ORIGINAL ARTICLE

Psychiatry and Clinical Psychopharmacology 2020;30(2):175-181
DOI:10.5455/PCP.20200221095546

Comparison of Drugs Prescribed by Psychiatrists and Child/Adolescent Psychiatrists

Volkan Aydin [a], **N. Ipek Kirmizi** [b], **Fatma Isli** [c], **Mesil Aksoy** [c], **Ahmet Akici** [a]

[a] *Department of Medical Pharmacology, Marmara University School of Medicine, Istanbul, Turkey,* [b] *Department of Pharmacology, Istanbul Medipol University School of Medicine, Istanbul, Turkey,* [c] *Turkish Medicines and Medical Devices Agency, Ministry of Health, Ankara, Turkey*

Abstract

Background: Drug utilization patterns may vary between children and adults even for similar indications. Psychiatry is one of the areas where differences of both diagnosis and drug utilization often vary between age groups, imposed by respective separate subspecialties and their prescribing patterns. The study aimed to compare utilization of drugs prescribed by psychiatrists and child/adolescent psychiatrists (CPs).

Methods: This study evaluated all electronic prescriptions that were generated by psychiatrists and CPs and registered to the national Prescription Information System in 2016. The drugs in these prescriptions were examined and compared in terms of physician groups.

Results: Among 1,150,621 prescriptions generated by psychiatrists and CPs during the study year, 94.2% (n=1,083,631) belonged to psychiatrists and the remaining 5.8% (n=66,990) to CPs. Psychiatrists were detected to prescribe significantly fewer nervous system drugs than CPs did (89.5% vs. 97.8%, p<0.001). Antidepressants constituted 57.4% of all nervous system drugs prescribed by psychiatrists, which was significantly lower in the prescriptions of CPs as 22.1% (p<0.001). Within antidepressants, SSRIs were significantly more preferred by CPs (91.4%) than that by psychiatrists (56.2%), (p<0.001). Centrally-acting sympathomimetics formed 46.6% of nervous system drugs prescribed by CPs compared to 2.4% of that by psychiatrists (p<0.001). Among these sympathomimetics, methylphenidate was the most commonly preferred drug by both CPs and psychiatrists (%84.6% vs. %68.6, respectively; p<0.001).

Conclusions: It seems that centrally-acting sympathomimetics constitute near half of the drugs preferred by CPs who tend to prescribe a limited number of different drugs. Contrarily, psychiatrists tend to prescribe wide spectrum of drugs, half of these being antidepressants. The study highlights some discrepancies of psychotropic drug use regarding approved indication and clinical practice for different age groups.

ARTICLE HISTORY

Received: Feb 21, 2020
Accepted: Apr 18, 2020

KEYWORDS: drug prescribing, psychiatry, child health, serotonin and noradrenaline reuptake inhibitors, antidepressive agents, methylphenidate

INTRODUCTION

Drug utilization patterns may vary between children and adults even for similar indications [1]. These variations mainly stem from the differences in incidence, course, and severity of certain diseases with their therapeutic response in childhood compared to that in adults. In addition, pharmacokinetic and pharmacodynamic factors could elicit important variations between children and adults with respect to drug use [2]. Psychiatry is one of the areas where differences of both diagnosis and drug utilization often vary between age groups, imposed by respective separate subspecialties, i.e. psychiatry and child/adolescent psychiatry, and their prescribing patterns. While child/adolescent psychiatrists (CPs) tend to predominantly prescribe for behavioural disorders and attention deficit hyperactivity disorder (ADHD), psychiatrists rather prescribe for depression, anxiety, and mood disorders [3–5]. The differences in diagnosis make the stimulants and antidepressants the first rank in these groups, respectively [6,7]. On the other hand, potential distinguishing and similar features of pharmacotherapy practice by these two relevant disciplines needs to be addressed in detail, especially considering their overlapping indications. However, the literature seems to lack a comprehensive pharmacoepidemiological study that comparably assesses prescribing metrics of psychiatrists and CPs.

Psychiatric drug utilization in both children and adults exhibits an increasing trend across the globe and also

Corresponding author: Ahmet Akici, E-Mail: aakici@marmara.edu.tr

To cite this article: Aydin V, Kirmizi NI, Isli F, Aksoy M, Akici A. Comparison of Drugs Prescribed by Psychiatrists and Child/Adolescent Psychiatrists. Psychiatry and Clinical Psychopharmacology 2020;30(2):175-181, DOI: 10.5455/ PCP.20200221095546

some debates exist about these medications' rational use [8–11]. Determination of potential differences between these two branches of specialists who prescribe such medications indicated only in certain conditions may help to develop better strategies directed at more rational pharmacotherapy in psychiatric disorders of both children and adults. This could also make an indirect contribution to estimate relative prevalence of these disorders. The study aimed to compare utilization of drugs prescribed by either psychiatrists or CPs.

METHODS

This study evaluated all electronic prescriptions that was registered in the national Prescription Information System (PIS) and generated by psychiatrists and CPs during year 2016. PIS is executed by Turkish Medicines and Medical Devices Agency under the Ministry of Health and encompasses all electronic prescriptions generated in healthcare institutions [12]. Only drug-oriented parameters were analysed in the study; patient data containing demographic characteristics were not included.

As of 2016, there were 78,620 specialist physicians in Turkey, among which the number of psychiatrists were near eight-fold that of CPs [13,14]. On the other hand, children (<18 years old) constituted 29.7% of the total population, almost 80 million inhabitants in this high-middle income country [15].

All the prescriptions generated by these specialist groups were examined with respect to their medications based on Anatomical Therapeutic Chemical (ATC) classification. Among all the drugs, those in the "N-Nervous System" category were analysed in detail: number of drugs per encounter at ATC-1 and ATC-2 levels; percentage of antidepressants and centrally-acting sympathomimetics; and percentage of selective serotonin reuptake inhibitors (SSRIs) and specific types of centrally-acting sympathomimetics. Additionally, ten most common nervous system drugs prescribed by these physicians were also determined.

The drugs prescribed by psychiatrists and CPs at ATC-2 level were compared in terms of subgroups classified as "psycholeptics" (N05), "psychoanaleptics" (N06), and "others" (N01-anesthetics, N02-analgesics, N03-antiepileptics, N04-antiparkinson drugs, N07-other nervous system drugs). Antidepressants were examined at ATC-4 level, and the percentages of SSRIs (N06AB) and non-SSRIs (N06AA, N06AG, N06AX) were compared. Centrally-acting sympathomimetics were compared at ATC-5 level as atomoxetin, methylphenidate, and modafinil.

Statistical Analysis

Statistical analyses were performed through SPSS 25.0 software. Data were expressed as mean ± standard deviation, minimum and maximum values and numbers and/or percentages where appropriate. Categorical variables of drug utilization by psychiatrists and CPs were compared through chi-square test to identify any statistical difference between the groups. An overall type I error of 5% was used to infer statistical significance.

RESULTS

Among a total of 1,150,621 electronic prescriptions generated by all psychiatrists and CPs in Turkey during the study year, 94.2% (n=1,083,631) belonged to psychiatrists and the remaining 5.8% (n=66,990) to CPs. Psychiatrists were found to prescribe 1,943,745 drugs (3,587,684 drug boxes), yielding a mean of 1.8±0.9 (range: 1-15) drugs per encounter. On the other hand, CPs prescribed 91,167 drugs (137,113 drug boxes) with a mean of 1.4±0.6 (range: 1-9) drugs per encounter. At ATC-1 level, psychiatrists were detected to prescribe significantly fewer nervous system drugs than CPs did (89.5% vs. 97.8%, p<0.001), (Table 1).

Table 1. Comparison of the percentages of drugs prescribed by psychiatrists and child/adolescent psychiatrists by their "N-nervous system" group and ATC-2 subgroup status.

Drug Group		Psychiatrist n (%)	Child/ adolescent psychiatrist n (%)	P-value*
All drugs	"N" group	1,739,619 (89.5)	89,148 (97.8)	<0.001
	Other than "N" group	204,126 (10.5)	2,019 (2.2)	
	Total	1,943,745 (100.0)	91,167 (100.0)	
ATC-2 subgroup	N06-Psychoanaleptics	1,055,043 (60.6)	61,835 (69.4)	<0.001
	N05-Psycholeptics	588,093 (33.8)	26,077 (29.2)	
	Others**	96,483 (5.6)	1236 (1.4)	
	Total	1,739,619 (100.0)	89,148 (100.0)	

Based on data of the Prescription Information System, Year 2016. *Chi-Square test, **N01-anaesthetics, N02-analgesics, N03-antiepileptics, N04-antiparkinson drugs, N07-other nervous system drugs.

In terms of nervous system drugs, mostly prescribed drugs were psychoanaleptics at ATC-2 level with a significantly higher prescription rate by CPs (69.4%) than the one by psychiatrists (60.6%, p<0.001). Contrarily, psycholeptics and other drugs at ATC-2 level were found to be significantly less prescribed by CPs compared to that by psychiatrists (29.2% vs 33.8%, [p<0.001] and 1.4% vs. 5.6%, [p<0,001]; respectively), (Table 1).

Antidepressants constituted 57.4% of all nervous system drugs prescribed by psychiatrists, which was significantly lower in the prescriptions of CPs as 22.1% (p<0.001). With respect to antidepressants, it was determined that SSRIs were significantly more preferred by CPs than that by psychiatrists (91.4% vs. 56.2%, respectively; p<0.001), (Table 2). Distribution of SSRIs at ATC-5 level showed mostly prescribed drugs as escitalopram (31.6%) and fluoxetine (51.1%) by psychiatrists and CPs, respectively (Figure 1).

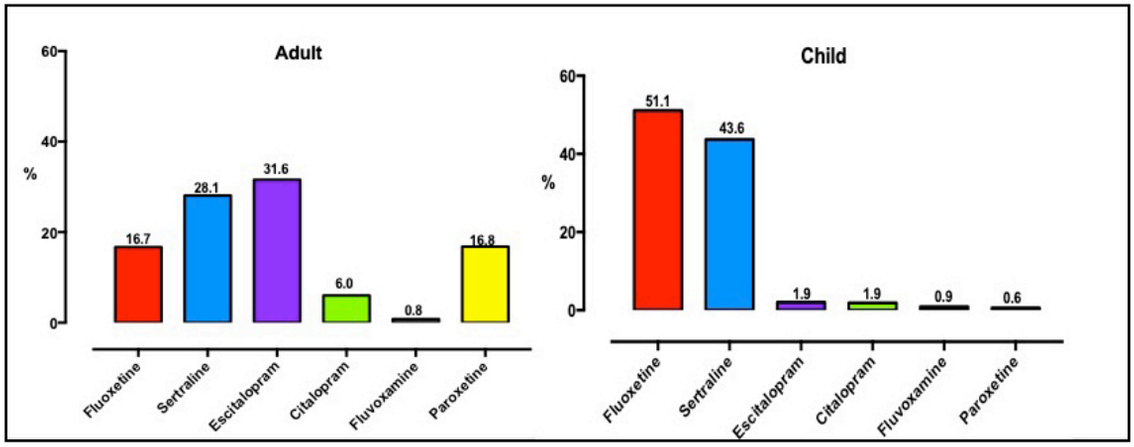

Figure 1. Distribution of the percentage of SSRIs prescribed by psychiatrists and child/adolescent psychiatrists (n=560,764 and n=18,019; respectively). SSRI, selective serotonin reuptake inhibitor

Table 2. Comparison of the percentages of drugs prescribed by psychiatrists and child/adolescent psychiatrists by their antidepressant and SSRI status.

Drug Group		Psychiatrist n (%)	Child/ adolescent psychiatrist n (%)	P-value
Nervous system drugs	Antidepressants	998,634 (57.4)	19,717 (22.1)	<0.001
	Other than antidepressants	740,985 (42.6)	69,431 (77.9)	
	Total	1,739,619 (100.0)	89,148 (100.0)	
Antidepressants	SSRI	560,764 (56.2)	18,019 (91.4)	<0.001
	Other than SSRIs*	437,870 (43.8)	1,698 (8.6)	
	Total	998,634 (100.0)	19,717 (100.0)	

* Prescribed antidepressants other than SSRIs (N06AB) with following ATC codes: N06AA, N06AF, N06AG, and N06AX. SSRI, selective serotonin reuptake inhibitor.

Centrally-acting sympathomimetics were found to form 46.6% of nervous system drugs prescribed by CPs compared to 2.4% of that by psychiatrists (p<0.001). Methylphenidate was the most commonly preferred drug by both physician groups, while significantly more predominantly in CPs than in psychiatrists (%84.6% vs. %68.6, p<0.001). Comparison of other centrally-acting sympathomimetics showed that atomoxetine was significantly more preferred by CPs (15.3% vs. 3.0%, p<0.001) and modafinil was significantly more prescribed by psychiatrists (28.4% vs. 0.1, p<0.001) than their counterparts (Table 3).

Among all nervous system drugs, CPs were detected to most commonly prescribe methylphenidate (39.4%), followed by risperidone (18.5%), fluoxetine (10.3%), sertraline (8.8%), and atomoxetine (7.1%). For psychiatrists, on the other hand, the most commonly preferred nervous system drug was escitalopram (10.2%), followed by sertraline (9.0%), quetiapine (8.4%), duloxetine (7.0%), and venlafaxine (6.3%), (Figure 2). The top ten most commonly prescribed drugs constituted 94.4% of all nervous system drugs in CPs, compared to 65.9% of that in psychiatrists. The remaining one-third of the nervous system drugs for psychiatrists included aripiprazole (3.8%), trazodone (3.8%), alprazolam (2.0%), citalopram (1.9%), methylphenidate (1.7%), valproate (1.6%), hydroxyzine (1.3%), biperiden (1.2%), paliperidone (1.1%), haloperidol (1.0%), sulpiride (0.8%), trifluoperazine (0.8%), buspirone (0.7%), modafinil (0.7%), clomipramine (0.7%), diazepam (0.7%), lithium (0.7%), lorazepam (0.7%), and various other drugs (12.0%).

Table 3. Comparison of the percentages of nervous system drugs prescribed by psychiatrists and child/adolescent psychiatrists by their centrally-acting sympathomimetic group and ATC-5 level status.

Drug Group		Psychiatrist n (%)	Child/ adolescent psychiatrist n (%)	P-value*
Nervous system drugs	Centrally acting sympathomimetics	42,588 (2.4)	41,546 (46.6)	<0.001
	Other than centrally acting sympathomimetics	1,697,031 (97.6)	47,602 (53.4)	
	Total	1,739,619 (100.0)	89,148 (100.0)	
Centrally acting sympathomimetics	Methylphenidate	29,234 (68.6)	35,139 (84.6)	<0.001
	Atomoxetine	1,268 (3.0)	6,369 (15.3)	
	Modafinil	12,086 (28.4)	38 (0.1)	
	Total	42,588 (100.0)	41,546 (100.0)	

Based on data of the Prescription Information System, Year 2016. *Chi-Square test.

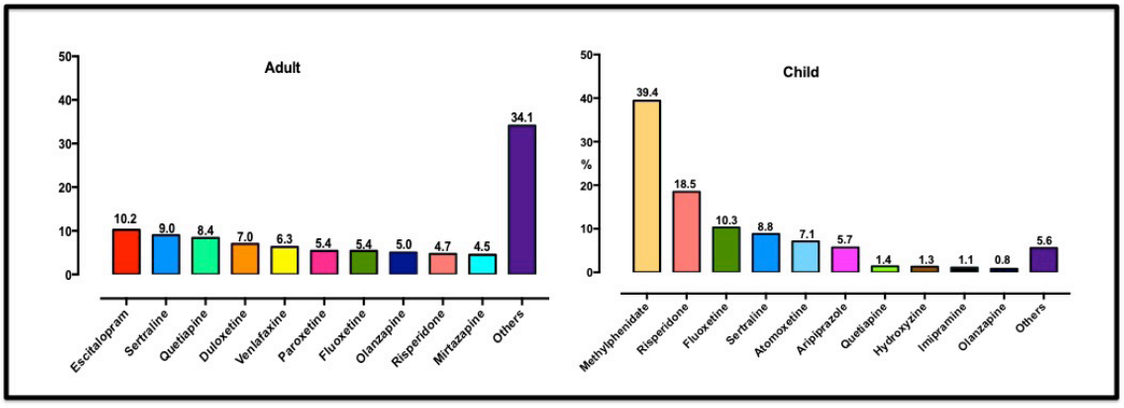

Figure 2. Distribution of the percentage of nervous system drugs prescribed by psychiatrists and child/adolescent psychiatrists in ATC 5 level (n=1,739,619 and n=89,148; respectively).

DISCUSSION

Prevalence of psychiatric disorders has increased globally, and the number of the reports examining the details of this subject from different aspects has rised [7–9,16]. A complementary approach such as prescription-based pharmacoepidemiological studies could be useful to assess the problem. In fact, analysis of prescriptions obtained from psychiatrists and CPs is expected to help to determine and compare distribution of psychiatric diagnoses in pediatric and adult populations. Though similar drug classes are deemed suitable for the same diagnoses in children and adults, possible variations in pharmacokinetic/pharmacodynamic parameters and adverse effect profiles between the groups may lead to the preference of any given drug over others in a particular indication. Our study has shown that while both CPs and psychiatrists mostly prescribed psychoanaleptics, their preferences within this drug class, e.g. antidepressants and centrally-acting sympathomimetics, varied.

The number of drugs per encounter was 25% higher in psychiatrists' prescriptions than that in CPs (1.8 vs. 1.4). Apart from the higher rate of psychiatric disorders in adults than in the children [13], this may result from increased prevalence of associated diseases with raising age. In fact, the literature reported elevated number of pharmacotherapy-requiring comorbidities as the age increased [17–19]. Consistently, we found that the percentage of non-nervous system drugs prescribed by psychiatrists were five-fold higher than that by CPs, which might be partly attributed to age-related increase in comorbidities.

At ATC-2 level, psychoanaleptics include antidepressants, psychostimulants/nootropics, anti-demans drugs whereas psycholeptics consist of antipsychotics, anxiolytics, and sedative hypnotics. In this study, both physician groups were found more likely to prescribe psychoanaleptics in their practice, while more prominent in CPs than psychiatrists (69.4% vs. 60.6%, respectively). On the other hand, psycholeptics, the second most commonly prescribed group, were more preferred by psychiatrists than CPs (33.8% vs. 29.2%, respectively). These differences might be partly explained by the limited number of medication-requiring indications in CP practice than that in general psychiatry practice [8,20] though the literature have demonstrated no studies that directly compared adult and pediatric patients for their variety of psychiatric diagnoses. Notwithstanding, the distribution of most frequently prescribed drugs between the study groups may give important clues regarding their preferences of pharmacotherapy: while the top ten prescribed nervous system drugs corresponded to near 95% of the total in CPs, this was about two-thirds in psychiatrists. Furthermore, near half of this frequently prescribed drugs by CPs were centrally-acting sympathomimetics, and further quarter consisted of antipsychotics, mostly including risperidone. Contrarily, wider variety of the distribution of drugs prescribed by psychiatrists could reflect the diversity of indications among adults.

Several reports showed increased utilization of antidepressants with debates about overuse of some drug groups [9,21,22]. Depression is more common among adults, and pharmacological treatment is indicated rather for the major depressive disorder subtype [8,23]. In this study, compared to CPs, psychiatrists were significantly more likely to prescribe antidepressants (22.1% vs. 57.4%). This at first sight might be well expected from higher prevalence of depression in adults, as depression ranked ninth (7.2%) among major diseases seen in ≥15-year-old population during the study year in Turkey [13]. While Turkey remains well below the average of OECD countries in terms of antidepressant utilization [9], the fact that antidepressants constituted more than half of all the prescribed drugs by psychiatrists may deserve further research to investigate rationality of such use among adult population. In fact, the prevalence of major depressive disorder in our country was reported as 12.6% in adolescents compared to 8.2% in adults [24,25]. While antidepressants are also indicated for anxiety, phobia, or obsessive compulsive disorders

(OCD) other than depression [26,27], study findings suggest the need for designing future research to probe the reasons behind this excessive prescribing practice among psychiatrists. On the other hand, their SSRI preference in favor of escitalopram, sertraline, and paroxetine appears more rational, as these agents were reported to have comparably higher therapeutic responsiveness and lower discontinuation rates in major depressive disorder than other antidepressants, including SSRIs [28].

Regarding antidepressant drugs, CPs were 1.6-fold more likely to prefer SSRIs (91.4%) than were psychiatrists (56.2%). Consistent with our finding, reports from the United States and Europe showed SSRIs as the most commonly utilized antidepressant group in children [29]. For SSRIs, CPs were found to mostly prescribe fluoxetine (51.1%) and sertraline (43.7%). In fact, the literature revealed these two agents at top places for SSRI use in children in many countries [29–31]. Relevant guidelines recommended fluoxetine as first-line treatment for pharmacological management of depression and anxiety disorders in children. Sertraline, however, is one of the options for patients with anxiety and OCD symptoms; and is recommended as the second-line treatment in fluoxetine-unresponsive depression where its efficacy is controversial [32,33]. In fact, Food and Drug Administration and European Medicines Agency approved fluoxetine for major depressive disorder in >8-year-old children and sertraline for OCD in >6-year-old children, with a boxed warning that stated increased risk of suicide by SSRIs in pediatric population [34–37]. While sertraline has the same approved indication in Turkey [38], fluoxetine does not have any particular statement for children in indications section at the summary of product characteristics of drug with a mere statement of "its use is not recommended in children" under special populations section [39]. A Turkish study reported prevalence of major depression and OCD in children as 1.4% and 0.2%, respectively [40]. Several such epidemiological studies regarding psychiatric disorders in pediatric population [24,41] suggest an often off-label use of pediatric SSRI, especially considering these drugs' approved indications. This further indicates the need for investigation of pediatric SSRI utilization with diagnosis-based studies and for subsequent interventions that aim to reduce off-label use of these drugs. This study implies that heterogeneity of these drugs in terms of CPs' practices, current guidelines, and cross-national variations of approved indications could be more important for vulnerable populations, e.g. children. Therefore, global harmonization is needed as much as possible for SSRI's labelling, especially in sections about pediatric use.

ADHD affects up to 3.4% of children, and mostly requires pharmacological treatment with stimulating agents like methylphenidate as well as non-drug interventions [4,42,43]. While its prevalence diminishes in adults, some patients continue to need pharmacotherapy during adolescence and afterwards [44,45]. Consistently, we found near 20-fold difference between psychiatrists and CPs in terms of prescribing ADHD drugs (2.4% vs. 46.6%, respectively). On the other hand, some concerns exist regarding overdiagnosis and overtreatment of the condition [10]. In our study, CPs were detected to prescribe mostly methylphenidate (84.3%) and atomoxetine (15.6%), where the predominance of the former was comparable with that in the published studies [46,47]. A study in Turkey reported ADHD to be responsible for 27% of psychiatric admissions among pre-school children [41]. In addition, incidence of depressive, anxiety, and psychotic disorders was reported to increase with age during childhood [48]. In this manner, it is remarkable that near one in every two drugs prescribed by CPs was a centrally-acting sympathomimetics, implying the need for future research to investigate rationality of diagnosis and pharmacotherapy of ADHD. On the other hand, controversies have emerged about the types of centrally-acting sympathomimetics to prescribe for target patient populations in transition from adolescence to young adults [43]. Higher prescription rates of modafinil in psychiatrists than that in CPs in our study might partly be attributed to an off-label use since it is only approved for epilepsy, narcolepsy, and febril convulsions yet may be used to manage ADHD [43,49]. This might be further supported by the fact that contrary to atomoxetine, which is only reimbursed for up to 25-year-old ADHD patients with an institutional drug dispensing form, modafinil could be prescribed regardless of patients' age and without dispensing form [50].

A critical aspect of our study is the relatively small number of CPs compared to the psychiatrist's group. While the number of children per CP was 110,239, the number of patients per psychiatrist was 32,009 in Turkey [14,51]. This smaller size of CP population might have led to the fact that some of the drugs detected in psychiatrists' prescriptions might be for pediatric patients. In addition, some of older adolescents might have applied to psychiatrists rather than CPs. This should also be considered in interpreting the differences of prescribing practices between these two branches. Finally, our study only analysed the data of drugs prescribed by psychiatrists and CPs, without matching these to patients' demographic or diagnostic information.

CONCLUSION

In conclusion, we compared the drug preferences of psychiatrists and CPs over >1 million of prescriptions they generated in an entire year. It seems that centrally-acting sympathomimetics constitute near half of the drugs preferred by CPs who tend to prescribe a limited number of different drugs. Contrarily, psychiatrists tend to prescribe with a more diverse spectrum of drug classes, yet half of these drugs consisted of antidepressants. Our study highlighted some discrepancies of psychotropic drug use with respect to the labelled indication and clinical practice, such as excessive off-label use of SSRIs in children. This further underlines the need for designing detailed indication-oriented studies to establish a solid background for interventions that aim to reduce off-label use of commonly prescribed psychiatric drugs.

Acknowledgements: The authors thank Esma Kadi and other respective staff/consultants of Turkish Medicines and Medical Devices Agency for their assistance in data collection from the Prescription Information System.

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

Conflict of Interest: The authors declare that they have no conflict of interest.

REFERENCES

[1] World Health Organization. Promoting Safety of Medicines for Children, 2007. ISBN: 978.924.1563437.

[2] Kearns GL, Abdel-Rahman SM, Alander SW, Blowey DL, Leeder JS, Kauffman RE. Developmental Pharmacology-Drug Disposition, Action, and Therapy in Infants and Children. N Engl J Med. 2003;349:1157-1167.

[3] Bronsard G, Alessandrini M, Fond G, Loundou A, Auquier P, Tordjman S, et al. The prevalence of mental disorders among children and adolescents in the Child Welfare System. Medicine (Baltimore). 2016;95(7):1-17.

[4] Polanczyk G V, Salum GA, Sugaya LS, Caye A, Rohde LA. Annual Research Review : A meta-analysis of the worldwide prevalence of mental disorders in children and adolescents. J Child Psychol Psychiatry. 2015;56(3):345-365.

[5] Doherty JO, Hannigan A, Hickey L, Meagher D, Cullen W, Connor R, et al. The prevalence and treatment of mental health conditions documented in general practice in Ireland. Ir J Psychol Med. 2018:1-8.

[6] Moore TJ, Mattison DR. Adult Utilization of Psychiatric Drugs and Differences by Sex,Age, and Race. JAMA Intern Med. 2017;177(2):274-275.

[7] Olfson M, Druss BG, Marcus SC. Trends in mental health care among children and adolescents. N Engl J Med. 2015;372(21):2029-2038.

[8] Mental health surveillance among children — United States, 2005-2011. MMWR Surveill Summ 2013; 62: Suppl 2: 1-35.

[9] OECD (2017), Health at a Glance 2017: OECD Indicators, OECD Publishing, Paris. doi:10.1787/health_glance-2017-en.

[10] Swanson JM, Volkow ND. Increasing use of stimulants warns of potential abuse. Nature. 2008;453(7195):586.

[11] Piovani D, Clavenna A, Bonati M. Prescription prevalence of psychotropic drugs in children and adolescents: an analysis of international data. Eur J Clin Pharmacol. 2019.

[12] Aksoy M, Alkan A, Isli F. Rational drug use promotional activities of ministry of health. Türkiye Klin J Pharmacol-Special Top. 2015;3(1):19-26.

[13] Turkish Ministry of Health. Health Statistics Yearbook 2016. Ankara; 2017.

[14] TC. Sağlık Bakanlığı. Ulusal Ruh Sağlığı Eylem Planı (2011-2023) [Turkish Ministry of Health, National Mental Health Action Plan (2011-2023)]. Ankara, 2011. ISBN:978-975-590-391-0.

[15] Ministry of Interior. [Number of People by Age in General Directorate of Civil Registration and Citizenship; 2016]. https://www.nvi.gov.tr/PublishingImages/Lists/PageContents/EditForm/Nufus Kutukleri Istatistigi.pdf. Date of Access: [16.01.2019]

[16] Belloni A, Morgan D, Paris V. Pharmaceutical expenditure and policies: past trends and future challenges. OECD Heal Work Pap. 2016;87:10-60.

[17] Piccirillo JF, Vlahiotis A, Barrett LB, Flood KL, Spitznagel EL, Steyerberg EW. The changing prevalence of comorbidity across the age spectrum. Crit Rev Oncol Hematol. 2008;67(2):124-132.

[18] Luppa M, Sikorski C, Luck T, Ehreke L, Konnopka A, Wiese B, et al. Age – and gender-specific prevalence of depression in latest-life – Systematic review and meta-analysis. J Affect Disord. 2012;136(3):212-221.

[19] Reisinger Walker E, Druss B. A public health perspective on mental and medical comorbidity. JAMA. 2016;316(10):1104-1105.

[20] Jones PB. Adult mental health disorders and their age at onset. Br J Psychiatry. 2013;202:5-10.

[21] Ilyas S, Moncrieff J. Trends in prescriptions and costs of drugs for mental disorders in England, 1998-2010. Br J Psychiatry. 2012;200(5):393-398.

[22] Mars B, Heron J, Kessler D, Davies N, Martin R, Thomas K, et al. Influences on antidepressant prescribing trends in the UK: 1995–2011. Soc Psychiatry Psychiatr Epidemiol. 2017;52(2):193-200.

[23] Kennedy SH, Lam RW, McIntyre RS, Tourjman S, Bhat V, Blier P, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 clinical guidelines for the management of adults with major depressive disorder: Section 3. Pharmacological Treatments. Can J Psychiatry. 2016;61(9):540-560.

[24] Toros F, Bilgin NG, Bugdayci R, Sasmaz T, Kurt O, Camdeviren H. Prevalence of depression as measured by the CBDI in a predominantly adolescent school population in Turkey. Eur Psychiatry. 2004;19(5):264-271.

[25] Topuzoglu A, Binbay T, Ulaş H, Elbi H, Tanik F, Zagli N, et al. The epidemiology of major depressive disorder and subthreshold depression in Izmir, Turkey: Prevalence, socioeconomic differences, impairment and help-seeking. J Affect Disord. 2015;181:78-86.

[26] Olfson M, Marcus SC. National patterns in antidepressant medication treatment. Arch Gen Psychiatry. 2009;66(8):848-856.

[27] Roest AM, De Jonge P, Williams CD, De Vries YA, Schoevers RA, Turner EH. Reporting bias in clinical trials investigating the efficacy of second-generation antidepressants in the treatment of anxiety disorders: A report of 2 meta-analyses. JAMA Psychiatry. 2015;72(5):500-510.

[28] Cipriani A, Furukawa TA, Salanti G, Chaimani A, Atkinson L, Ogawa Y, et al. 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(10128):1357-1366.

[29] Bachmann CJ, Aagaard L, Burcu M, Glaeske G, Kalverdijk L, Petersen I, et al. Trends and patterns of antidepressant use in children and adolescents from five western countries, 2005-2012. Eur Neuropsychopharmacol. 2016;26(3):411-419.

[30] Pottegård A, Bjerregaard BK, Glintborg D, Kortegaard LS, Hallas J, Moreno SI. The use of medication against attention deficit/hyperactivity disorder in Denmark: A drug use study from a patient perspective. Eur J Clin Pharmacol. 2013;69(3):589-598.

[31] Schröder C, Dörks M, Kollhorst B, Blenk T, Dittmann R, Garbe E, et al. Outpatient antidepressant drug use in children and adolescents in Germany between 2004 and 2011. Pharmacoepidemiol Drug Saf. 2016;26(2):170-179.

[32] National Institute for Health and Care Excellence. Using antidepressants in children and young people. 2018;(2018):1-13.

[33] Garland EJ, Kutcher S, Virani A, Elbe D. Update on the use of SSRIs and SNRIs with children and adolescents in clinical practice. J Can Acad Child Adolesc Psychiatry. 2016;25(1):4-10.

[34] Prozac Prescribing information (FDA). Available at: www.accessdata.fda.gov/drugsatfda_docs/label/2011/018936s091lbl.pdf Date of Access:[16.01.2019].

[35] European Medicines Agency. Prozac-Article 6(12) referral – Annex I, II,III, 2006. https://www.ema.europa.eu/documents/referral/prozac-article-6-12-referral-annex-i-ii-iii_en.pdf Date of Access:[16.01.2019].

[36] Zoloft Prescribing information (FDA). Available at: www.accessdata.fda.gov/drugsatfda_docs/label/2009/019839s070,020990s032lbl.pdf Date of Access:[16.01.2019].

[37] European Medicines Agency. Zoloft-Article 30 referral – Annex I, II,III,IV, 2009. www.ema.europa.eu/documents/referral/zoloft-article-30-referral-annex-i-ii-iii-iv_en.pdf Date of Access:[16.01.2019].

[38] Lustral Summary of Product Characteristics (Turkish Version). Available at: www.titck.gov.tr/kubkt Date of Access:[16.01.2019].

[39] Prozac Summary of Product Characteristics (Turkish Version). Available at: www.titck.gov.tr/kubkt Date of Access:[16.01.2019].

[40] Ercan ES, Bilaç Ö, Uysal Özaslan T, Akyol Ardic U. Prevalence of psychiatric disorders among Turkish children: the effects of impairment and sociodemographic correlates. Child Psychiatry Hum Dev. 2016;47(1):35-42.

[41] Coskun M, Kaya I. Prevalence and patterns of psychiatric disorders in preschool children referred to an outpatient psychiatry clinic. Anatol Clin. 2016;21(1):42-47.

[42] Thapar A, Cooper M. Attention deficit hyperactivity disorder. Lancet. 2016;387:1240-1250.

[43] Kooji SJ, Bejerot S, Blackwell A, Caci H, Casas-Brugue M, Carpentier P, et al. European consensus statement on diagnosis and treatment of adult ADHD: The European Network Adult ADHD. BMC Psychiatry. 2010;10(67):1-24.

[44] Singh SP, Tuomainen H. Transition from child to adult mental health services: Needs, barriers, experiences and new models of care. World Psychiatry. 2015;14(3):358-361.

[45] Zetterqvist J, Asherson P, Halldner L, Långström N, Larsson H. Stimulant and non-stimulant attention deficit/hyperactivity disorder drug use: Total population study of trends and discontinuation patterns 2006-2009. Acta Psychiatr Scand. 2013;128(1):70-77.

[46] Bachmann CJ, Wijlaars LP, Kalverdijk LJ, Glaeske G, Schuiling-Veninga C, Hoffmann F, et al. Trends in ADHD medication use in children and adolescents in five western countries, 2005–2012. Eur Neuropsychopharmacol. 2017;27(5):484-493.

[47] Chai G, Governale L, McMahon A, Trinidad J, Staffa J, Murphy D. Trends of outpatient prescription drug utilization in US children, 2002 – 2010. Pediatrics. 2017;130:23-31.

[48] Horwitz SM, Storfer-Isser A, Demeter C, Youngstrom E, Frazier T, Fristad M, et al. Use of outpatient mental health services among children of different ages: are younger children more seriously ill? Psychiatr Serv. 2014;65(8):1026-1033.

[49] Modiogen Summary of Product Characteristics (Turkish Version). Available at: www.titck.gov.tr/kubkt Date of Access:[16.01.2019].

[50] T.C. Sosyal Güvenlik Kurumu, Sağlık Uygulama Tebliği [Republic of Turkey, Social Security Institution, Health Practice Statement], 2015 .

[51] Turkish Statistical Institute. Regional Statistics of 2011. www.biruni.tuik.gov.tr/bolgeselistatistik/anaSayfa.do?dil=en Date of Access: [14.01.2019].