efficacy against acute suicidality and no robust tools to measure such improvement, the improvement of depressive symptoms is ranked as a top priority for these patients. Antidepressants constitute a key component of the first-line standard of care for patients with MDD and acute SI (Jaffe et al., 2019; Seifert et al., 2021) and are administered to patients soon after admission. However, conventional oral antidepressants are of limited use in the acute treatment phase due to their delayed onset of action, taking at least 4 weeks to reach their expected antidepressant effect (Machado-Vieira et al., 2010; Wasserman et al., 2012). Although there is some evidence in the literature regarding the use of IV ketamine to rapidly improve symptoms of depression as well as acutely reducing symptoms of suicidality (Dadiomov and Lee, 2019; Han et al., 2016; Dubovsky, 2018), dose-finding and large-scale studies are lacking and IV ketamine is not currently approved or recommended for the treatment of MDD with or without SI. This may explain the low number of psychiatrists in this research considering IV ketamine a standard treatment or being familiar with the use of this drug. More recently, the European Medicines Agency has approved esketamine, the S-enantiomer of ketamine and an N-methyl-D-aspartate receptor antagonist, in association with oral antidepressant therapy in adult patients with MDD, as acute-

short term treatment for the rapid reduction of depressive symptoms, which according to clinical judgment constitute a psychiatric emergency (EMA, 2021). The approval of this indication was based on two phase 3, double-blind, multicentre registration trials in patients with MDD and active SI with intent: ASPIRE I and ASPIRE II. In both trials, patients who received esketamine nasal spray, given in addition to comprehensive standard of care, exhibited a significantly greater reduction in depressive symptoms than those who received placebo nasal spray plus standard of care, measured 24 hours after first administration. This difference was, however, not observed when assessing suicidality (Fu et al., 2020; Ionescu et al., 2021). As this approval dates from 2021, its use in clinical practice could not be captured in this research.

In the absence of a rapid-acting and effective pharmacological treatment option, patients are often managed with temporary hospitalisation and anxiolytics, but these do not appropriately treat the underlying MDD. Acute non-pharmacological interventions such as ECT may also be considered in very specific, high-risk patients to rapidly induce remission of depressive symptoms (Wasserman et al., 2012). However, ECT is delivered in a controlled clinical setting under general anaesthetic, requiring a specific infrastructure that may not be readily available in the context of a psychiatric emergency. Furthermore, patients seem often reluctant to receive ECT due to the side effects and stigma related to treatment (Cusin and Dougherty, 2012).

According to the current research, use of ECT seems uncommon in many hospitals, and 40% of the psychiatrists surveyed mentioned not seeing it as standard of treatment or being unfamiliar/having no experience with this treatment. Also, if used, it is reserved for later stages of treatment, more often implemented 2 weeks or later after admission.

It is therefore not surprising that, despite the broad range of treatments used to manage these patients, 63% of respondents in the current study rated rapid onset of action as a key unmet need for treatments in these patients.

This study was designed and conducted in accordance with best

practice principles, including the development of the A&L grid, conjoint analysis experimental design, and statistical analyses (Bridges et al., 2011; Hauber et al., 2016; Orme, 2002). A qualitative phase was conducted to determine the relevance and importance of selected attributes as well as the participant's understanding of the wording of the attributes, which was critical to ensure the content validity of the survey. Input from these interviews, combined with subsequent pilot interviews, conducted as part of the rollout of the survey, were also important for validation of the study design, ensuring that survey content and the choice tasks participants were asked to complete were well-understood and reflected real-world decision-making.

The sample recruited to complete the survey was defined to reflect those treating the patient population of interest. The previously described inclusion criteria sought to ensure that participants completing the survey had adequate real-life experience with making decisions relevant to the choice tasks. All participants were decision makers, with responsibilities on the decision as to whether to discharge a patient with MDD hospitalised due to SI. Finally, the large sample achieved across multiple European countries gives confidence in the integrity of the data and analysis and that the participants represented views from across the region.

The choice-based conjoint approach allows replication of the real choice and trade-off behaviour that psychiatrists may experience in the practice setting; offers multiple alternatives, maximising respondents' attention; and has a high degree of sensitivity. This approach facilitates an understanding of respondents' trade-offs when making the discharge decision, including those of which the respondent may not be explicitly aware of through derived analysis of choices made.

4.1. Limitations

The following methodological limitations should be considered when interpreting the results. While the survey sample was robust and thought to be generally reflective of the psychiatrists treating the patient population of interest, the findings are specific to the population and cross-sectional design of this study and cannot be generalised more widely. Additionally, because the survey was conducted during the SARS2 COVID-19 pandemic, the participants' time was potentially more limited to complete the tasks.

Mean part-worth utilities and preference weights derived from conjoint analyses are dependent on the attributes and associated levels employed within the specific study. To maximise the study validity and generalisability of the findings, care was taken to ensure that attributes included covered the spectrum of characteristics of the patient of interest (Olsson et al., 2016). However, it is necessary to acknowledge the limitations of reducing the clinical prescribing decision down to a relatively small number of attributes in an area where we know subjective assessment of the patient's condition and individual circumstance play a large role in the decision to discharge. For example, the grid does not take into account the qualitative severity of any prior suicide attempts and method by which they took place. To focus on the clinical aspects of the discharge decision, the list of attributes included in the current study also did not include financial or budgetary considerations, which might also contribute to the decision-making process in real-world clinical practice either directly or indirectly through limited availability of healthcare resources. The current analysis may be considered to represent decisions made in an environment in which psychiatrists can assess the clinical and support needs of patients without the confounding influence of financial considerations.

Methods that rely on stated preference rather than observation of behaviour can be criticised in terms of reporter bias. The conjoint design requires respondents to evaluate hypothetical situations. The utilities calculated on this basis can only therefore reflect the value placed on each attribute level relative to the value placed on all other levels within the same attribute. The number of attributes included within this and other similar studies (Johnson et al., 2013; Liu et al., 2017; van

Overbeeke et al., 2019) are necessarily limited to fit with the feasible sample size to power analysis and to ensure the A&L grid does not become overly complex. Because the attribute and level of importance were calculated based on how physicians responded to the tasks on the online survey, the results only represent the described patient behaviour and not observed clinical behaviour. Hence, the study design limits the respondent's ability to respond meaningfully.

The advantages of using a conjoint-based approach included replicating real choice and trade-off behaviour that physicians may experience in their routine practice setting; showing multiple alternatives so that respondents had to pay attention to their decisions and choices; and a high degree of sensitivity, making it possible to understand what a respondent may trade for a more favourable level. The exercise can also reveal trade-offs of which the respondent themselves may be unaware.

Though conjoint methods better reflect the real-life decision-making than other survey methods, the choices made in response to the hypothetical scenarios lack the risk and real-life consequences, and emotion attached to such decisions. The choice task was based on the appropriateness to discharge a patient and thereby provides a robust measure of factors influencing the likelihood to discharge and their magnitude of influence on that decision. However, the task did not consider the actual likelihood that a given patient would be discharged in the real world. The results are dependent on adequate participant understanding of the survey and rely on the respondent providing the best possible answer choices based on a hypothetical patient rather than clinical data. Additionally, the cross-sectional approach does not allow us to draw conclusions about causality.

5. Conclusions

The decisions to admit and discharge patients with MDD hospitalised for acute SI are mostly driven by the severity of SI and the severity of MDD. Antidepressants with a rapid onset of action, which can quickly improve depressive symptoms, represent a key unmet need for these patients and may contribute to a higher likelihood of earlier discharge.

Further research is needed to provide more detail on the psychiatrist decision-making process, including the variables that could influence, or even prevent, patients' admission and/or accelerate their discharge.

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jad.2022.05.099>.

Data availability statement

The key data supporting the findings of this study are available within the article and its supplementary materials. Additional data may be obtained from the authors upon reasonable request.

Credit authorship contribution statement

A. Major, J. Anjo, and K. Hope designed and planned the study. K. Hope lead the team that conducted the study and processed the data. J. Anjo, M. Pompili, M. O'Hara, S. Borentain, T. Annus, and U. Lewitzka reviewed the data. M. Pompili, S. Borentain, and U. Lewitzka assessed the clinical validity and relevance of the findings. All authors participated in the manuscript development and approved the final version of the manuscript to be published.

Role of funding source

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Conflict of interest

Ute Lewitzka has received research grants from BMBF, AFSP, BMG, Dalhousie University, Gulinsky Stiftung, and Janssen-Cilag; honoraria for lecturing from Janssen-Cilag; and honoraria for advisory board

activity from Janssen-Cilag.

Kirsty Hope was an employee of Adelphi Research at the time of study completion.

Maurizio Pompili took part in advisory boards on esketamine and received consultation fees from Janssen, which are unrelated to this article. In the last 2 years, he has received lectures or advisory board honoraria or engaged in clinical trial activities with Angelini, Lundbeck, Janssen, Otsuka, Pfizer, Recordati, GSK, and Allergan, which are unrelated to this work.

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