

SEX-RELATED DIFFERENCES IN THE PHARMACOLOGICAL TREATMENT OF MAJOR DEPRESSION - ARE WOMEN AND MEN TREATED DIFFERENTLY?

Karin Schwalsberger^{1,2}, Bernd Reininghaus², Alexandra Reiter^{1,2}, Nina Dalkner¹, Eva Fleischmann¹, Frederike Fellendorf¹, Martina Platzer¹ & Eva Z. Reininghaus¹

¹Medical University of Graz, Department of Psychiatry and Psychotherapeutic Medicine, Graz, Austria

²Rehabilitation centre Justus Park Bad Hall, Bad Hall, Austria

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SUMMARY

Background: In the last decade, sex-related medicine has become an increasingly important area of research as insights in this field can improve treatment strategies and recovery. The aim of this study was to investigate sex-related differences in the prescription and kinds of psychopharmacological treatment in individuals with unipolar affective disorder.

Subjects and methods: Data collected on 388 patients attending a psychiatric rehabilitation clinic (194 females, 194 males, mean age 52.3 years, standard deviation 7.8 years), who were matched by age and severity of depression, were analyzed. Depression severity and information on drug type and quantity were assessed at the beginning of the rehabilitation program and compared between women and men.

Results: A significant difference between females and males was found in the frequency of prescribing bupropion (females: 3.61%, males: 12.89%; $p=0.001$) and mirtazapine (females: 5.15%, males: 13.40%; $p=0.005$). In terms of polypharmacy, the results showed that over 53% of the patients were taking two or more psychotropic substances as a long-term therapy and that 34% of them were taking three to five different substances. No sex-related differences were found concerning the number of psychotropic drugs taken by the patients.

Conclusion: The higher frequency of prescriptions for bupropion and mirtazapine in men might be explained by the adverse drug reactions of the drugs (e.g., fewer sexually adverse drug reactions, weight gain) and a known interaction with oral contraception. It remains unclear whether these aspects are taken into consideration for each patient in terms of their special needs and conditions or whether it is a decision based on the patient's sex. Given a similar severity of depression, men and women are prescribed a similar number of psychotropic substances. However, the high number of psychotropic drugs prescribed on average should be noted. Well-trained healthcare professionals should focus on regularly assessing and optimizing treatment regimens.

Key words: polypharmacy - treatment of major depression - sex-related differences

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INTRODUCTION

In the last 20 years, sex-related medicine has become an increasingly important area of research in mental disorders such as major depression (MD). To some extent, sex-related differences can be found in every field of medicine and every disease or illness. They have also been found in psychiatric diseases, with higher prevalence rates of MD presenting in women (Seifert et al. 2021). There is a body of research on sex-related differences in the treatment of MD, with women recording a higher intake rate of psychopharmacological drugs (Boyd et al. 2015, Estancial Fernandes et al. 2018). However, the existing research findings are inconsistent, and there are no evidence-based recommendations for sex-based treatments in MD. MD is a mood disorder that has significant effects on national healthcare systems and society in general. In Austria, there is a high prevalence of MD in the adult population, ranging between 9.9% and 15.6% (Łaszewska et al. 2018). Treatment strategies are occasionally based on trial and error. Importantly, up to 50% of patients do not respond to antidepressant treatment in the first instance, and only

30% remit in total (Rush et al. 2006). This leads to longer disease duration, with all its attendant consequences.

Interestingly, despite the well-known fact that MD is more prevalent in women, there is still no consensus as to whether there are sex-related differences in the effectiveness of antidepressants (Sramek et al. 2016). Some studies have found tricyclic antidepressants to be more effective in men (Glassman et al. 1977, Kornstein et al. 2000), while selective serotonin reuptake inhibitors (SSRIs) and monoamine oxidase (MAO) inhibitors have been found to respond better in women (Kornstein et al. 2000, Young et al. 2009). This effect seems to diminish once women enter menopause, which could imply that SSRIs are especially effective in the presence of estrogen (Kornstein et al. 2000). In contrast, Quitkin and colleagues (2002) analyzed 1746 patients and found no differences in treatment response to tricyclic antidepressants and the SSRI fluoxetine in men and women. Importantly, in this study, women showed a better response to MAO inhibitors than men (Quitkin et al. 2002). Several additional studies and meta-analyses have failed to find any sex-related

differences in terms of drug response (Kokras & Dalla 2017, Sramek et al. 2016, Thase et al. 1997, Wohlfarth et al. 2004).

Differences in antidepressant medication seem to predominantly underline individual biological differences rather than gender-related factors (Parker et al. 2011). Previous research has detected prescription trends that may indicate that men and women with major depressive disorder are treated differently when it comes to psychopharmacotherapy (Estancial Fernandes et al. 2018, Luo et al. 2020). A recent study found that mirtazapine and bupropion were more often prescribed to men. The reasons for these differences, however, are not fully understood (Seifert et al. 2021).

Another important aspect in the context of the effectiveness of psychopharmacotherapy is the number of drugs prescribed. It is well known that for the treatment of physical as well as mental health conditions, monotherapy should be preferred (Boskailo et al. 2017). Polypharmacy is defined as the intake of more than one medication for a patient's medical condition (National Association of State Mental Health Program Directors 2001). It is important to note that the term polypharmacy suggests that the number of drugs prescribed is higher than clinically indicated (Kukreja et al. 2013). Polypharmacy can increase the risk of adverse drug reactions, substance interactions cannot be fully predicted, and health costs are increasing with the number of drugs prescribed (Boskailo et al. 2017). Nevertheless, clinical practice shows a trend towards poly-pharmacological treatment in mentally ill patients (Ćurković et al. 2016, Rittmannsberger 2002). This increasingly common and debatable practice seems to be based less on evidence and more on subjective experience (las Cuevas & Sanz 2004).

The use of psychiatric polypharmacy has increased in the last decades. A detailed review (Rittmannsberger 2002) outlined that monotherapy was used with 47.8% of the psychiatric patients before 1980, decreasing to 31.1 % in 1980-1990, and further decreasing to 19.6% until 2000. The average number of an individual's psychotropic medication in 2000 was estimated at 2.9 and the percentage of psychiatric patients taking three or more psychotropic drugs lay at 49.7 %. More recent data from a sample of adults (n = 6.685) with depressive disorders showed a prevalence of 54.0% of polypharmacy in 2014–2015. The authors stated, that about half of the cases of polypharmacy are justified by augmentation strategies (Rhee & Rosenheck 2019). Psychiatric polypharmacy is not only widespread in adult patients but also in children and especially older patients (Kukreja et al. 2013). A Brazilian study examining 2475 psychiatric patients found that 85.7% of men and 84.9% of women with psychiatric diseases took two or more psychotropic drugs (Costa et al. 2017). The average number of drugs used was 2.98, with no significant sex-related difference.

To date, evidence of sex-related differences in psychiatric polypharmacy were seldomly investigated. Two studies found no sex-related differences concerning single vs. multiple psychotropic drug use (Boskailo et al. 2017, Costa et al. 2017), but showed that associated factors of psychotropic drug intake differ between men and women. Polypharmacy in men was found to be associated with white skin color, lack of occupation, greater number of self-reported health problems and insomnia. In women, multiple psychotropic drug intake was associated with advanced age, higher education and multiple diagnosed chronic diseases (Fernandes et al. 2018). Further findings support the hypothesis that men as well as patients at a young age are more vulnerable to psychiatric polypharmacy (25-45 years) (las Cuevas & Sanz 2004). In older people there is a tendency to polypharmacy which is stronger in females compared to males (Gulla et al. 2016). A recent study found, that women more often than men take four or more drugs (Seifert et al. 2021).

The aim of this study was to explore sex-related differences in the prescription of drugs in MD as well as in polypharmacy in MD. We hypothesized (1) that depressed women differ from depressed men concerning the kind of medication prescribed and (2) that depressed women differ from depressed men concerning the number of drugs prescribed.

SUBJECTS AND METHODS

Study subjects were recruited from a psychiatric rehabilitation clinic in Austria between April 2015 to March 2016. The clinic was specialized in the treatment of psychiatric conditions, such as affective and anxiety disorders and patients were treated there after acute psychiatric hospital care. All inpatients between the ages of 18 and 75 were included in the study if they gave written informed consent. From all study participants (n=697), patients with MD (International classification of Diseases (ICD)-10 diagnoses F33.x and F32.x) were selected. In a next step, women and men were matched based on their scores in the Beck's Depression Inventory version II (BDI-II (Kühner et al. 2007)) and their age. The remaining subjects (n=388) were included in the current analyses. This process assured that potential differences between groups were neither influenced by the severity of depressive symptoms nor age. Additionally, an equal sample size of females and males could be achieved. Socio-demographic data and treatment history were collected by questionnaires which were developed by the study team and sent to the patients prior to admission to the clinic.

Assessment of disease severity and medication

For the diagnose of the severity of depression one self-report questionnaire (Beck Depression Inventory-II

(BDI-II) (Kühner et al. 2007) and one external assessment questionnaire, the Hamilton Depression Scale (HAM-D) (Hamilton 1960) were used. The BDI-II assesses the severity of depressive symptoms on the basis of 21 items and was filled out by the patients at the time of admission to the rehabilitation clinic. The items include questions about mood, sleep, eating habits, sex drive, and suicidal tendencies. The HAM-D is an external assessment to measure the severity of depression based on 21 symptoms or symptom complexes. The HAM-D and the current medication of the patient was assessed during admission by a medical doctor. The BDI-II was completed by the patient in the presence of a clinical psychologist. Categories for medications prescribed were built, including SSRIs, serotonin and norepinephrine reuptake inhibitors (SNRIs), tricyclics, norepinephrine and dopamine reuptake inhibitors (NDRIs), noradrenergic and specific serotonergic antidepressants (NaSSAs), trazodone, atypical antipsychotics, typical antipsychotics, lithium, hypnotics and antiepileptics.

Study design and statistic analysis

Sex-related differences at the time of admission were analyzed in a cross-sectional observational study design. This data collection was part of a large burn-out study (for detailed description of the study see (Reininghaus et al. 2019).

In order to answer the question whether depressed men differ from depressed women in the medical treatment of MD, all relevant variables (*kind of drug prescribed* and *number of drugs prescribed*) were compared between women and men. Chi-square tests were used to calculate differences in prescription of drugs. Because of multiple testing, the false discovery rate was used for alpha-error correction. Sex-related differences in the number of drugs prescribed was calculated with the t-test. Due to the large sample size a normal distribution can be assumed. A Pearson's correlation analysis was performed to investigate an association between number of drugs and age.

Ethics vote

The study protocol was approved by the Ethics-Committee of the Federal State Upper Austria. All procedures were in accordance with the standards of the Declaration of Helsinki in 1995 (as revised in Edinburgh 2000).

RESULTS

Sample description

On the whole, data from 697 patients was collected. 465 patients of the sample were diagnosed with MD and therefore included in the study. After the matching

process, 194 female and 194 male participants remained for further analysis. The mean (M) age of the participants was 52.3 years with a standard deviation (SD) of 7.8 years (females: $M=53.9$; $SD=7.4$ / males: $M=51.8$; $SD=8.1$) and the mean body mass index (BMI) was 27.2 ($SD=5.06$; females: $M=27.0$; $SD=5.6$ / males: $M=27.3$; $SD=4.4$). The occupational fields of the participants were mainly education, police force, army and government service. 32.5% of females and 22.9% of males had graduated from college/university, while 30.7% females and 24.7% males were high school graduates. The residual patients had a lower education level. All patients were diagnosed with MD and did not differ significantly in the HAMD Score (females: $M=11.02$; $SD=6.35$ /males: $M=12.49$; $SD=7.36$, $p=0.074$), nor the BDI - Score (females: $M=20.25$ $SD=10.23$ /males: $M=20.08$; $SD=10.83$; $p=0.770$). The mean scores indicate a mild to moderate severity of depression. A Mann-Whitney-U Test was performed since the variables HAMD score and BDI score were not normally distributed. See table 1 for an overview.

Table 1. Sample description

Demographics of subjects	Females (n=194)	Males (n=194)
Mean Age (SD)	53.9 (7.4)	51.8 (8.1)
BMI (SD)	27.0 (5.6)	27.3 (4.4)
Education		
College/University	32.5%	22.9%
High school	30.7 %	24.7%
Lower education	36.8%	52.4%
Score of Becks Depression Inventory* (SD)	11.02 (6.35)	12.49 (7.36)
Mann-Whitney-U Test result	$z=-1.789$, $p=0.074$	
Sore of Hamilton Depression Scale* (SD)	20.25 (10.23)	20.08 (10.83)
Mann-Whitney-U Test result	$Z=-0.293$, $p=.770$	

n= sample size; SD= Standard Deviation; *Scores indicate a mild to moderate severity of depression

Psychological comorbidities

The most frequent psychological comorbidity for females as well as males were the Z73 diagnoses: problems related to life management difficulty – e.g. burnout (females=22.2%; males=29.4%), followed by diagnoses of F4 - Neurotic, stress-related and somatoform disorders (females=16.5%; males=14.9%), diagnoses of F1 - mental and behavioral disorders due to psychoactive substance use (females=4.6%; males 11.3%) and after that diagnoses of F6 - disorders of adult personality and behavior (females=2.6%; males 4.6%). Sex-related differences were calculated with the χ^2 – test. No significant differences were found, except for the F1 – disorders, where men had a significantly higher value than women (females:4.6%, males: 11.3; $p=0.023$). See table 2 for an overview.

Table 2. Sex-related differences in psychological comorbidity

Diagnose groups ICD-10	Female n=194 % (n)	Male n=194 % (n)	χ^2 - value	p - value
F0 Organic, including symptomatic, mental disorders	0	0.52 (1)	-	-
F1 Mental and behavioral disorders due to psychoactive substance use	4.64 (9)	11.34 (22)	5.050	0.023
F2 Schizophrenia, schizotypal and delusional disorders	0	0	-	-
F3 Mood [affective] disorders (F32/F33 excluded)	0	1.03 (2)	-	-
F4 Neurotic, stress-related and somatoform disorders	16.49 (32)	14.95 (29)	0.175	0.780
F5 Behavioral syndromes associated with physiological disturbances and physical factors	2.58 (5)	1.03 (2)	-	-
F6 Disorders of adult personality and behavior	2.58 (5)	4.64 (9)	1.170	0.415
F7 Mental retardation	0	0	-	-
F8 Disorders of psychological development	0	0	-	-
F9 Behavioral and emotional disorders with onset usually occurring in childhood and adolescence	0	0.52 (1)	-	-
Z73 Problems related to life management difficulty – e.g. burnout	22.16 (43)	29.38 (57)	2.640	0.131

χ^2 Value = Value of Chi-Square Test; n = number of patients

Table 3. Sex-related differences in prescription of medication, descriptive and statistical results

Medication substance	Female (n=194)		Male (n=194)		χ^2 - value	p - value*
	%	n	%	n		
SSRIs	48.45	94	37.63	73	4.64	0.031
SNRIs	23.71	46	24.74	48	0.06	0.813
Tricyclics	4.64	9	2.06	4	1.99	0.158
NDRIs	3.61	7	12.89	25	11.04	0.001*
NaSSAs	5.15	10	13.40	26	7.84	0.005*
Trazodone	41.75	81	35.05	68	1.84	0.175
Atypical neuroleptics	11.86	23	12.37	24	1.02	0.600
Typical neuroleptics	7.73	15	5.15	10	1.07	0.301
Lithium	0.00	0	0.52	1	1.00	0.317
Hypnotics	7.73	15	8.25	16	0.04	0.851
Antiepileptics	6.70	13	6.19	12	0.04	0.836

* = significant using a false discovery rate of 0.05; χ^2 value= value of Chi-Square test; n = number of patients;

SSRIs = selective serotonin reuptake inhibitors; SNRIs = serotonin and norepinephrine reuptake inhibitors;

NDRIs = norepinephrine and dopamine reuptake inhibitors; NaSSAs= noradrenergic and specific serotonergic antidepressants

Table 4. Sex-related differences in number of different psychotropic drugs in percentage

Number of drugs	All patients% (n=388)	Female % (n=194)	Male % (n=194)
0	15.5	15.5	15.5
1	32.0	32.0	32.0
2	34.5	33.5	35.6
3	13.9	14.4	13.4
4	3.1	3.1	3.1
5	1.0	1.5	0.5

% = percent of females/males; n = number of patients

Medication kind of drugs prescribed

Sex-related differences were found in the frequency of the prescription of the NDRI/Bupropion (females: 3.61%, males: 12.89%; $p=0.001$) and the NaSSA/Mirtazapine (females: 5.15%, males: 13.40%; $p=0.005$). Both

drugs were found to be prescribed to men significantly more frequently than to women. For descriptive and statistical results see table 3. No significant differences between females and males were found concerning the prescriptions of the following substances: SSRIs, SNRIs, tricyclics, trazodone, atypical antipsychotics, typical antipsychotics, lithium, hypnotics and antiepileptics see table 3.

Number of drugs prescribed

Nearly half of the patients (48.4%) took two or three substances. There was no significant difference in the number of drugs per person found between females ($M=1.62$; $SD=1.10$) and males ($M=1.58$; $SD=1.04$; $t(386)=0.38$; $p=0.704$). Of the female patients 52.5% and of the male patients 52.6% were taking two or more psychotropic drugs. The sex-related differences in the number of different psychotropic drugs in percentage can be found in table 4. There was no correlation found

between age and number of drugs taken ($r=-0.057$, $p=0.262$). When calculated separately, there was no significant differences found in men ($r=0.010$, $p=0.895$), however a tendency was found in women ($r=-0.129$, $p=0.073$).

DISCUSSION

The aim of this study was to investigate sex-related differences in the pharmacological treatment of, namely the kind and number of psychotropic drugs prescribed for MD to in-patients of a psychiatric rehabilitation clinic in Austria. Sex-related differences, concerning the frequency of certain drug prescriptions were identified given a similar severity of depression and age between women and men. Male patients were taking mirtazapine almost three times and bupropion almost four times more often than female patients. The number of psychotropic drugs was similar in women and men, with the average patient taking 1.5 drugs.

Mirtazapine is a NaSSA, which is predominantly used in the treatment of MD. The efficacy of mirtazapine is equivalent to tricyclic antidepressants. Importantly, the increase of bodyweight and appetite is precipitated more likely by mirtazapine than by comparable antidepressants (Holm & Markham 1999). The association of mirtazapine and sex has not been investigated thoroughly. Two studies investigated sex differences in the context of mirtazapine treatment: The first study found that young male patients treated with mirtazapine showed an approximately 50 percent higher plasma level than female patients and older males (Timmer et al. 2000). Secondly, a study conducted by Borbobia and colleagues (Borobia et al. 2009) suggested that women had a faster mirtazapine metabolism than men due to differences in the genotype of the enzyme cytochrome P450 (CYP) 2D6. The differences found in both studies were marginal and did not justify an adjustment of the mirtazapine dose (Timmer et al. 2000). Nevertheless, a higher plasma level might imply a better antidepressive response and could lead to a higher frequency of prescription in men, supporting our results. In line with this, recent research on rats also showed that the antidepressant effect of mirtazapine appears to be stronger in male rats (Álvarez & Fernández-Guasti 2020). Among different drugs influencing the enzymes responsible for eliminating mirtazapine (Zhou 2009), oral contraceptives should be highlighted (Hägg et al. 2001), as they could be responsible for sex-related prescription differences. In addition to CYP2D6, drugs inhibiting or stimulating the enzymes CYP1A2 and CYP3A4 are known to influence mirtazapine (Anttila & Leinonen 2001) as for example oral contraceptives (Granfors et al. 2005, Zhang et al. 2018). Furthermore, mirtazapine is known to cause fewer sexual adverse drug reactions than serotonergic antidepressants as well (Bet et al. 2013, Rothmore 2020). The additional use of mirta-

zapine is even recognized as an option to treat SSRI-induced sexual dysfunction (Atmaca et al. 2011). One study suggested that men may be at higher risk of experiencing sexual dysfunction (Preeti et al. 2018). These facts, as well as the appetite and weight increasing effect in many patients might be reasons why mirtazapine is not as frequently prescribed in women as in men. Due to sex specific stereotypes and culturally influenced beauty standards, women might feel an elevated need to refrain from mirtazapine, instead preferring antidepressants which are less likely to lead to an increased bodyweight or even lower appetite. However, other psychotropic drugs such as second-generation antipsychotic drugs or lithium also have a high risk of causing weight gain (McKnight et al. 2012, Usher et al. 2013), and this study failed to find a difference in the prescription of lithium between men and women. This could be explained by the results of a current meta-analysis by Gomes-da-Costa and colleagues (2021) that found lithium to be associated with weight gain, however, only in the short term. There were no significant differences to placebo groups when comparing long-term changes in weight. Bupropion is an antidepressant and smoking cessation drug, inhibiting the reuptake of both dopamine and norepinephrine (NDRI) and acting as an antagonist at nicotinic acetylcholine receptors (Dwoskin et al. 2006). This drug is a substrate of the enzyme CYP2B6 (Flockhart 2007), which is induced by estrogen (Higashi et al. 2007). This interaction might explain prescription differences, as it could lead to unexpected treatment outcomes in women taking contraceptives. Although it has been suggested that the efficacy of bupropion does not differ between the different sexes (Papakostas et al. 2007), another study showed that women might have both a higher maximum plasma concentration and higher elimination half-life than men (Stewart et al. 2001). Additionally, (Barrett et al. 2017) found that women might be more susceptible to the dopaminergic reward-enhancing effects of bupropion, making them more vulnerable for medication abuse (Cummings et al. 2014). Furthermore, the sexual adverse drug reactions of bupropion should be considered: In comparison to other antidepressants, bupropion induces increased libido more frequently (Vanderkooy et al. 2002) and shows the occurrence of less adverse sexual adverse drug reactions (Modell et al. 1997). Interestingly, lower plasma levels of bupropion have been found in smokers than in non-smokers (Scherf-Clavel et al. 2019). This should be taken into consideration, as the percentage of men consuming tobacco is higher than that of women among individuals with MD (Li et al. 2017). There might be sex-related differences in medication adherence when treating MD, however, the nature of these differences remains unclear. As stated in several reviews and studies, the results range from there being no sex-related differences (Jawad et al. 2018), contradicting findings (Levin et al.

2016) and to both male (Corréard et al. 2017) and female (Bates et al. 2010) sex being related to low adherence. Regrettably, literature on adherence in MD with regard to specific medication is scarce. These results show the importance of investigating the interactions of antidepressants and other drugs, especially in relation to CYP enzymes.

In general, mirtazapine tends to be prescribed for patients with insomnia, since its effect on sleep quality is well established (Winokur et al. 2003, Savarese et al. 2015) and bupropion tends to be prescribed for patients with fatigue (Rujescu et al. 2020). Thus, sex differences in symptoms accompanying MD should be investigated. This study did not investigate sex differences in specific symptoms of depression, however multiple studies exploring this topic failed to find different somatic symptom patterns in depressed female vs. male patients (Parker & Brotchie 2010). Some studies found that sleep problems (Frank et al. 1988, Kornstein et al. 2000, Leibenluft et al. 1995, Marcus et al. 2005), changes in eating habits and weight (Frank et al. 1988, Leibenluft et al. 1995, Wilhelm & Parker 1989) as well as anxiety (Kornstein et al. 2000, Marcus et al. 2005, Wilhelm & Parker 1989) and somatization (Frank et al. 1988, Kornstein et al. 2000, Marcus et al. 2005) are more common in females. Thus, the higher prescription rate of mirtazapine and bupropion in men cannot be explained by differences in symptoms. Further research is needed to investigate this topic.

In contrast to our expectations, the number of psychotropic medications was similar in women and men, with the average patient taking 1.5 drugs. We did not find any effect of age concerning the number of drugs prescribed, probably due to a very homogeneous sample. The majority of the sample were between the age of 40 and 60. However there was a statistically trend, suggesting, that older women have a higher likelihood of polypharmacy. The study results suggest that, given a similar severity of depression, men and women are prescribed a similar number of psychotropic substances, which might change in older age. Still, compared with previous studies, the number and percentages were lower than expected (Carmona-Huerta et al. 2019, Costa et al. 2017, Rhee & Rosenheck 2019, Rittmannsberger 2002). This could indicate that the tendency towards polypharmacy in Austria is not as severe yet. Furthermore, the severity of depression of the study subjects was ranging from mild to moderate. The comparative studies (Boyd et al. 2015, Estancial Fernandes et al. 2018, Seifert et al. 2021) investigated larger population samples of depressed patients, with a broader spectrum of severity including highly severe cases as well. Hence, the results of this study could serve as a more accurate assessment, comparing women and men with a similar severity of depression. This was not the case in any other study. Research shows, that women tend to seek help earlier and more frequently than men (Kuehner 2003, 2017) and men tend to self-

medicated with illegal drugs and alcohol instead of consulting a professional (Brownhill et al. 2005). Furthermore, if in a professional setting, women more willingly give information about their emotional state compared to men (Kilmartin 2005). Thus, the number of undiagnosed men with MD might be higher than in women (Brownhill et al. 2005). Therefore, simply comparing samples of depressed males and females without a standardized diagnosis as well as a matching of severity and age could result in a biased outcome. Future research should focus on researching sex and gender differences across different levels of severity as well as in severity-matched samples.

Nonetheless, trend toward polypharmacy is alarming. Clinical outcomes and quality of care of affected patients are uncertain and come with an increased risk of drug-drug interaction (Mojtabai & Olfson 2010). A strategy to prevent as well as change treatment regimens, that are neither helpful nor healthy, should therefore be implemented. Psychopharmacological drugs are prescribed not only by psychiatrists but often also by general practitioners (Gudd et al. 2020), especially with regard to the elderly, who are at greater risk for receiving potentially inadequate medication (Hefner et al. 2021). Additionally, information about the current drug intake of a patient is not always accurate and complete. In many cases, patients are simply asked what medication they are taking and they do not know exactly. This can lead to suboptimal medical treatment regimens (Ekedahl et al. 2011, Fourrier-Réglat et al. 2010, Grimaldi-Bensouda et al. 2012).

Better psychopharmacological training for doctors prescribing these drugs regularly, is needed. Furthermore, the problem of polypharmacy should be brought to awareness to medical health care professionals. Some sort of monitoring and controlling of the drug prescriptions for patients with mental disorders through a psychiatrist/or similar qualified professional is required to optimize treatment and recovery of patients with MD. Electronical storage of Information about current medication, as well as guidelines to assist in the decision process could be helpful to realize such goals.

Strengths and novelty

To the knowledge of the author, a similar study, which compared the treatment regimens of female and male patients with MD in a matched, case-control study design has not been performed before. No differences in age or severity of depressive symptomatology could be found, which improves the validity of the comparison. Moreover, the psychological comorbidities of the female and male study subjects were very similar which further improves the validity of the results. This study can provide an insight in the status quo of treatment regimens in Austria and demonstrate areas of improvement. In order to enable individual therapy, which improves treatment success immensely, studies like this are crucial.

Limitations

This study had a number of limitations, which need to be outlined. Firstly, the study population was not representative for the whole adult population, 94% were over forty years old. Therefore, the results should be interpreted predominantly for this age group. Secondly, there was a rather high homogeneity of the study population. Due to the local health insurance politics only employees of the state were admitted to this rehabilitation clinic. The homogeneity of the study population guarantees a higher validity of the data for this population because of a smaller error chance. On the other hand, it loses some of its representability for the whole population of Austria. Thirdly, information about drugs dosages was not obtained. There are still a considerable number of unanswered questions, concerning sex-related differences in the treatment of MD. Further investigations are needed to fully understand these differences.

CONCLUSION

All in all, depressed females and males showed more similarities than differences concerning the treatment of MD. Nevertheless, prescription differences were found in the prescription of Bupropion and Mirtazapine. These differences might be explained by the adverse drug reactions of the drugs (weight gain, less sexual adverse drug reactions). Additionally, the intake of oral contraception is known to have an interaction with both substances. It remains unclear if these aspects are taken into consideration for each patient with their special needs and conditions. Further investigation is needed to determine if preconceptions related to the patient's sex affect the selection of the prescript drug, rather than scientific knowledge and medical guidelines.

Given a similar severity of depression, men and women are prescribed a similar number of psychotropic substances, however, the high number of psychotropic drugs prescribed on average should be noted. Ideally, the treatment regimen should include prescribing as many substances as necessary and as little as possible. This does not seem to be the case right now, neither in women nor men. Health care professionals should focus on assessing and optimizing treatment regimens regularly. This should be performed by experts in the field of mental disorders and psychotropic drugs. Some kind of electronical storage of medication information could prove to be helpful to realize these goals.

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Contribution of individual authors:

Karin Schwalsberger: idea, concept and design of the article, writing of manuscript, continuous reviewing and approval of the final version.

Bernd Reininghaus: planning of study design, continuous reviewing and approval of the final version.

Alexandra Reiter: data collection, continuous reviewing and approval of the final version.

Nina Dalkner: literature research, advising the study design, continuous reviewing and approval of the final version.

Eva Fleischmann: literature research, reviewing and approval of the final version.

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Correspondence:

Karin Schwalsberger, MA
Medical University of Graz, Department of Psychiatry and Psychotherapeutic Medicine
Auenbruggerplatz 31, 8036 Graz, Austria
E-mail: karin.schwalsberger@stud.medunigraz.at