OPEN SUBMISSIONS

mhc MENTAL HEALTH CLINICIAN

ORIGINAL RESEARCH Open Access

Cardiometabolic management in severe mental illness requiring an atypical antipsychotic

Allison Schmitz, PharmD[1]; Melissa Rohrich, PharmD, BCPS[2]; William Newman, MD, FACP[3]; Pamela Wolf, PharmD, BCPP[4]

How to cite: Schmitz A, Rohrich M, Newman W, Wolf P. Cardiometabolic management in severe mental illness requiring an atypical antipsychotic. Ment Health Clin [Internet]. 2017;7(2):81-7. DOI: 10.9740/mhc.2017.03.081.

Abstract

Introduction: Cardiometabolic management was evaluated in patients with diabetes and a severe mental illness that require treatment with an atypical antipsychotic.

Methods: Seventy-four patients with diabetes and a severe mental illness treated with an atypical antipsychotic from the Fargo Veterans' Affairs Health Care System were included in this retrospective study. Primary end points analyzed the change in hemoglobin A1c (Hgb A1c), blood pressure, and low-density lipoprotein (LDL) cholesterol 12 months prior to and 12 months following the initiation of an atypical antipsychotic. Secondary end points evaluated changes specific to clozapine and olanzapine. Additional secondary end points evaluated the medication management for cardiometabolic disease prior to and following atypical antipsychotic initiation.

Results: In the 12 months following atypical antipsychotic initiation, there were no statistically significant changes in metabolic parameters. Mean Hgb A1c increased from 6.9% to 7.2% ($P=.47$), mean systolic blood pressure decreased slightly from 132 to 127.8 mm Hg ($P=.97$), mean diastolic blood pressure decreased slightly from 79.6 to 76.6 mm Hg ($P=.19$), and mean LDL remained unchanged at 104.4 mg/dL ($P=.92$). Medications to control cardiometabolic disease increased substantially following atypical antipsychotic initiation; 35.1%, 39.2%, and 39.2% of patients were started on one or more new antihyperglycemics, antihypertensives, and statins, respectively.

Discussion: Patients had a significant increase in prescriptions to manage cardiometabolic disease in the 12 months following initiation of an atypical antipsychotic. Although medications to manage cardiometabolic disease increased, the actual metabolic parameters did not significantly change during the same time period.

Keywords: schizophrenia, psychotic disorders, diabetes, atypical antipsychotics

[1] (Corresponding author) Mental Health Clinical Pharmacy Specialist, Fargo VA Health Care System, Fargo, North Dakota, allison.schmitz@va.gov, ORCID: http://orcid.org/0000-0001-6663-7985; [2] Chief of Pharmacy Services, Fargo VA Health Care System, Fargo, North Dakota, ORCID: http://orcid.org/0000-0001-6564-9140; [3] Chief of Endocrinology, Fargo VA Health Care System, Fargo, North Dakota; Professor of Medicine and Acting Chair, Department of Internal Medicine, University of North Dakota School of Medicine & Health Sciences Southeast Campus, Fargo, North Dakota, ORCID: http://orcid.org/0000-0002-5712-9265; [4] Mental Health Clinical Pharmacy Specialist, Fargo VA Health Care System, Fargo, North Dakota, ORCID: http://orcid.org/0000-0001-8609-4527

Disclosures: A.S. owns stock in Eli Lilly and Company. P.W. does consulting on behalf of aripiprazole (Abilify) for Otsuka Pharmaceuticals. No other authors of this manuscript have any conflicts of interest to declare.

Introduction

Diabetes is one of the most common chronic disease states in the United States, and with it comes significant morbidity as well as mortality.[1] Diabetes is more prevalent

in patients with schizophrenia or bipolar disorders than in the general population.[2-7] Glycosylated hemoglobin (Hgb A1c), blood pressure, and low-density lipoprotein cholesterol (LDL) are 3 objective measurements clinicians target to minimize negative outcomes.

Well-respected guidelines, including the American Diabetes Association's Standard of Medical Care in Diabetes 2013, the Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III), and the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC 7), recommend targeting an Hgb A1c <7%, blood pressure <130/80 mm Hg, and LDL <100 mg/dL, respectively.[8-10] Following the data collection for this study, new hypertension and lipid guidelines have been published. According to the 2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults, the newest blood pressure recommendation is <140/90 mm Hg.[11] The 2013 American College of Cardiology/American Heart Association Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults concludes lipid management should focus on statin intensity rather than an LDL target of <100 mg/dL.[12]

Increased diabetes prevalence in severe mental illness is likely multifactorial, including the impact of the illness itself, associated medication-induced metabolic side effects, sedentary lifestyle, poor diet, and limited access to quality health care.[13-20] Atypical antipsychotics carry a class warning for weight gain, dyslipidemia, diabetes, and accelerated cardiovascular disease. Atypical antipsychotics display activity at a number of receptors, and those associated with cardiometabolic side effects include the serotonin receptor 5HT2C, muscarinic receptor M3, and histaminic receptor H1. Antagonized H1 and 5HT2C receptors are associated with weight gain, which can partly be explained by an increase in appetite.[21] Insulin regulation can be disrupted and reduced by antagonizing the M3 receptor.[22] Researchers theorize atypical antipsychotics may have additional activity because not all cardiometabolic side effects can be fully explained by weight gain or the known receptor activity.

All of these factors, along with cardiovascular disease, contribute to the reduced life expectancy of patients with schizophrenia.[7,23] Published research predominantly focuses on the risk of developing diabetes with atypical antipsychotic treatment. The hypothesis was that patients treated with atypical antipsychotics for severe mental illnesses with comorbid diabetes would have poorly controlled diabetes. This retrospective study evaluates changes in Hgb A1c, blood pressure, and LDL, and associated medication prescribing.

Methods

Study Design

Prior to initiation, this study was reviewed and approved by the University of South Dakota Institutional Review Board and the Fargo Veterans' Affairs Health Care System (VAHCS) Research and Development Committee. Informed consent was waived. This retrospective study was a single-site study conducted at the Fargo VAHCS. Inclusion criteria for the study required an active diagnosis according to ICD-9 coding of both diabetes mellitus and a severe mental illness at the time of data collection (November-December 2013) and treatment with an atypical antipsychotic. Severe mental illnesses included a psychotic or bipolar spectrum disorder. Psychotic disorders included schizophrenia, schizoaffective disorder, schizophreniform disorder, psychotic disorder not otherwise specified, and delusional disorder. Bipolar spectrum disorders included bipolar 1 disorder, bipolar 2 disorder, bipolar disorder not otherwise specified, and cyclothymia. All atypical antipsychotics prescribed at the Fargo VAHCS were included in the study and are as follows: clozapine, olanzapine, risperidone, paliperidone, quetiapine, ziprasidone, and aripiprazole. Veterans were included in the study if receiving conventional antipsychotics in addition to an atypical antipsychotic. Exclusion criteria included deceased individuals or individuals who elected to fill their antipsychotic prescriptions at private pharmacies outside of the Fargo VAHCS. Veterans were not excluded if they received other prescription medications at private pharmacies. All living patients within the Fargo VAHCS and meeting criteria at the time of data collection were included in the study.

Primary end points analyzed the change in Hgb A1c, blood pressure, and LDL before and after the initiation of an atypical antipsychotic. Vitals and laboratory values were averaged during the 12 months prior to and 12 months following the initiation of the atypical antipsychotic. Secondary end points evaluated the change in Hgb A1c, blood pressure, and LDL specific to olanzapine or clozapine because these agents carry the greatest metabolic risk.

The prevalence of prescriptions for diabetes, blood pressure, and dyslipidemia was also evaluated as a secondary end point in the 12 months prior to and 12 months following initiation of the atypical antipsychotic. All oral and injectable diabetes medications in addition to all antihypertensives were evaluated and included in the analysis. Only HMG-CoA reductase inhibitors or "statins" were gathered for the dyslipidemia indication.

Statistical Analysis

The index date was the date when the first atypical antipsychotic was prescribed for each patient and was not

TABLE 1: Demographics of 74 study participants

	Mean ± SD	Median (Q Range)	Minimum	Maximum
Continuous variables				
Age, y	52.9 ± 9.1	60.0 (11.0)	31.0	82.0
Body mass index, kg/m^2	34.6 ± 6.2	32.7 (9.4)	23.5	49.4
Diabetes duration, y	5.9 ± 4.1	5.5 (6.0)	1.0	17.0
Medications, no.	14.2 ± 5.9	13.0 (8.0)	1.0	34.0
Atypical antipsychotic use duration, y	8.6 ± 5.8	8.5 (10.1)	0.1	18.9
	%	95% CI		
Categoric variables				
Male[a]	87.8	78.2-93.6		
Hypertension	73.0	61.8-81.8		
Dyslipidemia	86.5	76.6-92.6		

CI = confidence interval.

[a]Female participants represented the remainder of study participants at 12.2%.

required to occur within a specific time period for inclusion in this study. The change in Hgb A1c, blood pressure, and LDL is presented as both the mean with the standard deviation and the median with the interquartile range. Secondary end points looking specifically at olanzapine and clozapine were calculated in the same fashion as the primary end points, with the exception that the initiation date of olanzapine and clozapine was used as the index date. The paired *t* test was used to compare continuous variables whose difference in preatypical and postatypical antipsychotic use approximated a normal distribution. Only those individuals having both 12 months preatypical and 12 months postatypical antipsychotic values were used for statistical calculations. Lastly, for the secondary end points evaluating the prescription medication management of diabetes, blood pressure, and dyslipidemia, either the χ^2 or the Fisher exact test was used. SAS 9.3 (Cary, North Carolina) was used for all calculations.

Results

A total of 74 patients were included in the study. A total of 155 patients were excluded. There were 2 patients who filled their atypical antipsychotic at a private pharmacy, and the remaining 153 patients were deceased. Demographics were obtained and analyzed (Table 1). The primary end points compared Hgb A1c, blood pressure, and LDL 12 months prior to and in the 12 months following atypical antipsychotic exposure. In the 12 months prior to initiation of an atypical antipsychotic, 16%, 35%, and 19% of patients had Hgb A1c, blood pressure, and LDL values, respectively, available. In the 12 months following the initiation of an atypical antipsychotic, monitoring improved, and 54%, 88%, and 55% of patients had Hgb A1c, blood pressure, and LDL, respectively, available to analyze. There were no statistically significant changes in metabolic parameters in the 12 months following initiation of an atypical antipsychotic. Mean Hgb A1c increased from 6.9% to 7.2% ($P = .47$), mean systolic and diastolic blood pressures decreased slightly, and mean LDL remained unchanged (Table 2).

Secondary end points analyzed if olanzapine and clozapine caused worsening of Hgb A1c, blood pressure, and LDL more than atypical antipsychotics as a class. Small numbers limited the applicability of the results. Forty study participants were included in the olanzapine subgroup. Patients exposed to olanzapine had a worsen-

TABLE 2: Primary end point changes in diabetes parameters—average value 12 months prior to atypical antipsychotic use and 12 months following initiation (N = 74)

	Preatypical Antipsychotic Use (12 mo)			Postatypical Antipsychotic Use (12 mo)			
Variable	No.	Mean ± SD	Median (Q Range)	No.	Mean ± SD	Median (Q Range)	*P* Value
A1c, %	12	6.9 ± 1.3	6.4 (2.2)	40	7.2 ± 1.7	6.6 (1.5)	.47
Systolic blood pressure, mm Hg	26	132.0 ± 11.0	136.3 (20.0)	65	127.8 ± 17.0	127.5 (14.6)	.97
Diastolic blood pressure, mm Hg	26	79.6 ± 8.9	81.3 (12.2)	65	76.6 ± 10.4	78.5 (9.4)	.19
LDL, mg/dL	14	104.4 ± 33.9	110.0 (44.3)	41	104.4 ± 34.2	99.0 (45.0)	.92

LDL = low-density lipoprotein.

TABLE 3: Change in diabetes parameters with olanzapine—average value 12 months prior to atypical antipsychotic use and 12 months following initiation (N = 40)

Variable	Preatypical Antipsychotic Use (12 mo)			Postatypical Antipsychotic Use (12 mo)			*P* Value
	No.	Mean ± SD	Median (Q Range)	No.	Mean ± SD	Median (Q Range)	
A1c, %	9	6.9 ± 1.4	6.1 (2.0)	19	7.3 ± 1.8	6.5 (2.5)	.11
Systolic blood pressure, mm Hg	24	132.7 ± 8.6	135.6 (12.2)	37	129.0 ± 20.0	131.5 (15.4)	.90
Diastolic blood pressure, mm Hg	24	79.7 ± 7.6	80.1 (6.8)	37	77.1 ± 11.6	79.0 (8.7)	.46
LDL, mg/dL	13	113.2 ± 34.3	119.9 (36.3)	19	117.1 ± 40.8	115.5 (73.0)	.99

LDL = low-density lipoprotein.

ing of mean Hgb A1c from 6.9% to 7.3% ($P = .11$). Mean systolic and diastolic blood pressures decreased slightly and LDL increased slightly in patients receiving olanzapine (Table 3). Evaluating clozapine's effect on Hgb A1c, blood pressure, and LDL was limited by the small sample size of 12 patients. In the clozapine subgroup, mean Hgb A1c improved from 7.8% to 6.8% ($P = .07$). Mean systolic blood pressure decreased slightly, whereas mean diastolic blood pressure and LDL increased slightly in patients receiving clozapine (Table 4).

Additional secondary end points compared the prescription history for diabetes, hypertension, and dyslipidemia medications in relationship to the initiation of an atypical antipsychotic. After the initiation of an atypical antipsychotic, monitoring of Hgb A1c, blood pressure, and LDL improved, and aggressive medication management was apparent. In the 12 months prior to atypical antipsychotic use, 16.2%, 16.2%, and 10.8% of patients were initiated on one or more new medications for diabetes, hypertension, and dyslipidemia, respectively. In the 12 months following atypical antipsychotic initiation, 35.1%, 39.2%, and 39.2% of patients were started on one or more new medications for diabetes, hypertension, and dyslipidemia, respectively (Table 5).

Discussion

Contrary to our hypothesis, this study indicates veterans with a severe mental illness and comorbid diabetes are well managed within the Fargo VAHCS. Changes in Hgb A1c, blood pressure, and LDL in the 12 months prior to and 12 months following the initiation of an atypical antipsychotic were minor and failed to reach statistical significance. Although study participants were required to have diabetes in addition to a psychotic or bipolar spectrum disorder, it is important to acknowledge that diabetes may not have been diagnosed until 12 months or more after starting the atypical antipsychotic. It is also possible that the trend of increasing Hgb A1c may have reached statistical significance if all patients had had appropriate monitoring available or if a greater number of patients had been analyzed.

Other published literature supports our findings that initiation of an atypical antipsychotic does not worsen cardiometabolic parameters. An inpatient study conducted by Krosnick and Wilson[24] evaluated diabetes control in patients with schizophrenia and determined achieving adequate glycemic control is possible when treated with atypical antipsychotics with appropriate and aggressive treatment for hyperglycemia. The applicability of these results is limited in the outpatient mental health setting because the study was conducted in a controlled inpatient environment. Weiss et al[25] concluded patients with severe mental illnesses were managed similarly for diabetes in comparison with patients without a severe mental illness, but applicability of their findings is limited, because only 94 of the 214 patients had an antipsychotic documented on their medication list. Dixon et al[26] determined that patients with diabetes

TABLE 4: Change in diabetes parameters with clozapine—average value 12 months prior to atypical antipsychotic use and 12 months following initiation (N = 12)

Variable	Preatypical Antipsychotic Use (12 mo)			Postatypical Antipsychotic Use (12 mo)			*P* Value
	No.	Mean ± SD	Median (Q Range)	No.	Mean ± SD	Median (Q Range)	
A1c, %	5	7.8 ± 1.4	7.1 (2.0)	10	6.8 ± 1.3	6.4 (1.7)	.07
Systolic blood pressure, mm Hg	7	130.7 ± 8.6	130.4 (7.2)	11	129.7 ± 12.0	124.6 (23.3)	.50
Diastolic blood pressure, mm Hg	7	79.0 ± 5.6	80.3 (7.3)	11	80.9 ± 6.8	78.9 (13.6)	.15
LDL, mg/dL	6	106.1 ± 29.7	97.8 (60.6)	6	112.9 ± 45.4	118.0 (77.0)	.92

LDL = low-density lipoprotein.

TABLE 5: Medication management, preatypical versus postatypical

Drug Category Added	No.	New Medications Initiated Preatypical (12 mo), %	95% CI	No.	New Medications Initiated Postatypical (12 mo), %	95% CI	*P* Value
All atypicals	74			74			
Diabetes		16.2	9.4-26.5		35.1	25.3-46.5	<.01
Blood pressure		16.2	9.4-26.5		39.2	28.9-50.6	<.01
Statin		10.8	5.4-20.2		39.2	28.8-50.6	<.01
Olanzapine	40			40			
Diabetes		17.5	8.4-32.4		32.5	20.1-48.1	.12
Blood pressure		15.0	6.7-29.6		30.0	18.1-45.6	.11
Statin		12.5	5.1-26.7		27.5	16.1-43.0	.09
Clozapine	12			12			
Diabetes		16.7	3.8-46.2		33.3	13.8-61.2	.35
Blood pressure		25.0	8.5-54.0		58.3	31.9-80.6	.21
Statin		8.3	0.0-37.9		41.7	19.4-68.1	.16

CI = confidence interval.

and a schizophrenia spectrum disorder or a major mood disorder had lower mean Hgb A1c values compared with patients with diabetes without a mental illness. Nevertheless, these results too were limited because patients were not required to be on an atypical antipsychotic, and individuals included in the major mood disorder study arm included those with major recurrent depression. Individuals with major recurrent depression may have higher functioning and insight into both their psychiatric and medical illnesses.

A particularly intriguing observation was the trend of lowering of Hgb A1c in the clozapine group. Although not statistically significant, patients prescribed clozapine experienced a drop in the mean Hgb A1c from 7.8% to 6.8% ($P = .07$). Reasons for this unexpected finding are unclear because one would expect this high cardiometabolic risk agent to increase, rather than decrease, the Hgb A1c. Possible explanations include patients prescribed clozapine require frequent lab monitoring, which may lead to increased use of health care resources in the form of provider visits, home health services, or social program assistance. In contrast to clozapine, olanzapine patients' Hgb A1c trended up from 6.9% to 7.3% ($P = .11$), as one would expect. The discrepancy between clozapine and olanzapine indicates that although medications and their associated side effect profiles play a role in diabetes and its management, other factors may contribute to outcomes.

Improved metabolic monitoring was apparent following the initiation of an atypical antipsychotic. Monitoring at baseline was suboptimal. Monitoring labs and vitals increased considerably following initiation of an atypical antipsychotic. Although monitoring increased significantly, clinicians must continue to strive to further improve monitoring.

Aggressive medication management was evident by the sizable increases in new prescriptions for diabetes, hypertension, and dyslipidemia. In contrast with our findings, Nasrallah et al[27] concluded that diabetes was undertreated in patients with schizophrenia. Kreyenbuhl et al[28] concluded patients with serious mental illnesses and diabetes were less likely to receive HMG-CoA reductase inhibitors, angiotensin-converting enzyme inhibitors, or angiotensin receptor blockers than patients without a serious mental illness. Interventions were apparent in our study to control diabetes, indicating that clinicians are mindful of the significant cardiometabolic risk in this unique patient population. Differing conclusions in VA populations versus private health care populations may highlight differences between the two health care systems and limit the external validity of the results. Coordinating mental health and primary care services in the private health care system may be more difficult in comparison with the VAHCS; obstacles may include problems accessing medical records, incomplete or unknown medical history, insurance issues, expensive prescription drug costs, and limited social program assistance. Additional research with greater patient numbers, including individuals receiving their health care in the private health care system, is warranted to further evaluate care in individuals with severe mental illnesses. Nevertheless, the interventions seen in this study attest to quality health care and the coordination of care between mental health and primary care clinicians within the VAHCS.

Limitations of this study include: retrospective design, lack of a control group, single center, small patient numbers, predominantly male sex, only included veterans, and did not evaluate medication adherence. This study also only evaluated Fargo VA prescriptions. It is possible that patients could have elected to fill some of their prescriptions at private pharmacies, but because of the design of VA pharmacy benefits, it is unlikely that many in this patient population would have elected to use private pharmacies. Intended indications were not evaluated and antihypertensive medications used for other common indications, including loop diuretics and alpha 1 antagonists, may have been prescribed for other indications. In addition, all of the study was conducted within the Fargo VAHCS. Overall generalizability may be limited because this study consisted of a predominantly male population and only included veterans. Various socioeconomic issues may be more pronounced and contribute to access to or quality of health care more within the private health care system.

Lastly, this study was conducted before the 2013 American College of Cardiology/American Heart Association Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults was published and implemented into practice. In the absence of contraindications, most patients with diabetes should receive an HMG-CoA reductase inhibitor.[12] In the future, aggressively treating these high-risk patients according to guideline recommendations will be important to minimize cardiovascular disease in this particularly vulnerable patient population. As these guidelines become the standard of practice, it is our expectation that even more study participants will be started on an HMG-CoA reductase inhibitor.

Conclusion

In conclusion, patients requiring an atypical antipsychotic for a psychotic or bipolar spectrum disorder had a significant increase in prescriptions for medications to manage diabetes, hypertension, and dyslipidemia in the 12 months following the index prescription. Although medications to manage cardiometabolic disease increased, the actual metabolic parameters (Hgb A1c, blood pressure, and LDL) did not significantly change during the same time period. Monitoring of laboratory values and vitals increased after atypical antipsychotics were initiated, but this remains an identifiable area for improvement. New prescriptions to manage cardiometabolic disease increased substantially following initiation of an atypical antipsychotic, indicating primary care clinicians are making appropriate interventions to control cardiometabolic disease when necessary. Although atypical antipsychotics can cause cardiometabolic side effects, clinicians have the ability to attenuate these unwanted side effects with aggressive medication interventions.

Acknowledgments

This material is the result of work supported with resources and the use of facilities at the Fargo Veterans Affairs Health Care System. The contents do not represent the views of the US Department of Veterans Affairs or the US Government.

References

1. FAST FACTS Data and Statistics about Diabetes [Internet]. Alexandria (VA): American Diabetes Association [cited 2014 Jun 4]. Available from: http://professional.diabetes.org/admin/UserFiles/o%20%20Sean/FastFacts%20March%202013.pdf
2. Dixon L, Weiden P, Delahanty J, Goldberg R, Postrado L, Lucksted A, et al. Prevalence and correlates of diabetes in national schizophrenia samples. Schizophr Bull. 2000;26(4):903-12. PubMed PMID: 11087022.
3. Subramaniam M, Chong SA, Pek E. Diabetes mellitus and impaired glucose tolerance in patients with schizophrenia. Can J Psychiatry. 2003;48(5):345-7. PubMed PMID: 12866342.
4. van Winkel R, De Hert M, Van Eyck D, Hanssens L, Wampers M, Scheen A, et al. Prevalence of diabetes and the metabolic syndrome in a sample of patients with bipolar disorder. Bipolar Disord. 2008;10(2):342-8. DOI: 10.1111/j.1399-5618.2007.00520.x. PubMed PMID: 18271914.
5. Cohen D, Stolk RP, Grobbee DE, Gispen-de Wied CC. Hyperglycemia and diabetes in patients with schizophrenia or schizoaffective disorders. Diabetes Care. 2006;29(4):786-91. DOI: 10.2337/diacare.29.04.06.dc05-1261. PubMed PMID: 16567816.
6. American Diabetes Association. Standards of medical care in diabetes–2013. Diabetes Care. 2013;36 Suppl 1:S11-66. DOI: 10.2337/dc13-S011. PubMed PMID: 23264422.
7. National Heart, Lung, and Blood Institute. The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Bethesda (MD): National Institutes of Health; 2003 Dec. NIH Publication No.: 03-5233.
8. National Heart, Lung, and Blood Institute. Detection, evaluation, and treatment of high blood cholesterol in adults. Bethesda (MD): National Institutes of Health; 2001 May. NIH Publication No.: 01-3670.
9. Suvisaari J, Perälä J, Saarni SI, Härkänen T, Pirkola S, Joukamaa M, et al. Type 2 diabetes among persons with schizophrenia and other psychotic disorders in a general population survey. Eur Arch Psychiatry Clin Neurosci. 2008;258(3):129-36. DOI: 10.1007/s00406-007-0762-y. PubMed PMID: 17990051.
10. Enger C, Weatherby L, Reynolds RF, Glasser DB, Walker AM. Serious cardiovascular events and mortality among patients with schizophrenia. J Nerv Ment Dis. 2004;192(1):19-27. DOI: 10.1097/01.nmd.0000105996.62105.07. PubMed PMID: 14718772.
11. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). JAMA. 2014;311(5):507-20. DOI: 10.1001/jama.2013.284427. PubMed PMID: 24352797.
12. Stone NJ, Robinson JG, Lichtenstein AH, Bairey Merz CN, Blum CB, Eckel RH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American

Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014;63 (25 Pt B):2889-934. DOI: 10.1016/j.jacc.2013.11.002. PubMed PMID: 24239923.
13. Ryan MC, Collins P, Thakore JH. Impaired fasting glucose tolerance in first-episode, drug-naive patients with schizophrenia. Am J Psychiatry. 2003;160(2):284-9. DOI: 10.1176/appi.ajp.160.2.284. PubMed PMID: 12562574.
14. Casey DE. Metabolic issues and cardiovascular disease in patients with psychiatric disorders. Am J Med. 2005;118 Suppl 2:15S-22S. PubMed PMID: 15903291.
15. Spoelstra JA, Stolk RP, Cohen D, Klungel OH, Erkens JA, Leufkens HGM, et al. Antipsychotic drugs may worsen metabolic control in type 2 diabetes mellitus. J Clin Psychiatry. 2004;65(5):674-8. PubMed PMID: 15163254.
16. American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists, North American Association for the Study of Obesity. Consensus development conference on antipsychotic drugs and obesity and diabetes. Diabetes Care. 2004;27(2):596-601. PubMed PMID: 14747245.
17. Marder SR, Essock SM, Miller AL, Buchanan RW, Casey DE, Davis JM, et al. Physical health monitoring of patients with schizophrenia. Am J Psychiatry. 2004;161(8):1334-49. DOI: 10.1176/appi.ajp.161.8.1334. PubMed PMID: 15285957.
18. Connolly M. Lifestyle and physical health in schizophrenia. Adv Psychiatric Treat. 2005;11(2):125-32. DOI: 10.1192/apt.11.2.125.
19. Gothelf D, Falk B, Singer P, Kairi M, Phillip M, Zigel L, et al. Weight gain associated with increased food intake and low habitual activity levels in male adolescent schizophrenic inpatients treated with olanzapine. Am J Psychiatry. 2002;159(6):1055-7. DOI: 10.1176/appi.ajp.159.6.1055. PubMed PMID: 12042200.
20. Brown S, Birtwistle J, Roe L, Thompson C. The unhealthy lifestyle of people with schizophrenia. Psychol Med. 1999;29(3):697-701. PubMed PMID: 10405091.
21. Stahl SM. Antipsychotic agents. In: Stahl SM. Stahl's essential psychopharmacology. 4th ed. New York: Cambridge University Press; 2013:129-236.
22. Stahl SM. Antipsychotic agents. In: Stahl SM. Stahl's essential psychopharmacology. 3rd ed. New York: Cambridge University Press; 2008:327-451.
23. Newman SC, Bland RC. Mortality in a cohort of patients with schizophrenia: a record linkage study. Can J Psychiatry. 1991;36(4):239-45. PubMed PMID: 1868416.
24. Krosnick A, Wilson MG. A retrospective chart review of the clinical effects of atypical antipsychotic drugs on glycemic control in institutionalized patients with schizophrenia and comorbid diabetes mellitus. Clin Ther. 2005;27(3):320-6. DOI: 10.1016/j.clinthera.2005.02.017. PubMed PMID: 15878385.
25. Weiss AP, Henderson DC, Weilburg JB, Goff DC, Meigs JB, Cagliero E, et al. Treatment of cardiac risk factors among patients with schizophrenia and diabetes. Psychiatr Serv. 2006;57(8):1145-52. DOI: 10.1176/appi.ps.57.8.1145. PubMed PMID: 16870966.
26. Dixon LB, Kreyenbuhl JA, Dickerson FB, Donner TW, Brown CH, Wohlheiter K, et al. A comparison of type 2 diabetes outcomes among persons with and without severe mental illnesses. Psychiatr Serv. 2004;55(8):892-900. DOI: 10.1176/appi.ps.55.8.892. PubMed PMID: 15292539.
27. Nasrallah HA, Meyer JM, Goff DC, McEvoy JP, Davis SM, Stroup TS, et al. Low rates of treatment for hypertension, dyslipidemia and diabetes in schizophrenia: data from the CATIE schizophrenia trial sample at baseline. Schizophrenia Res. 2006;86(1-3):15-22. DOI: 10.1016/j.schres.2006.06.026. PubMed PMID: 16884895.
28. Kreyenbuhl J, Dickerson FB, Medoff DR, Brown CH, Goldberg RW, Fang LJ, et al. Extent and management of cardiovascular risk factors in patients with type 2 diabetes and serious mental illness. J Nerv Ment Dis. 2006;194(6):404-10. DOI: 10.1097/01.nmd.0000221177.51089.7d.