

A ONE-DAY CROSS-SECTIONAL STUDY OF ANTIDEPRESSANTS PRESCRIPTION PATTERNS IN PUBLIC MENTAL HEALTH SERVICES: CLINICAL GUIDELINES VS REAL CLINICAL PRACTICE IN RUSSIA

Alexey Pavlichenko¹, Daria Smirnova^{2,3}, Daria Susloparova¹, Timur Syunyakov^{1,4} & George Kostyuk¹

¹Mental-health Clinic № 1 named after N.A. Alexeev, Moscow, Russia

²International Centre for Education and Research in Neuropsychiatry, Samara State Medical University, Samara, Russia

³Department of Psychiatry, Narcology, Psychotherapy and Clinical Psychology, Samara State Medical University, Samara, Russia

⁴Zakusov Institute of Pharmacology, Moscow, Russia

SUMMARY

Background: Antidepressants (AD) are widely used in the treatment of mood disorders and administered for mental disorders coded across other diagnostic categories. However, inaccuracy in AD prescription may lead to unresponsive cases, decreased compliance, and treatment discontinuation. Following a one-way cross-sectional study design, we aimed to analyze the AD prescription patterns in routine clinical practice in Moscow, as compared to clinical guidelines, taking the capital as representative of the Russian national experience.

Subjects and methods: We studied 537 medical case records of inpatients and outpatients who had received treatments on an arbitrarily chosen day, focusing on classes, doses, drug combinations, and switching patterns for AD prescription. All statistical calculations (descriptive statistics, between group comparisons using Fisher exact, binomial and Pearson chi-square tests, significant at two-tailed $p < 0.05$) were performed with the IBM SPSS 27.

Results: 15% of inpatients and 52% of outpatients with mental disorders received ADs. ADs were prescribed for major depressive disorder and other diagnoses, including the majority of schizophrenia spectrum disorders and non-organic conditions. Selective serotonin reuptake inhibitors, particularly fluvoxamine, were used most often for outpatient and inpatient settings, but at lower average dose rather than recommended, while tricyclic ADs were more likely to be correctly administered for severe depression. ADs were often prescribed within combined treatment rather than monotherapy, but clinical recommendations were not strictly followed in relation to the drug choice, combination with antipsychotic agents and switching strategies.

Conclusions: The clinical reality of AD prescriptions in the studied psychiatric setting differed from the clinical guidelines, insofar as the choice of AD medication did not always follow evidence-based recommendations. Choice and dosage of ADs should properly follow duration and severity of the illness, and the clinical profile of disorders.

Key words: antidepressants - clinical guidelines - depression - monotherapy - prescription patterns

Abbreviations: AD - antidepressant; AD+ - antidepressants were prescribed; AD- - antidepressants were not prescribed; AGO - agomelatine; MAO - monoamine oxidase inhibitors; MDD - major depressive disorder; n/a - data non available; SD - standard deviation; SNRI - serotonin norepinephrine reuptake inhibitors; SSRI - selective serotonin reuptake inhibitors; TAU - treatment as usual; TCA - tricyclic antidepressants; VOR - Vortioxetine

* * * * *

INTRODUCTION

Widespread use of antidepressant (AD) medications in general medical practice and psychiatric services raises a variety of concerns among professionals and the patient community (Kendrick et al. 2020). Notably, the prescription rate of ADs has been increasing in recent decades due to a greater proportion of patients with major depressive disorder (MDD) receiving long-term treatment and the higher frequency of prescriptions at first contact; general practitioners do not always take into account the severity of the state, resulting in prescription of inadequate doses of ADs (Bosman et al. 2016, Kendrick et al. 2015, Moore et al. 2009, National Centre of Health Statistics 2011, Spies et al. 2004). Furthermore, these trends lead to the increased number

of patients' self-reports on negative side-effects or ineffectiveness of ADs, changing attitudes towards psychopharmacotherapy, and declines in patient compliance, all of which cause barriers for treatment continuation and optimization (Agius & Bonnici 2017, Van Geffen et al. 2007). This state of affairs emphasizes the importance of adopting strategies aiming to improve the accuracy in prescription of ADs in general practice (e.g., REDUCE program in the UK) (Kendrick 2021).

Among the numerous approved ADs, the particular choice for treatment of MDD is generally based on (i) symptomatology profile of the subject, (ii) medical comorbidities, (iii) previous efficacy, (iv) the profile of available compounds, (v) tolerability profile, (vi) individual preferences, and (vii) family history (Fabbri et al. 2018). A recent meta-analysis of AD studies by

Cipriani et al. (2018) demonstrated that (i) all approved agents were more effective than placebo, (ii) the drop-out rate was lower for agomelatine and fluoxetine, (iii) agomelatine, amitriptyline, escitalopram, mirtazapine, paroxetine, venlafaxine, and vortioxetine were more effective than other antidepressant agents, and (iv) patients had greater tolerance for agomelatine, citalopram, escitalopram, fluoxetine, sertraline, and vortioxetine. An international study on AD prescription patterns showed that (i) selective serotonin reuptake inhibitors (SSRIs) were the most frequently prescribed subclass of drugs across all institutions, (ii) ADs were prescribed for states other than MDD in 40% of cases, (iii) the newer ADs (e.g., vortioxetine) were prescribed more often, while (iv) the prescription of tricyclic agents has declined significantly (Chee et al. 2015). Among Asian countries, escitalopram is the AD of choice in India and Korea, as compared to fluoxetine in Indonesia and Thailand, fluvoxamine in Malaysia and Singapore, mirtazapine in Japan, sertraline in China, and trazadone in Taiwan (Chee et al. 2015). These patterns may have arisen in relation to pharmacogenetic differences in drug metabolism (Jessel et al. 2020) or indirect influence of pharmaceutical industry. On the other hand, the experience of the University Clinic of Belgrade showed that prescription patterns varied significantly according to the criterion of severity of depression; whereas tricyclic drugs were the first choice for severe depression with psychotic features, SSRIs were used for moderate depression. Furthermore, younger psychiatrists prescribed newer ADs (e.g., venlafaxine, tianeptine, mirtazapine, bupropion, trazadone) more often than did their elder colleagues (Marić et al. 2012).

According to the current Russian and International evidence-based clinical guidelines, (i) antidepressants represent the first-line choice for the treatment of moderate and severe depression, (ii) in particular, amitriptyline and clomipramine are more effective than SSRIs for inpatients, (iii) escitalopram (20 mg) serves as the first choice for severe cases, (iv) venlafaxine, escitalopram, and sertraline are more effective than other SSRIs, (v) appropriate combinations of antidepressants, mood-stabilizers and antipsychotic drugs should be prescribed as recommended in clinical guidelines (e.g. quetiapine (A-evidence level), aripiprazole (A) or lithium (A) as first-line treatments; risperidone (A), olanzapine (B), or mirtazapine (B) as second-line treatments) (Mosolov et al. 2016, Cleare et al. 2015). ADs are also used in therapy of bipolar disorder (Goodwin et al. 2016), schizophrenia (Gregory et al. 2017, Whitehead et al. 2003), and personality disorders (Lieb et al. 2010, Timäus et al. 2019), equally in outpatient and inpatient healthcare settings. There are a number of reports on the off-label prescriptions of antidepressants (Skånland & Ciešlar-Pobuda 2019, Wong et al. 2017).

Bauer et al. (2009) demonstrated that an algorithm-based treatment approach leads to better outcomes and less frequent switching of antidepressants, as compared to treatment as usual (TAU) strategies in depression. The primary factors for consideration in the algorithm include duration, severity, and symptom profile of depression (Cleare et al. 2015). "Despite the availability and distribution of a variety of expert-based guidelines, only a fraction of patients are actually treated according to guidelines" (Kraus et al. 2019).

Following a one-way cross-sectional study design, we aimed to analyze the AD treatment strategies in routine clinical practice in Moscow, focusing on the similarities and differences in the ADs' use, and their application in Russian outpatients vs inpatients with mental disorders. Taking into account the frequent deviations from clinical guidelines as presented across the professional literature, we also aimed to compare the indications of ADs and switching strategies in real clinical practice as compared to clinical guidelines, taking Moscow as representative of the Russian national experience.

SUBJECTS AND METHODS

The survey settings included outpatient and inpatient facilities of the Mental-health Clinic №1 named after N.A. Alexeev and day hospital of the Psychoneurological Dispensary №13 in Moscow, Russia. The Ethics committee of the Mental Health Clinic №1 named after N.A. Alexeev granted approval of the study protocol, which was in accordance with the Helsinki declaration. We studied all medical case records of inpatients and outpatients who had received or attended treatments on an arbitrarily chosen day (20.12.2019; n=537, Table 1). The study sample included medical records with diagnoses grouped according to the following ICD-10 categories: F01-09 (n=172, 32.03%), F10-19 (n=1, 0.18%), F20-29 (n=298, 55.49%), F30-39 (n=32, 5.96%), F40-48 (n=8, 1.49%), F50-59 (n=15, 2.79%), F60-69 (n=2, 0.37%), F70-79 (n=8, 1.49%). Psychiatrists (19 males, 38 females, Median age = 39.4 y.o., Min=28, Max=72) who prescribed the ADs had on average 12.6 years of clinical practice (Min=1, Max=45). The list of administered ADs is presented in Table 2. All statistical calculations were performed with the IBM SPSS Statistics Professional 27 version (IBM Corp. 2020). We applied a descriptive analysis to all the data; between group comparisons (when applicable) were performed using Fisher exact test, binominal/proportion test, Pearson chi-square test and statistical significance was considered at two-tailed $p < 0.05$.

RESULTS

Analysis of case records from 537 patients who were treated on the day of investigation, of whom 102 (18.99%) were prescribed ADs. Across this one-day

Table 1. The antidepressant prescriptions according to the ICD-10 diagnostic categories among inpatients and outpatients on the day of investigation

ICD-10 Categories	Antidepressants' prescription				Total	Total n=537
	Inpatient		Outpatient			
	Yes	No	Yes	No	Yes	No
F01 to F09: Mental disorders due to known physiological conditions, including	19 (3.54%)	145 (27.00%)	2 (0.37%)	6 (1.12%)	21 (3.91%)	151 (28.12%)
F01-03. Dementia	3 (0.56%)	80 (14.90%)	n/a	n/a	3 (0.56%)	80 (14.90%)
F04-09. Non-dementia	16 (2.98%)	65 (12.10%)	2 (0.37%)	6 (1.12%)	18 (3.35%)	71 (13.22%)
F10 to F19: Mental and behavioral disorders due to psychoactive substance use	0 (0%)	1 (0.19%)	n/a	n/a	0 (0%)	1 (0.19%)
F20 to F29: Schizophrenia, schizotypal, delusional, and other non-mood psychotic disorders, including	21 (3.91%)	243 (45.25%)	18 (3.35%)	16 (2.98%)	39 (7.26%)	259 (48.23%)
F20, 22-29. Schizophrenia and psychotic disorders	13 (2.42%)	235 (43.76%)	14 (2.61%)	16 (2.98%)	27 (5.03%)	251 (46.74%)
F21. Schizotypal disorder	8 (1.49%)	8 (1.49%)	4 (0.74%)	0 (0%)	12 (2.23%)	8 (0.74%)
F30 to F39: Mood (affective) disorders, including	19 (3.54%)	6 (1.12%)	7 (1.30%)	0 (0%)	26 (4.84%)	6 (1.12%)
F31. Bipolar disorder	3 (0.56%)	4 (0.74%)	n/a	n/a	3 (0.56%)	4 (0.74%)
F32-33. Major depressive disorder	16 (2.98%)	2 (0.37%)	7 (1.30%)	0 (0%)	23 (4.28%)	2 (0.37%)
F40 to F48: Anxiety, dissociative, stress-related, somatoform and other nonpsychotic mental disorders, including	4 (0.74%)	4 (0.74%)	n/a	n/a	4 (0.74%)	4 (0.74%)
F40-41. Anxiety disorders	1 (0.19%)	0 (0%)	n/a	n/a	1 (0.19%)	0 (0%)
F43. Reaction to severe stress, and adjustment disorders	3 (0.56%)	4 (0.74%)	n/a	n/a	3 (0.56%)	4 (0.74%)
F50 to F59: Behavioral syndromes associated with physiological disturbances and physical factors	10 (1.86%)	5 (0.93%)	n/a	n/a	10 (1.86%)	5 (0.93%)
F60 to F69: Disorders of adult personality and behavior	n/a	n/a	0 (0%)	2 (0.37%)	0 (0%)	2 (0.37%)
F70 to F79: Intellectual disabilities	1 (0.19%)	5 (0.93%)	1 (0.19%)	1 (0.19%)	2 (0.37%)	6 (1.12%)
Comorbid mental disorders	0 (0%)	1 (0.19%)	n/a	n/a	0 (0%)	1 (0.19%)
Total	74 (13.78%)	410 (76.35%)	28 (5.21%)	25 (4.66%)	102 (18.99%)	435 (81.01%)
						537 (100%)

Table 2. The variety of antidepressant prescriptions in the inpatient vs outpatient services and the cases of switching on the day of investigation

Antidepressant (AD)	Prescription		Prescribed dose (mg)				Prescribed for MDD cases by the criterion of depression severity				Cases of switching Switched/Administered (% share)
	Inpatient	Outpatient	Total*	Mean	-95%CI	95%CI	Mild	Moderate	Severe	Total	
Agomelatine	8 (6.67%)	1 (0.83%)	9 (7.50%)	28.13	-3.74	59.99	0 (0%)	1 (4.35%)	0 (0%)	1 (4.35%)	2/9 (22.22%)
Amitriptyline	5 (4.16%)	3 (2.50%)	8 (6.67%)	68.57	17.13	34.51	2 (8.70%)	0 (0%)	2 (8.70%)	4 (17.39%)	1/7 (14.29%)
Clomipramine	9 (7.50%)	5 (4.17%)	14 (11.67%)	66.36	39.19	93.54	2 (8.70%)	1 (4.35%)	1 (4.35%)	4 (17.39%)	4/11 (36.36%)
Duloxetine	2 (1.67%)	0 (0%)	2 (1.67%)	90.00	26.27	153.73	0 (0%)	1 (4.35%)	0 (0%)	4 (17.39%)	1/2 (50%)
Escitalopram	2 (1.67%)	2 (1.67%)	4 (3.33%)	13.33	-38.70	65.37	1 (4.35%)	0 (0%)	0 (0%)	4 (17.39%)	0/4 (0%)
Fluoxetine	5 (4.17%)	1 (0.83%)	6 (5.00%)	40.00	-0.31	80.31	1 (4.35%)	0 (0%)	0 (0%)	1 (4.35%)	0/6 (0%)
Fluvoxamine	25 (20.83%)	9 (7.50%)	34 (28.33%)	105.88	90.43	121.34	6 (26.09%)	0 (0%)	0 (0%)	6 (26.09%)	4/34 (11.76%)
Imipramine	0 (0%)	2 (1.67%)	2 (1.67%)	150.00	86.27	213.73	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1/2 (50%)
Mianserine	1 (0.83%)	0 (0%)	1 (0.83%)	30.00	-60.13	120.13	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0/1 (0%)
Milnacipran	3 (2.50%)	0 (0%)	3 (2.50%)	50.00	-40.13	140.13	1 (4.35%)	0 (0%)	0 (0%)	1 (4.35%)	0/3 (0%)
Mirtazapine	1 (0.83%)	0 (0%)	1 (0.83%)	30.00	-60.13	120.13	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0/1 (0%)
Paroxetine	4 (3.33%)	3 (2.50%)	7 (5.83%)	31.67	-5.13	68.46	1 (4.35%)	1 (4.35%)	0 (0%)	2 (8.70%)	0/7 (0%)
Pirlindole	2 (1.67%)	2 (1.67%)	4 (3.33%)	93.75	48.69	138.81	0 (0%)	1 (4.35%)	0 (0%)	1 (4.35%)	0/4 (0%)
Sertraline	4 (3.33%)	0 (0%)	4 (3.33%)	108.33	56.30	160.37	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1/4 (25%)
Trazodone	4 (3.33%)	1 (0.83%)	5 (4.17%)	50.00	-40.13	140.13	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0/5 (0%)
Venlafaxine	14 (11.67%)	1 (0.83%)	15 (12.50%)	108.75	80.25	137.25	0 (0%)	0 (0%)	1 (4.35%)	1 (4.35%)	0/15 (0%)
Vortioxetine	0 (0%)	1 (0.83%)	1 (0.83%)	20.00	-70.13	110.13	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1/1 (100%)
Total*	89 (74.17%)	31 (25.83%)	120 (100%)	-	-	-	14 (60.87%)	5 (21.74%)	4 (17.39%)	23 (100%)	15/102 (14.71%)

* Number of the antidepressants prescriptions, including cases of combined treatments and drugs switching

extracted sample, outpatients (AD+: n=28, 52.83%; AD-: n=25, 47.17%) were treated using ADs significantly more often than inpatients (AD+: n=74, 15.29%; AD-: n=410, 84.71%), $\chi^2(1, N=537) = 43.75, p < 0.001$, Cohen's $w = 0.285$. The majority of ADs prescriptions were related to the ICD-10 diagnoses of (i) F2 schizophrenia spectrum disorders, and (ii) F3 mood disorders, as well as (iii) F0 organic mental disorders, for both inpatients and outpatients (see Table 1 for details). In particular, ADs were prescribed proportionally more often for outpatients (AD+: n=14, 46.75%; AD-: n=16, 53.33%) rather than inpatients (AD+: n=13, 5.24%; AD-: n=235, 94.76%) with schizophrenia and psychotic disorders ($\chi^2(1, N=537) = 52.40, p < 0.001$, Cohen's $w = 0.312$), while other comparisons by ICD-10 categories for inpatients vs outpatients were not significant.

Among ADs prescriptions of the SSRI class, in particular fluvoxamine prevailed both among inpatients and outpatients (see Table 2 for details). The average doses and CI of ADs used are presented in Table 2. Patients were prescribed with ADs of the following pharmacological classes (Spearman ranking is n/a due to small sample size): 1) SSRI (n=52, 50.98%), 2) tricyclic antidepressants (TCA: n=20, 19.61%), 3) sero-

tonin-norepinephrine reuptake inhibitors (SNRI; n=13, 12.75%), 4) agomelatine (AGO, n=8, 7.84%), 5) monoamine oxidase inhibitors (MAO; n=4, 3.92%), 6) new/vortioxetine (VOR, n=1, 0.98%). The binominal test indicated that in the whole study sample, ADs monotherapy (n=11, 10.78%) was observed significantly less often than as compared to combination treatment of ADs and other medication classes (e.g., antipsychotic agents in cases of schizophrenia spectrum disorders) (n=91, 89.22%) (hypothesis 0.50, N=102, $p < 0.001$). Fisher exact test did not show significant differences in relation to monotherapy versus combined treatment approaches for ADs use in the inpatient department (monotherapy: n=4, 3.92%; combined treatment: n=70, 68.63%) as compared to the outpatient unit (monotherapy: n=0, 0%; combined treatment: 28, 27.45%), $p = 0.271$. In cases of schizophrenia spectrum disorders, fluvoxamine was also the drug which was combined with antipsychotics in the majority of 36.59% (30 out of 82) cases of combined ADs therapy with antipsychotics (such as quetiapine (n=7), olanzapine (n=6) and risperidone (n=5); the same trend was observed for all ADs' combinations with antipsychotic medications, (16 cases of quetiapine, 15 of olanzapine and 12 of risperidone),

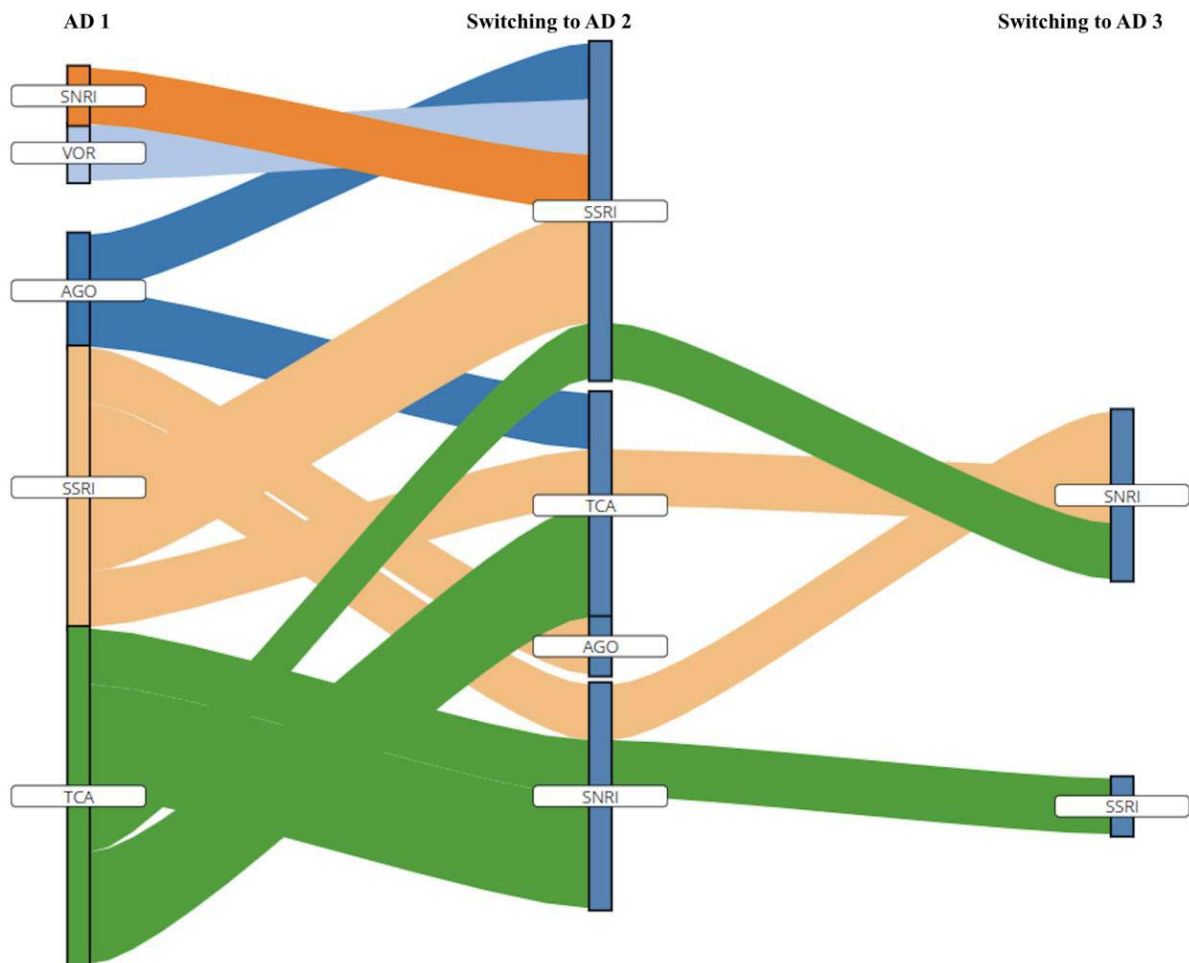


Figure 1. The patterns of antidepressants switching strategies as presented on the day of investigation

as compared to other ADs. Fluvoxamine was also prescribed at lower than recommended doses (the average doses of prescribed ADs are presented in Table 2). As for the criterion of severity of MDD, fluvoxamine was prescribed for mild depression while amitriptyline both for mild and severe depression. Different classes of ADs have been used in the treatment of mild to moderate depression, but only TCA have been prescribed for severe depression. (see Table 2 for details).

According to the binominal test, continuation of AD treatment ($n=87$, 85.29%), which had been prescribed since the beginning of treatment, was observed significantly more often than switching the AD ($n=15$, 14.71%), (hypothesis 0.50, $N=102$, $p<0.001$). The same pattern characterized the inpatient study samples (continuation: $n=12$, 16.22%; switching: $n=62$, 71.26%) and outpatient (continuation: $n=3$, 10.71%; switching: $n=25$, 89.29%; $p=0.755$). The details of switching patterns as presented with the pharmaceutical names of ADs are described in Table 2, with AD class presented in Figure 1.

DISCUSSION

A one-day cross-sectional study in Russian mental health services demonstrated that approximately 19% of patients with mental disorders in the whole study sample, including more than half of outpatients (52.83%, 28 out of 53), received ADs. This result matches well with international outpatient practice (e.g., 52.00% of outpatients with mental disorders use ADs, Tokumitsu et al. 2020). Besides the indications for patients with diagnosis of mood disorders (F3), the majority of ADs prescriptions were registered in patients with diagnosis of schizophrenia spectrum disorders (F2) and organic mental disorders (F0), in particular, significantly more often in outpatients rather than inpatients with F2 diagnoses. These findings also resemble those obtained in an international study showing that ADs were prescribed for states other than MDD in 40% of cases (Chee et al. 2015). However, we note that this pattern of AD prescription in our study sample was related to the way in which Russian clinicians coded mental disorders, often failing to code depression as a secondary or comorbid state, despite describing the presence of a clinical state of depression in such patients. The procedure of diagnostic coding in hierarchical manner of the most severe or basal mental condition can lead to inadequate statistical reports related both to incorrect depression prevalence rates and ADs indications marked as being inconsistent with clinical guidelines.

Our study demonstrated that the SSRIs class of ADs dominated among the prescription lists, such as previously reported in European and Asian studies (Agius & Bonnici 2017, Chee et al. 2015, Cipriani et al. 2018). However, fluvoxamine was used in our sample more often than all other ADs classes and among the various SSRIs. An international study demonstrated that

fluvoxamine was the first choice ADs also in Malaysia and Singapore (Chee et al. 2015). Nonetheless, accepted national and international guidelines recommend prescription of escitalopram at a dose of 20 mg as the first choice for severe cases of depression, while venlafaxine, escitalopram, and sertraline are thought to be more effective than other SSRIs (Mosolov et al. 2016, Cleare et al. 2015). Taking into account the availability of various ADs in the studied services, we suppose that the free access and contracted availability of fluvoxamine led to prioritization of its prescription, despite clinical recommendations for a rational decision-making approach. We hypothesize that the same factor of hospital provision with particular antipsychotic drugs influenced the outcome of the most frequent combination with ADs. A case in point was the finding that fluvoxamine was frequently prescribed along with olanzapine and risperidone after the correctly prioritized quetiapine; according to the guidelines, quetiapine and aripiprazole (A-evidence level) are recommended as first-line treatments, and risperidone (A), olanzapine (B), or mirtazapine (B) as second-line treatments only (Mosolov et al. 2016, Cleare et al. 2015).

The average doses of ADs drugs were lower than recommended, which is important result insofar that inadequate doses can lead to serious issues related to the long-term outcomes of treatment of patients with depression (Bosman et al. 2016, Cleare et al. 2015, Kendrick et al. 2015, 2021, Moore et al. 2009, National Centre of Health Statistics 2011, Spies et al. 2004). Fluvoxamine, venlafaxine, and then clomipramine ranked as the most frequently prescribed ADs among inpatients, whereas the ranking was fluvoxamine, amitriptyline, and then clomipramine for the outpatient settings. In particular for cases of MDD, different ADs were used for mild and moderate forms, while only TCAs were accurately prescribed for severe MDD. According to guidelines, TCAs represent the first choice of treatment for severe episodes and for an inpatient population (Marić et al. 2012). Combination of ADs with drugs of other classes significantly predominated over monotherapy, a finding that likely relates to the small study sample and the variety of diagnostic categories other than MDD considered on the day of investigation. Switching patterns among the investigated cases, such as switching from primary administration of a TCA to an SNRI as the second choice and SSRI as the third choice, demonstrated that clinicians relied on factors other than clinical recommendations across prescription practices.

CONCLUSIONS

A one-day cross-sectional study of ADs use in mental health services in Moscow demonstrated that (i) 15% of inpatients and 52% of outpatients with mental disorders received treatments with antidepressants.

sant agents. ADs were prescribed for (ii) MDD and other diagnoses, including schizophrenia spectrum disorders, (iii) SSRIs, in particular fluvoxamine, were used more often in both outpatient and inpatient settings, but at lower average dose rather than is recommended, while TCAs had been correctly administered for severe MDD, (iv) mostly within combined treatment rather than monotherapy, and (v) in cases of combination with antipsychotics and for AD switching strategies, clinical recommendations were not followed accurately. The study sample was small in consideration of the number of factors and medications categories, thus calling for further research. However, the clinical reality of AD prescriptions in psychiatric settings in the Russian capital differed in some respects from clinical guidelines, insofar as the drug choice even by experienced clinicians was often at odds with the relevant factors of duration, severity or clinical profile of disorders, which should be definitely prioritized within the evidence-based decision-making approach.

Limitations of the study

The study sample is small, and further research should include patient populations from other cities and centres. Detailed analysis of factors related to AD prescription should be performed to afford a better understanding of contributing factors and to help reform prescription patterns in accordance to the guidelines. In ongoing research, we are analyzing the patterns of AD switching in patients, taking into account diagnostic categories and the AD dosages, which was not presently applicable due to the study sample size.

Acknowledgements:

Authors express their gratitude to Professor Paul Cumming of the Institute of Nuclear Medicine, Inselspital, Bern University, Bern, Switzerland, School of Psychology and Counselling and IHBI, Queensland University of Technology, Brisbane, Australia, and International Centre for Education and Research in Neuropsychiatry, Samara, Russia, for his valuable recommendations and detailed review of the paper.

Conflict of interest: None to declare.

Contribution of individual authors:

Alexey Pavlichenko & Daria Susloparova collected the data and designed the project with the advice from George Kostyuk.

Alexey Pavlichenko, Daria Smirnova & Timur Syunyakov analyzed the data.

Daria Smirnova wrote the first draft of the manuscript.

Alexey Pavlichenko, Timur Syunyakov & George Kostyuk had revised the first draft upon input from all co-authors.

References

1. Agius M & Bonnici H: *Antidepressants in use in clinical practice. Psychiatr Danub* 2017; 29(Suppl 3):S667-671
2. Bauer M, Pfennig A, Linden M, Smolka MN, Neu P, Adli M: *Efficacy of an algorithm-guided treatment compared with treatment as usual: a randomized, controlled study of inpatients with depression. J Clin Psychopharmacol* 2009; 29:327-33. doi:10.1097/JCP.0b013e3181ac4839
3. Bosman RC, Huijbregts KM, Verhaak PF, Ruhé HG, van Marwijk HW, van Balkom AJ, Batelaan NM: *Long-term antidepressant use: a qualitative study on perspectives of patients and GPs in primary care. Br J Gen Pract* 2016; 66:e708-19. doi:10.3399/bjgp16X686641
4. Cipriani A, Furukawa TA, Salanti G, Chaimani A, Atkinson LZ, Ogawa Y, Leucht S, Ruhe HG, Turner EH, Higgins JPT, Egger M, Takeshima N, Hayasaka Y, Imai H, Shinohara K, Tajika A, Ioannidis JPA, Geddes JR: *Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis. Lancet* 2018; 391:1357-1366. doi:10.1016/S0140-6736(17)32802-7
5. Chee KY, Tripathi A, Avasthi A, Chong MY, Sim K, Yang SY, Glover S, Xiang YT, Si TM, Kanba S, He YL, Lee MS, Chiu HF, Kuga H, Mahendran R, Udormatn P, Kallivayalil RA, Tanra AJ, Maramis M, Shinfuku N, Shen WW, Tan CH, Sartorius N: *International study on antidepressant prescription pattern at 40 major psychiatric institutions and hospitals in Asia: A 10-year comparison study. Asia Pac Psychiatry* 2015; 7:366-74. doi:10.1111/appy.1217
6. Cleare A, Pariante CM, Young AH, Anderson IM, Christmas D, Cowen PJ, Dickens C, Ferrier IN, Geddes J, Gilbody S, Haddad PM, Katona C, Lewis G, Malizia A, McAllister-Williams RH, Ramchandani P, Scott J, Taylor D, Uher R: *Members of the Consensus Meeting. Evidence-based guidelines for treating depressive disorders with antidepressants: A revision of the 2008 British Association for Psychopharmacology guidelines. J Psychopharmacol* 2015; 29:459-525. doi:10.1177/0269881115581093
7. Fabbri C, Zohar J, Serretti A: *Pharmacogenetic tests to guide drug treatment in depression: Comparison of the available testing kits and clinical trials. Prog Neuropsychopharmacol Biol Psychiatry* 2018; 86:36-44. doi:10.1016/j.pnpbp.2018.05.007
8. Goodwin GM & Haddad PM: *Evidence-based guidelines for treating bipolar disorder: Revised third edition recommendations from the British Association for Psychopharmacology. Journal of Psychopharmacology* 2016; 30:495-55
9. Gregory A, Mallikarjun P, Uptegrove R: *Treatment of depression in schizophrenia: systematic review and meta-analysis. Br J Psychiatry* 2017; 211:198-204. doi:10.1192/bjp.bp.116.190520
10. Jessel CD, Mostafa S, Potiriadis M, Everall IP, Gunn JM, Bousman CA: *Use of antidepressants with pharmacogenetic prescribing guidelines in a 10-year depression cohort of adult primary care patients. Pharmacogenet Genomics* 2020; 30:145-152. doi:10.1097/FPC.0000000000000406
11. Kendrick T: *Strategies to reduce use of antidepressants. Br J Clin Pharmacol* 2021; 87:23-33. doi:10.1111/bcp.14475

12. Kendrick T, Stuart B, Newell C, Geraghty AWA, Moore M: Changes in rates of recorded depression in English primary care 2003–2013: time trend analyses of effects of the economic recession, and the GP contract quality outcomes framework (QOF). *J Affect Disord* 2015; 180:68-78. doi:10.1016/j.jad.2015.03.040
13. Kraus C, Kadriu B, Lanzenberger R, Zarate CA Jr, Kasper S: Prognosis and improved outcomes in major depression: a review. *Transl Psychiatry* 2019; 9:127. doi:10.1038/s41398-019-0460-3
14. Lieb K, Völlm B, Rücker G, Timmer A, Stoffers JM: Pharmacotherapy for borderline personality disorder: Cochrane systematic review of randomised trials. *Br J Psychiatry* 2010; 196:4-12. doi:10.1192/bjp.bp.108.062984
15. Marić NP, Stojiljković DJ, Pavlović Z, Jasović-Gamsić M: Factors influencing the choice of antidepressants: a study of antidepressant prescribing practice at University Psychiatric Clinic in Belgrade. *Vojnosanit Pregl* 2012; 69:308-13
16. Moore M, Yuen HM, Dunn N, Mullee MA, Maskell J, Kendrick T: Explaining the rise in antidepressant prescribing: a descriptive study using the general practice research database. *BMJ* 2009. doi:339:b3999 10.1136/bmj.b3999
17. Mosolov SN, Kostyukova EG, Ladyzhensky MY: The algorithm of biological treatment of the acute episode of the recurrent depressive disorder. *Current treatment of mental disorders* 2016; 3:27-40
18. National Center for Health Statistics. *Health: United States, 2010, with special feature on death and dying*. 2011. [https://www.cdc.gov/nchs/data/10.pdf](https://www.cdc.gov/nchs/data/hus/10.pdf)
19. Skånland SS, Cieślak-Pobuda A: Off-label uses of drugs for depression. *Eur J Pharmacol* 2019; 865:172732. doi:10.1016/j.ejphar.2019.172732
20. Spies T, Mokking H, de Vries RP, Grol R: GP often chooses antidepressants independent of depression severity. *Huisarts Wet* 2004; 47:364-367
21. Timäus C, Meiser M, Bandelow B, Engel KR, Paschke AM, Wiltfang J, Wedekind D: Pharmacotherapy of borderline personality disorder: what has changed over two decades? A retrospective evaluation of clinical practice. *BMC Psychiatry* 2019; 19:393. doi:10.1186/s12888-019-2377-z
22. Tokumitsu K, Yasui-Furukori N, Adachi N, Kubota Y, Watanabe Y, Miki K, Azekawa T, Edagawa K, Katsumoto E, Hongo S, Goto E, Ueda H, Kato M, Yoshimura R, Nakagawa A, Kikuchi T, Tsuboi T, Shimoda K, Watanabe K: Real-world clinical features of and antidepressant prescribing patterns for outpatients with bipolar disorder. *BMC Psychiatry* 2020; 20:555. doi:10.1186/s12888-020-02967-5
23. Van Geffen EC, van der Wal SW, van Hulst R, de Groot MC, Egberts AC, Heerdink ER: Evaluation of patients' experiences with antidepressants reported by means of a medicine reporting system. *Eur J Clin Pharmacol* 2007; 63:1193-1199. 10.1007/s00228-007-0375-4
24. Whitehead C, Moss S, Cardno A, Lewis, G: Antidepressants for the treatment of depression in people with schizophrenia: a systematic review. *Psychol Med* 2003; 33:589-599
25. Wong J, Motulsky A, Abrahamowicz M, Egale T, Buckeridge DL, Tamblyn R: Off-label indications for antidepressants in primary care: descriptive study of prescriptions from an indication based electronic prescribing system. *BMJ* 2017; 356:j603. doi:10.1136/bmj.j603

Correspondence:

Assoc. Prof. Daria Smirnova, MD, PhD
International Centre for Education and Research in Neuropsychiatry & Department of Psychiatry,
Narcology, Psychotherapy and Clinical Psychology, Samara State Medical University
18 Gagarina Street, 443 079 Samara, Russia
E-mail: daria.smirnova.md.phd@gmail.com