# Perspective on shared decision-making for depression and anxiety disorders in clinical practice: a qualitative and quantitative exploration

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# Chapter 2

## Clinical and sociodemographic associations with treatment selection in Major Depression

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## ABSTRACT

*Objective*: To investigate treatment selection in a naturalistic sample of MDD outpatients and the factors influencing treatment selection in specialized psychiatric care.

*Method*: Multinomial Logistic Regression analysis investigated associations between treatment selection and patients' sociodemographic and clinical characteristics, using retrospective chart review data and Routine Outcome Monitoring (ROM) data of MDD outpatients.

*Results*: Of the patients included for analyses (N = 263), 34% received psychotherapy, 32% received an antidepressant (AD) and 35% received a combination. Men were more likely than women to receive AD with reference to psychotherapy ($OR_{AD}$ = 5.57, 95% CI 2.38–13.00). Patients with severe depression and patients with AD use upon referral, prescribed by their general practitioner, were more likely to receive AD ($OR_{severe\ depression}$ = 5.34, 95% CI 1.70–16.78/$OR_{AD\ GP}$ = 9.26, 95% CI 2.53–33.90) or combined treatment ($OR_{severe\ depression}$ = 6.32, 95% CI 1.86–21.49/$OR_{AD\ GP}$ = 22.36, 95% CI 5.89–83.59) with respect to psychotherapy. More severe patients with AD upon referral received combined treatment less often compared to psychotherapy (OR = 0.14, 95% CI 0.03–0.68).

*Conclusion*: AD prescriptions in primary care, severity and gender influenced treatment selection for depressive disorders in secondary psychiatric care. Other factors such as the accessibility of treatment and patient preferences may have played a role in treatment selection in this setting and need further investigation.

# INTRODUCTION

Worldwide, major depressive disorder (MDD) is highly prevalent in general populations[1-3]. In the Netherlands, the overall lifetime prevalence of MDD is approximately 20%. Of these patients, almost half (46%) suffers from a comorbid psychiatric disorder and only 30% receive some form of treatment[4]. Patients with anxiety and/or depressive complaints consult their general practitioner (GP) first, and may be treated in primary care (with either antidepressants by their GP or CBT by a psychologist/psychotherapist) before they are referred to specialized psychiatric care, i.e. secondary care and, in case of therapy resistance tertiary care.

To treat MDD, treatment guidelines recommend a stepped-care approach that uses a range of effective therapy options, in a specific order, depending on patient severity profiles and their response to previous treatments[5-7]. Clinical guidelines recommend psychotherapy, for example, Cognitive Behavioral Therapy (CBT) or Interpersonal Psychotherapy (IPT), Medication/antidepressants (ADs) or a combination of both. These treatments are considered equally suitable and efficacious for MDD[3-7], but they are not effective for all patients[8]. The guidelines mention that psychotherapy is effective for mild to moderate depression, medication is suggested for moderate to severe depression and combined treatment is more effective and indicated for severe or chronic forms of depression, suggesting that pharmacological treatment (with or without psychotherapy) is more appropriate in more severe forms of depression. Current clinical guidelines explicitly advise to involve patients and to gain their consent in treatment. In this context, important factors are interpersonal or psychosocial problems, patient preferences, results of previous treatments of the patient, side-effects of medication, family history of MDD or pragmatic issues, such as waiting lists for treatment[7]. However, guidelines cannot stipulate completely how treatment decisions should be made[9-11].

Diagnosing and treating psychiatric disorders can be complex because clinicians must balance biological-, psychological- and social factors[12]. Considering that no 'best' treatment exists and that both treatments are recommended in the guidelines, decisions regarding how to treat MDD are 'preference sensitive', that is, the best choice depends on how patients value the benefits versus the harms and on other fac- tors important to the decisional process[13,14]. There is little evidence to guide clinicians in this process and the initial choice to treat a patient with AD, psychotherapeutic treatment or a combination of both[15].

The process to determine treatment selection for depressive disorders in clinical practice is still poorly understood, and research on this topic in secondary psychiatric care is scarce. Little is known about actual treatment selection of patients and clinicians in routine clinical practice; the same is true for the specific clinical and sociodemographic factors associated with this selection[16]. Such information would illuminate the process of making treatment decisions in clinical practice; it would also propel the development and implementation of

future decision-making interventions and the development of new (international) treatment guidelines for MDD.

### Aims of the study

The aim of the present study was to analyze patients' socio- demographic and clinical factors in relation to treatment selection in a naturalistic sample of outpatients with MDD in a secondary mental health care setting.

## MATERIALS AND METHODS

### Overview

For this retrospective cohort study, we used an existing dataset from psychiatric outpatients treated at the Dutch Mental Health Care Provider GGZ Rivierduinen. We captured diagnostic and socio- demographic data from routine clinical practice from the Routine Outcome Monitoring (ROM) baseline assessment[17]. Next, we combined ROM data with clinical data, i.e. primary diagnosis (made by the clinician) and treatment modalities, captured from an earlier retrospective chart review by van der Lem et al. (2011)[18-20]. Based on the literature and the availability in our database, we selected the following sociodemographic and clinical variables for our analyses: age, gender, ethnic background, education, marital status, living situation and employment status, i.e. personal characteristics of the patient; co- morbidity, symptom severity and AD use upon referral (medical history), i.e. clinical characteristics of the patient. We investigated the association between these independent variables and the treatment modalities of psychotherapy, medication, or both to determine the influence of specific sociodemographic and clinical factors on treatment selection.

### Data sources

*ROM*

The Leiden Routine Outcome Monitoring Study is a naturalistic study among adult (age 18 to 65 years) outpatients at GGZ Rivierduinen. General practitioners (GPs) in primary care refer patients for specialized treatment of mood-, somatoform- and/or anxiety disorders. Reasons for patient referral to GGZ Rivierduinen are (i) more severe, recurrent, or refractory depression, (ii) the presence of comorbid psychiatric or somatic disorders and (iii) sometimes a preference for psychotherapy. As part of routine clinical practice, all patients are asked to complete an extensive battery of psychometric measures. De Beurs et al.[17] describe the procedure in more detail. All patient data from the Leiden Routine Outcome Monitoring Study are stored anonymously in the Psychiatric Academic Registration Leiden (PAREL) database and are accessible for research purposes only.

*Retrospective chart review*

We captured data on treatment modalities and primary diagnoses made by clinicians from a chart review conducted by van der Lem et al.[19] as part of a study assessing the generalizability of AD and psychotherapy efficacy trials[18-20]. The study included all adult (18–65 years) outpatients with a DSM-IV diagnosis of a current MDD, according to MINI-Plus 5.0.0[21] who sought treatment at GGZ Rivierduinen between January 2002 and January 2007. Of this population, van der Lem et al.[19] selected all patients with at least one ROM follow-up assessment (N=626). Next, an extensive chart review was conducted to collect additional information, such as patients' primary clinical diagnoses and treatment modalities.

The medical ethics committee of the Leiden University Medical Centre (LUMC) approved both studies, and informed consent was obtained from all participants.

## Patients

Between 2002 and 2007, the ROM baseline assessment included a standardized diagnostic interview, the Mini-International Neuropsychiatric Interview Plus (MINI-Plus; Dutch version 5.0.0)[21], a questionnaire on sociodemographic and socioeconomic data, disease specific severity scales and generic questionnaires. All patients with sufficient mastery of the Dutch language who were able to complete computerized and written questionnaires were eligible for ROM. Our study population was selected based on the MINI-Plus, that is, all patients meeting the diagnostic criteria of a current MDD diagnosis. The MINI-Plus has good psychometric properties: interrater reliability between 0.88 and 1.00, test–retest reliability between 0.76 and 0.93. In order to investigate a homogenous group of patients, we further restricted the sample to patients who were also given a primary diagnosis of MDD by their clinician, independently from the results of the MINI-Plus. This variable was captured from the retrospective chart review. In the current sample, a clinician (a psychiatrist or resident in training supervised by a psychiatrist or psychotherapist) determined the clinical/primary diagnosis – the most relevant diagnosis and the main focus of treatment according to that clinician- using his or her clinical skills, via a clinical interview in order to determine the presence/absence of a DSM-IV diagnosis[22].

## Outcome

Patients in the study population received different types of treatment for their depression of which most (85%) were in line with ((in)ternational) guidelines[20]. We captured three major categories of the treatment modalities from the chart review[18,19]: 1) 'psychotherapy' (mostly cognitive behavioral therapy (CBT) only or interpersonal psychotherapy (IPT) only, as recommended in the guidelines); 2) 'AD' (antidepressant only, which were: selective serotonin reuptake inhibitor (SRRI), serotonin norepinephrine reuptake inhibitor (SNRI) or tricyclic antidepressant (TCA), accordant with clinical guidelines for pharmacological treatment of depression in secondary care. Adequacy of the dosage was not included in the study.); and 3) 'combined treatment' (combination of an AD and CBT or IPT).

## Patient characteristics

The sociodemographic variables were available from a self-report questionnaire in ROM that assessed age, gender, ethnic background, education, marital status, living situation and employment status. A Dutch background was assumed when the patient and both parents were born in the Netherlands. Education was categorized into two levels: 'low' (no education and primary education – up to and including junior general secondary education or preparatory secondary vocational education) and 'high' (senior secondary general education or senior secondary vocational education – up to and including higher education, pre-university education, higher professional education, or higher academic education, i.e., university). Marital status was categorized into 'married/cohabitating' and 'not married/not cohabitating'. Living situation was categorized into two categories: 'alone' or 'with partner and/or family'. Employment status was categorized into 'job' (employed full- or part-time) and 'no job' (unemployed, retired or on sick leave).

We captured clinical variables from ROM measurements and the retrospective chart review. We used other diagnoses on the MINI-Plus 5.0.0 to assess comorbidity, which was divided into two categories: 'no' (depression only) and 'yes' (depression and one or more Axis I diagnosis – mostly anxiety disorder). Depression severity was assessed using the revised Beck Depression Inventory (BDI-II)[23]. The BDI-II, a widely used self-report instrument, measures the severity of depression, and reflects the diagnostic criteria for MDD described in the DSM-IV[24]. The BDI-II has shown good internal consistency, reliability, and validity[25]. For our analyses, we used the BDI-II total score, which was composed of the summation of 21 questions, each answer being scored on a scale value of 0–3. According to clinical practice guidelines, BDI-II total scores were divided into two categories: 'severe depression' (BDI-II total score of > 28 points) or 'mild to moderate depression' (BDI-II total score of < 29 depressive symptoms).

We captured information on AD use (at or prior to referral) from the chart review and divided it into yes/no categories.

## Statistical analyses

Data are presented as N (%) or mean (± SD), as appropriate. Sociodemographic and clinical characteristics of patients in the three treatment groups were compared using univariable multinomial logistic regression analysis. Independent associations of treatment groups were assessed using multivariable multinomial logistic regression analyses, with individual psychotherapy as a reference category. Odds Ratios (OR) represent the odds that a certain treatment modality was selected given the occurrence of a sociodemographic or clinical categorical variable or one unit increase in the value of a continuous variable: age (in years). For the multivariable analyses, all candidate determinants achieving significance levels of $p \leq .25$ in the univariable analyses were selected. This P-value criterion reduces the initial number of variables in the model but also minimalizes the risk of missing important variables[26,27]. Failure to achieve significance ($p \geq .05$) in the resulting multivariable model

prompted removing variables, except for age and gender, which were forced into the model as possible confounders. Statistical analyses were performed using IBM SPSS Statistics Version 25.0[28].

## Post Hoc analyses

Because of the findings regarding treatment from the GP upon referral and severity, post hoc analyses were performed to investigate whether treatment prescribed by the GP was continued in secondary care, using crosstabs. In addition, interactions of AD upon referral with gender, age and severity respectively were added to univariable and multivariable analyses.

# RESULTS

## Sample characteristics

Fig. 1 shows the flow chart of patients included in the study. Of the 263 patients that were included for analyses, 34% received psychotherapy, 32% AD and 35% received a combined treatment. The study population had a mean age of 40 years (SD = 11) and consisted of mostly women (65%). Patients were primarily Dutch (86%), 50% were married/cohabitating, 51% lived alone, 60% were highly educated and 64% were unemployed. Slightly more than half of patients (55%) had a comorbid psychiatric disorder according to the MINI-Plus 5.0.0, 58% suffered from a severe depression according to the BDI-II. 58% of the patients were using and AD upon referral, in 61% of these cases, medication was continued in secondary care as monotherapy (36%) or combination therapy (61%).

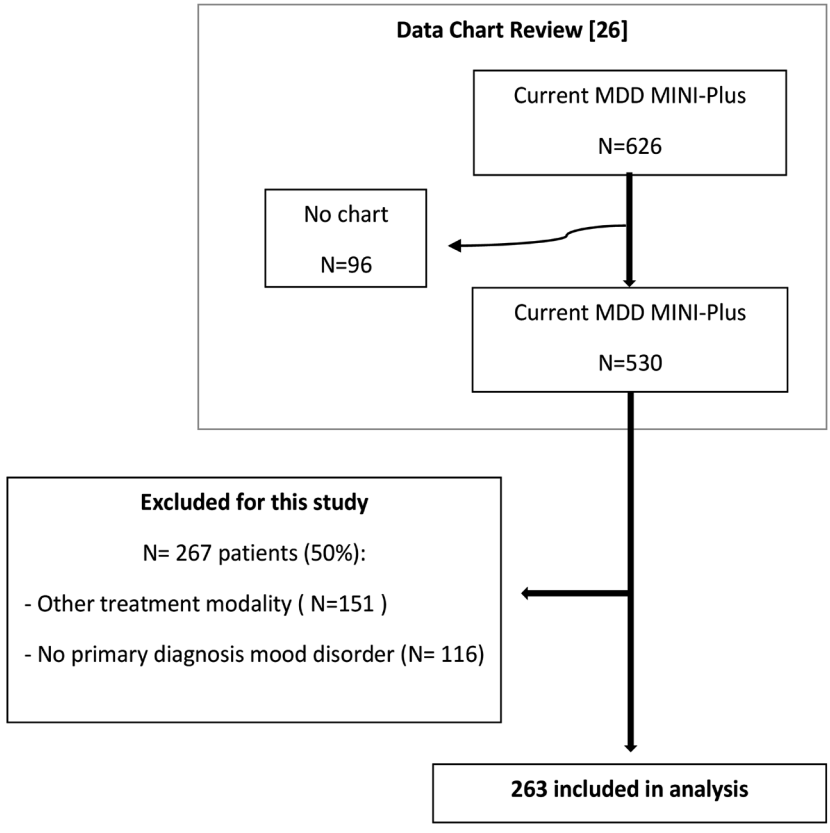


**Figure 1** *Flowchart of inclusion.*

Table 1 shows the characteristics of our study population according to treatment selection. Patients who exclusively received psychotherapy had a lower mean age, almost half had a mild to moderate depression and more than half (57%) were not using an AD upon referral. Half of the patients who exclusively received an AD (51%) were male.



Table 1 Sample *characteristics of N = 263 patients with Major Depression.*

| | **Total** N = **263** | **Psychotherapy** N = **88 (34%)** | **Antidepressant** N = **83 (32%)** | **Combination** N = **92 (35%)** |
|---|---|---|---|---|
| *Personal Characteristics* | | | | |
| Age (years ± *SD*) | 40± 11 | 36 ± 11 | 42 ± 10 | 41 ± 11 |
| Gender (*n*, %) | | | | |
| Male | 93 (35%) | 24 (27%) | 47 (56%) | 22 (24%) |
| Female | 170 (65%) | 64 (73%) | 36 (43%) | 70 (76%) |
| Ethnicity (*n*, %) | | | | |
| Dutch | 199 (86%) | 70 (89%) | 60 (83%) | 69 (85%) |
| Non Dutch | 33 (14%) | 9 (11%) | 12 (17%) | 12 (15%) |
| Marital Status (*n*, %) | | | | |
| Married/cohabitating | 116 (50%) | 38 (48%) | 37 (51%) | 41 (51%) |
| Not married/ cohabitating | 116 (50%) | 41 (52%) | 35 (49%) | 40 (49%) |
| Living Situation (*n*, %) | | | | |
| Alone | 118 (51%) | 43 (54%) | 35 (49%) | 40 (49%) |
| With partner / family | 114 (49%) | 36 (46%) | 37 (51%) | 41 (51%) |
| Education (*n*, %) | | | | |
| High | 138 (60%) | 50 (63%) | 37 (51%) | 51 (63%) |
| Low | 94 (41%) | 29 (37%) | 35 (49%) | 30 (37%) |
| Employment (*n*, %) | | | | |
| Job | 84 (36%) | 31 (39%) | 26 (36%) | 27 (33%) |
| No job | 148 (64%) | 48 (61%) | 46 (64%) | 54 (67%) |
| *Clinical Characteristics* | | | | |
| Comorbidity[a] (MINI-Plus) | | | | |
| Comorbidity | 144 (55%) | 45 (51%) | 46 (55%) | 53 (58%) |
| No Comorbidity | 119 (45%) | 43 (49%) | 37 (45%) | 39 (42%) |
| Severity[b] | | | | |
| Severe depression | 149 (58%) | 39 (45%) | 55 (68%) | 55 (62%) |
| Mild to moderate depression | 107 (42%) | 48 (55%) | 26 (32%) | 33 (38%) |
| AD upon referral[c] (*n*, %) | | | | |
| Yes | 151 (58%) | 26 (30%) | 55 (68%) | 70 (78%) |
| No | 108 (42%) | 62 (70%) | 26 (32%) | 20 (22%) |

[a] One or more comorbid diagnosis on Axis I according to the MINI-Plus.
[b] Symptom severity assessed with the Beck Depression Inventory (BDI-II). Total scores > 29 points indicate severe depression, total scores < 29 indicate mild to moderate depression.
[c] Patients using an antidepressant upon referral, prescribed by the General Practitioner.

## Associations with treatment selection

Table 2 shows the results of the univariable and multivariable multinomial logistic regression, expressed as the odds that a patient received an AD or combined treatment with respect to psychotherapy. Univariable analyses revealed significant differences between treatment groups for age, gender, severity, and AD upon referral. The ORs of the univariable analyses show that older patients were slightly more likely than younger patients to receive an AD or a combined treatment with respect to psychotherapy ($OR_{AD}$ = 1.05, 95% CI 1.02–1.08 per year; $OR_{combined\ treatment}$ = 1.04, 95% CI 1.01–1.07 per year). Male patients were more likely to receive an AD with respect to psychotherapy ($OR_{AD}$ = 3.48, 95% CI 1.84–6.60). Patients with severe depression were more likely than patients with mild to moderate depression to receive an AD or combined treatment with respect to psychotherapy ($OR_{AD}$ = 2.60, 95% CI 1.39–4.89; $OR_{combined\ treatment}$ = 2.05, 95% CI 1.12–3.75). With respect to psychotherapy, patients who already used an AD upon referral were more likely to receive an AD than patients not using an AD upon referral ($OR_{AD}$ = 5.04, 95% CI 2.62–9.70); they were even more likely than patients not using an AD upon referral to receive combined treatment with respect to the exclusive use of psychotherapy ($OR_{combined\ treatment}$ = 8.35, 95% CI 4.25–16.41). To reveal possible interaction between the effects of age with gender and severity with age and gender, respectively, we also entered the interaction terms for these variables into the univariable analyses, which were significantly associated with treatment selection, see Table 2.

Based on the results of the univariable analyses, post hoc univariate analyses for the interaction of AD upon referral with age, gender and severity were performed. These analyses showed significant associations with treatment selection (see Table 2). The variables age, gender, education, severity and AD upon referral and interaction terms were entered in the multivariable analysis. This multivariable nominal logistic regression analysis revealed significant associations between male gender, severity, AD upon referral and the interaction of severity and AD upon referral with treatment selection. Men were more likely than women to receive an AD with respect to psychotherapy ($OR_{AD}$ = 5.57, 95% CI 2.38–13.00). Patients with severe depression were more likely than patients with mild to moderate depression to receive AD ($OR_{AD}$ = 5.34, 95% CI 1.70–16.78) or a combined treatment ($OR_{combined\ treatment}$ = 6.32, 95% CI 1.86–21.49) with respect to psychotherapy. Patients who used an AD upon referral were more likely than patients not using an AD upon referral to receive either AD ($OR_{AD}$ = 9.26, 95% CI 2.53–33.90) or a combined treatment with respect to psychotherapy ($OR_{combined\ treatment}$ = 22.36, 95% CI 5.89–83.59). Patients with severe depression and AD upon referral were less likely to receive combination therapy with respect to psychotherapy ($OR_{combined\ treatment}$ = 0.14, 95% CI 0.03–0.68). Despite statistical significance in the univariable analyses, age was not significantly associated with treatment selection in the multivariable model and no interactions were found.

**Table 2** Univariable and multivariable odds ratios[a] of sociodemographic and clinical determinants of treatment choice in *N* = 263 MDD patients.

| | Univariable Analyses | | | Multivariable Analyses | | |
|---|---|---|---|---|---|---|
| **Medication** Base case: Individual Psychotherapy | **Odds Ratio** | **95% CI** | **p value** | **Odds Ratio** | **95% CI** | **p value** |
| *Personal Characteristics* | | | | | | |
| Age** | 1.05 | 1.02–1.08 | **0.001** | 1.03 | 0.99–1.07 | 0.20 |
| Male gender*** | 3.48 | 1.84–6.60 | **<0.001** | 5.57 | 2.38–13.00 | **<0.001** |
| Non Dutch ethnicity | 1.56 | 0.61–3.95 | 0.35 | | | |
| Not married/cohabitating | 0.88 | 0.46–1.66 | 0.69 | | | |
| Living alone | 0.79 | 0.42–1.50 | 0.48 | | | |
| Low education | 1.63 | 0.85–3.13 | 0.14 | | | |
| Unemployed | 1.14 | 0.59–2.21 | 0.69 | | | |
| *Clinical Characteristics* | | | | | | |
| Comorbidity[b] | 1.19 | 0.65–2.17 | 0.58 | | | |
| Severe depression[c] ** | 2.64 | 1.39–4.89 | **<0.01** | 5.34 | 1.7–16.78 | **<0.01** |
| Medical History (previous experience) | | | | | | |
| AD upon referral[d] *** | 5.04 | 2.24–9.70 | **<0.001** | 9.26 | 2.53–33.90 | **0.001** |
| Interactions | | | | | | |
| Age*Male gender | 1.07 | 1.03–1.10 | **<0.001** | | | |
| Age*Female gender | 1.03 | 1.00–1.07 | **<0.05** | | | |
| Age*Severe depression | 1.06 | 1.03–1.10 | **<0.001** | | | |
| Age*Mild-moderate depression | 1.04 | 1.01–1.07 | **<0.05** | | | |
| Male gender*Severe depression | 18.09 | 5.58–58.58 | **<.0.001** | | | |
| Male gender*Mild-moderate depression | 4.10 | 1.48-11.40 | **<0.01** | | | |
| Female gender*Severe depression | 3.17 | 1.25–8.03 | **<0.05** | | | |
| Post Hoc[e] | | | | | | |
| AD upon referral*Age | 1.06 | 1.03-1.09 | **<0.001** | | | |
| Ad upon referral*Male gender | 21.26 | 6.97-64.88 | **<0.001** | | | |
| Ad upon referral*Female gender | 5.72 | 2.32-14.08 | **<0.001** | | | |
| No AD upon referral*Male gender | 3.91 | 1.50-10.23 | **<0.01** | | | |
| AD upon referral*Severe depression | 10.20 | 4.06-25.60 | **<0.001** | | | |
| AD upon referral*Mild-moderate depression | 7.22 | 2.40-21.68 | **<0.001** | | | |
| No AD upon referral* Mild-moderate depression | 2.96 | 1.11-7.86 | **<0.001** | | | |
| **Combined Treatment** | | | | | | |
| Personal Characteristics | | | | | | |
| Age** | 1.0 | 1.01–1.07 | **<0.01** | 1.01 | 0.98–1.05 | 0.46 |
| Male Gender | 0.84 | 0.43–1.64 | 0.61 | 1.65 | 0.69–3.97 | 0.38 |
| Non-Dutch ethnicity | 1.35 | 0.54–3.42 | 0.52 | | | |
| Not married/cohabitating | 0.90 | 0.49–1.68 | 0.75 | | | |
| Living alone | 0.82 | 0.44–1.52 | 0.52 | | | |
| Low education | 1.01 | 0.53–1.93 | 0.97 | | | |
| Unemployed | 1.29 | 0.68–2.46 | 0.44 | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Clinical Characteristics | | | | | | |
| Comorbidity[b] | 1.30 | 0.72–2.34 | 0.40 | | | |
| Severe Depression[c] * | 2.05 | 1.12–3.75 | **<0.05** | 6.32 | 1.86–21.49 | **<0.01** |
| Medical History (experience) | | | | | | |
| AD upon referral[d] *** | 8.35 | 4.25–16.41 | **<0.001** | 22.36 | 5.89–83.59 | **<0.001** |
| Interactions | | | | | | |
| Age*Male gender | 1.04 | 1.00–1.07 | **<0.05** | | | |
| Age*Female gender | 1.04 | 1.01–1.07 | **<0.01** | | | |
| Male gender*Severe depression | 2.78 | 0.94–8.27 | 0.07 | | | |
| Male gender*Mid-moderate depression | 0.49 | 0.18–1.37 | 0.17 | | | |
| Female gender*Severe depression | 1.48 | 0.74–2.97 | 0.27 | | | |
| Severe depression*Age | 1.05 | 1.02–1.08 | **<0.01** | | | |
| Mild-moderate depression*Age | 1.03 | 1.00–1.06 | 0.33 | | | |
| Post Hoc[e] | | | | | | |
| AD upon referral*Age | 1.04 | 1.01-1.0 | **<0.05** | | | |
| Ad upon referral*Male gender | 8.31 | 2.77-24.96 | **<0.001** | | | |
| Ad upon referral*Female gender | 7.77 | 3.56-16.95 | **<0.001** | | | |
| AD upon referral*Severe depression | 15.68 | 5.60-43.86 | **<0.001** | 0.14 | 0.03-0.68 | **<0.05** |
| AD upon referral*Mild-moderate depression | 18.78 | 5.97-59.07 | **<0.001** | | | |
| No AD upon referral*severe depression | 3.84 | 1.28-11.53 | **<0.05** | | | |

[a] Odds ratio, 95% CI and *p* value by univariable and multivariable multinomial logistic regression (stepwise method); forward entry:
age, gender (forced), education, severity, medication upon referral and interaction terms.
[b] One or more co morbid diagnosis on Axis I according to the MINI-Plus
[c] > 29 points on the Beck Depression Inventory (BDI-II).
[d] Patients using an antidepressant upon referral, mostly prescribed by the General Practitioner.
[e] Post Hoc univariable multinomial logistic regression for interaction terms with AD upon referral
* *p* value <.05, ** *p* value <.01, *** *p* value < .001.

## DISCUSSION

Our study is one of the few that identifies specific factors associated with treatment selection for MDD in routine clinical practice in a secondary psychiatric care setting. Treatment selection for MDD seemed mostly in line with clinical guideline recommendations. We found a variation in selected treatments that can be partly explained by severity. We found no evidence for distinct sociodemographic patient profiles to explain this variation, but we found a few factors that might be noteworthy.

First, we found a strong association between treatment selection and AD use upon referral. Patients who already used an AD when referred by their GP were most likely to continue this treatment in secondary mental health care – exclusively or in combination with psychotherapy. Often the same medication was continued, but in almost 40% of the cases it was switched to another AD. In the Netherlands, patients with depression visit their GP first. Patients may be treated with AD by their GP in primary care and are referred to secondary care when they do not respond well to this treatment[7,29] or when psychotherapy is recommended. As there are waiting lists for psychotherapy, an AD can be prescribed to bridge the delay. Often, the

patients referred to secondary mental health care are more severely ill, have comorbidity, do not respond to first-step treatment options and/or are difficult to treat; therefore, they may need pharmacological therapy, which is also suggested in the guidelines. Our results do show that patients with severe depression are more likely to be treated exclusively with AD or combination therapy – compared to psychotherapy only. However, because we assessed the association independent of symptom severity and comorbidity, our finding may also be explained by other factors. It is possible that the medication was continued because it takes up to six weeks for ADs to attain a therapeutic effect, and they had not been prescribed/ used for such a period[7]. Sometimes when patients are already on an AD (prescribed by their GP), doses require adjusting or patients must switch to another AD. Discontinuation of an AD is known to cause withdrawal effects, which in addition to relapses, could influence future effectiveness of ADs in the same patient[30]. Psychiatrists and patients likely hesitate to abruptly discontinue an AD to avoid the adverse effects of medication withdrawal. Our results also show that patients with severe depression, who already use ADs upon referral, are more likely to receive psychotherapy only, compared to combination therapy. Possibly, because these patients have too little response and/or may experience too many side – effects from the AD therapy. Our results indicate that decisions to treat patients with an AD in primary care significantly impact future treatment options and selection in secondary psychiatric care.

Second, we found that men were less likely to receive psychotherapy – a result found in one other study in primary care[31]. Studies that investigated gender differences in relation to offered or received treatments are rare and results are inconclusive[31]. Clinical guidelines do not suggest that pharmacological treatment is especially more effective in men, nor is there unequivocal evidence that men respond better to medication or less to psychotherapy compared to woman[7,32]. Studies suggest that men and women show different symptom profiles and that men often exhibit the same symptoms more severely than women, or seek help later, which might explain why men and women receive different treatments[31,33,34]. In which case being male itself does not necessarily leads to pharmacological treatment, but this treatment selection is indirectly based on severity. Van Noorden et al.[35] found no gender differences in MDD outpatients regarding disease severity based on a clinician-rated severity scale, the Montgomery Asberg Depression Rating Scale (MADRS), and found slightly higher severity ratings for women on a patient-rated severity scale (BDI-II)[35]. Another explanation could be that men preferred being treated with medication and not with psychotherapy. Several studies on patient preferences report that men more readily accept pharmacological therapies and that women showed a preference for psychotherapy[36,37]. However, in a recent review paper on patient preferences for psychological versus pharmacological treatment of depressive and anxiety disorders, the authors found no significant differences in treatment preference between men and women[38]. In this context, Sierra Hernandez et al.[34] suggested that there is a common unfounded (yet persuasive) belief that men dislike psychotherapy. They studied the treatment preferences of male and female psychiatric outpatients and

found that men had either a preference for psychotherapy over pharmacological treatment or for no treatment. Furthermore, men and women's preference patterns did not differ significantly[35]. The assumption of a clinician that men are more responsive to or have a preference for ADs, because they are less 'talkative' than women, may explain our finding.
Patient preferences and personal aspects of patients are considered to be deciding factors in the treatment selection according to clinical guidelines. The patients in our study more often received an AD (exclusively or in combination with psychotherapy). It is possible that the patients in our population preferred to be treated with ADs or that the setting, specialized secondary care, is explaining this finding. However, studies on patient treatment preferences for MDD showed that patients often prefer psychotherapy to pharmacotherapy[38-40]. Several studies in primary and psychiatric care identified several sociodemographic influencing factors associated with patient treatment preferences for depression, such as age, ethnicity, social/cultural background, education and income[34,36,37,41]. If patient preferences played a substantial role, we would expect more patients' sociodemographic characteristics to be significantly associated with treatment selection.
Clinicians' preferences may have directed the decisional process. In routine clinical practice, the clinical judgment of the clinicians determines the main focus of treatment and consequently the treatment options offered. Our results indicate that previous treatments prescribed by the GP and ratings of severity – often made by the psychiatrist – are leading when selecting a treatment in secondary care. Studies on treatment variations in different settings indicated that physicians' preferences and practice styles influenced clinical practice[42] and that physicians often made unilateral decisions that were based on their own preferences rather than patient preferences[43-45]. Furthermore, the importance of clinician factors in treatment decisions was found in studies on treatment decision-making for psychiatric problems – mostly primary care settings[31-46]. In many cases, clinicians' treatment decisions are based on personal life experiences and attitudes rather than professional characteristics[46].

## Strengths and limitations

A strength of our study was that we used data from a naturalistic treatment-seeking population in a secondary mental health care setting. Additionally, our use of ROM data provided us with a variety of sociodemographic and clinical information.
Some limitations. First, variables were dichotomized because of their skewed distributions, which adversely affected statistical power. Second, the study population was relatively small, which explains the wide confidence intervals. We divided the outcome variable, treatment modality, into three treatment groups, which resulted in low frequencies in some cells. Consequently, our sample size was too small to perform subgroup analyses for comorbidity and ethnicity. Third, due to our study design, our findings are not generalizable to a broader population nor is it possible to say anything about causal relationships. Finally, information on patient treatment preferences and data on clinician characteristics were not available.

As a result, it was not possible to investigate associations of these factors with treatment selection, and it is therefore not possible to draw any conclusions about if and how patient preferences, nor how clinicians played a role in the decisional process. At the time of our data collection, Shared Decision Making (SDM) was in its infancy, and to this date, SDM is not yet widely implemented in mental health care[42,47,48]. Future research should explore the specific clinician characteristics that influence treatment selection as well as the role of clinician and patient preferences in treatment decision-making for depressive disorders in secondary care.

## Conclusions

Treatment selection for MDD in secondary care is according clinical guidelines and severity seems a deciding factor. Our study also indicates that when referred patients already use an AD upon referral, their medication is not stopped or changed to non-pharmacological treatment, reflecting the impact of treatment decisions made in primary care. Accessibility and availability of CBT/psychotherapy in primary and secondary care are likely to play a part. Current ((in)ternational) clinical guidelines emphasize combination therapy for severe MDD[49-51], which can only be offered to patients, when psychotherapeutic treatments are accessible, without waiting lists. Furthermore, to include patients' personal characteristics and preferences in the decisional process, as (Dutch) clinical guidelines highly recommend, efforts must be made to make all treatment options equally available to all patients.

## Conflict of interest

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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