Identification of High-Risk Coronary Heart Disease Patients Receiving Atypical Antipsychotics: Single Low-Density Lipoprotein Cholesterol Threshold or Complex National Standard?

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Objective: Although psychiatric patients have a shortened life expectancy due to increased coronary heart disease (CHD), early identification of high-risk patients and targeted prevention for reduction of low-density lipoprotein (LDL) cholesterol are suboptimal in clinical care. We aimed to compare the accuracy of a single LDL-cholesterol intervention threshold of > 130 mg/dL (recently proposed for psychiatric patients) with that of the more complex LDL-cholesterol targets defined by the National Cholesterol Education Panel (NCEP). The study was performed in patients receiving second-generation antipsychotics (SGAs), a medication class associated with CHD risk.

Method: Three hundred fifty-six psychiatric patients receiving SGAs underwent standard LDL-cholesterol target assessments upon admission to the hospital between August 1, 2004, and March 1, 2005. The expert consensus–recommended > 130-mg/dL LDL-cholesterol threshold was used to determine false-negative results among patients with above-target NCEP-defined LDL cholesterol and false-positive results in the group with below-target NCEP-defined LDL cholesterol.

Results: The > 130-mg/dL threshold misclassified 15 (14.9%) of 101 high-risk patients and 31 (12.2%) of 255 low-risk patients (mean ± SD 10-year CHD risk: 23.1% ± 12.2% and 2.1% ± 2.2%, respectively). Results were similar in the 171 schizophrenia patients. Misclassified patients with above-target LDL cholesterol were more likely than correctly identified patients to have diabetes (p = .0002), greater 10-year CHD risk (p = .0006), higher age (p = .0008), metabolic syndrome (p = .0018), and past CHD events (p = .0025). No distinguishing factors for false-positive cases could be identified.

***Conclusions*:** The > 130-mg/dL LDL-cholesterol intervention threshold operated poorly in our psychiatric population. To avoid substandard care, NCEP-defined LDL-cholesterol targets should be used for the routine detection of psychiatric patients treated with antipsychotics who require interventions to decrease CHD risk.

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Patients with psychotic disorders die of cardiovascular disease at substantially higher rates than do individuals without mental illness of similar age, gender, socioeconomic class, and access to health care resources.[1,2] A recent study demonstrated a dramatic 25-year decrease in life expectancy among public mental health patients across 8 U.S. states compared to the general population, mostly driven by a markedly increased absolute risk for premature death from coronary heart disease (CHD).[3] Reasons for this significantly decreased longevity are related to increased prevalence rates of modifiable risk factors for CHD, namely obesity, metabolic syndrome, diabetes mellitus, dyslipidemia, and smoking, all of which are 1.5-fold to 5-fold higher in patients with severe mental illness compared to the general population.[4–6] Alarmingly, the rates of metabolic syndrome[7] and CHD mortality[8] compared to the general population are greatest in patients younger than 45 and 49 years, respectively. Moreover, there has been an increasing recognition that antipsychotic treatment, especially the growing use of second-generation antipsychotics (SGAs), is related to the increased rates of obesity, metabolic syndrome, diabetes mellitus, dyslipidemia, and CHD.[4,9–12]

Unfortunately, the high prevalence of metabolic abnormalities in the mentally ill occurs in the context of insufficient monitoring[13–15] and management[16,17] of these abnormalities in clinical practice, contributing further to the shortened life expectancy from CHD in psychiatric populations. This reality has prompted recommendations for the monitoring and treatment of weight gain as well as the components of the metabolic syndrome in psychiatric populations receiving antipsychotics, with the goal being to improve health outcomes in the mentally ill.

A recent review[18] of published national and international guidelines and recommendations found a general consensus regarding the need for structured and proactive monitoring, as well as facilitation of access to appropriate clinical care for relevant abnormalities. Areas of dissent identified by the authors included the selection of psychiatric patients requiring monitoring, duration of monitoring intervals, utility of different measures of glucose metabolism, and the threshold at which switching to a lower-risk antipsychotic should be considered. Taken together, these guidelines focus on the assessment of the 5 parameters of the metabolic syndrome at baseline and at regular follow-up intervals: (1) body weight and waist circumference, (2) blood pressure, (3) fasting blood glucose, (4) high-density lipoprotein (HDL) cholesterol, and (5) triglyceride levels.[18]

Differences exist among these guidelines and recommendations[18] regarding the need for fasting blood glucose assessments versus allowing for random glucose and/or hemoglobin A_{1c} assessments, which are considered neither valid nor reliable screening tests for hyperglycemia and risk for diabetes. Moreover, the proposed time points varied widely across these guidelines. For example, recommendations for the measurement of weight ranged from "each clinical visit" to "quarterly." Recommendations for blood pressure assessments ranged from "quarterly" or "biannually" to "at 3 months and annually thereafter" to "as needed" or to not being mentioned at all. Proposed blood sugar assessments ranged from time points "at 6 and 12 weeks with quarterly measurements thereafter" to assessments "at 3 or 4 months and biannually or annually thereafter." Finally, recommended frequencies of blood lipid measurements ranged from "biannually" or "every 2 years" to measurement "at 3 months and every 5 years thereafter."[18] This variation points to the need for studies of the time course of metabolic abnormalities in specific patient and treatment groups, studies that could empirically guide the rational selection of measurement intervals.

As indicated above, available recommendations for the metabolic monitoring of psychiatric patients call for the assessment of hypertriglyceridemia, a common metabolic abnormality in patients receiving SGAs.[4,9–12,16] Importantly, however, triglycerides contribute to an excess of atherogenic lipoprotein cholesterol particles, which were recognized as central by the National Cholesterol Education Program (NCEP) when creating the current standards for the recognition and management of CHD risk.[19] The NCEP identified elevated levels of low-density lipoprotein (LDL) cholesterol, which contribute to the atherogenic toxicity of abnormal lipid levels, as the major cause of CHD and postulated elevated LDL cholesterol as the primary target of therapeutic interventions to reduce CHD. Individualized LDL-cholesterol therapeutic targets of < 100 mg/dL, < 130 mg/dL, and < 160 mg/dL were defined that are subsequently established for each patient by taking into account medical history, major risk factors for CHD, and the calculated 10-year risk for CHD events.[19] The NCEP guidelines were based on evidence produced by randomized trials of statins (for a review, see reference 20). Moreover, the LDL-cholesterol target of < 100 mg/dL for high-risk patients and those with diabetes has been validated in trials published since 2001.[20,21] On the other hand, controlled lipid-lowering drug trials have not been conducted in psychiatric populations.

A substantial number of SGA-treated patients have above-target LDL cholesterol but do not receive appropriate interventions to reduce the risk of CHD.[17] The issue of monitoring and prevention of metabolic risk factors was discussed by an authoritative group of psychopharmacologists at The Mount Sinai Conference on the Pharmacotherapy of Schizophrenia in October 2002. In the consensus panel recommendation published in the widely read journal of the American Psychiatric Association in 2004,[22] these experts recommended, regarding LDL-cholesterol monitoring and management, a referral to a primary care provider or dietary and pharmacologic interventions for schizophrenia patients with LDL cholesterol > 130 mg/dL, proposing this value as a single and simplified threshold that incorporates presence of a severe mental illness as a risk factor for CHD. This threshold was selected after panel deliberation following expert advice and was based on national guidelines published in 1988.[23]

A single intervention threshold of > 130 mg/dL is substantially different from the U.S. standard,[19] which allows for < 160 mg/dL for low-risk patients but requires LDL-cholesterol levels of less than 100 mg/dL for very high-risk patients. In view of suboptimal monitoring[13–15] and inappropriate intervention rates[16,17] for metabolic disturbances in patients receiving antipsychotics, the proposal of a different, simplified threshold could be justified if the recommendation would lead to improved care of mentally ill patients. However, no such evidence is currently available to support this deviation from the NCEP national standard. In addition, the expert recommendations did not take into account the existence of subgroups of patients with past medical history of CHD, diabetes, dyslipidemia, or arterial hypertension (all prevalent among the severely mentally ill) who very likely require

LDL-cholesterol levels below 130 mg/dL for effective risk reduction.

Therefore, the aim of the current study was to test the accuracy of the proposed single intervention threshold of LDL cholesterol > 130 mg/dL compared to the tripartite NCEP standard in a cohort of psychiatric patients receiving SGAs.

METHOD

Setting and Patient Population

Data were collected from the records of 458 psychiatric inpatients treated with SGAs at the time of admission to a 208-bed psychiatric hospital. The sample was randomly selected from 1420 consecutive admissions between August 1, 2004, and March 1, 2005. One hundred two subjects were excluded from this report, leading to a total sample of 356 patients with complete data. Reasons for exclusion were (1) age younger than 20 years or older than 79 years (N = 49) and (2) missing data that were required to calculate the 10-year risk for CHD and the LDL-cholesterol target (N = 53). The participants were representative of a population with severe and unstable psychiatric disorders. The Institutional Review Board of the North Shore–Long Island Jewish Health System approved the study.

Laboratory Tests

The fasting lipid levels were measured spectrophotometrically with the Chemistry Immuno Analyzer, Model AU2700 (Olympus America, Melville, N.Y.).

Calculation of the LDL-Cholesterol Therapeutic Target

We first assessed the past medical history for CHD or CHD-equivalent disorders (i.e., diabetes mellitus, peripheral arterial disease, abdominal aortic aneurysm, and symptomatic carotid artery disease). This assessment was followed by a determination of the number of major risk factors for CHD, i.e., age greater than 44 years for men and 54 years for women, cigarette smoking, hypertension (blood pressure ≥ 140/90 or receiving treatment with antihypertensive medication), HDL cholesterol < 40 mg/dL, or history of premature CHD in first-degree relatives (men younger than 55 years and women younger than 65 years). High-density-lipoprotein cholesterol levels of ≥ 60 mg/dL removed 1 risk factor from the total count. As per NCEP definition, HDL-cholesterol cutoffs are similar for men and women in the assessment of CHD risk.[19]

Finally, we calculated the 10-year risk of CHD, expressed as a percentage. For nondiabetic patients, the 10-year CHD risk was calculated with the NCEP version of the Framingham score, a gender-specific instrument that assigns specific points for age, HDL cholesterol, and systolic blood pressure, as well as total cholesterol and cigarette smoking, in an age-dependent fashion.[19] A total score of 12–14 points in men and 20–22 points in women is equivalent to a 10% to < 20% 10-year CHD risk. A total score of ≥ 15 points in men and ≥ 23 points in women is equivalent to a ≥ 20% CHD risk over the next 10 years.[19] For patients with diabetes, a version of the Framingham algorithm was used that assigns points for the presence of diabetes.[24]

The LDL-cholesterol targets for therapeutic intervention are established according to the calculated 10-year risk of CHD, number of risk factors, and/or past medical history detailed above[19] and consist of the following 3 risk categories: (1) < 100 mg/dL for patients with CHD, CHD equivalents, or a 10-year CHD risk > 20%; (2) < 130 mg/dL for patients with ≥ 2 risk factors or a 10-year CHD risk of 10%–20%; and (3) < 160 mg/dL for patients with 0–1 risk factors and a 10-year CHD risk of < 10%.[19] These cutoff values were compared with each patient's admission LDL cholesterol to identify individuals with above-target LDL cholesterol.

Data Analyses

We identified all patients in the entire sample who were misclassified by the single intervention threshold of > 130 mg/dL, i.e., false-negative in the NCEP-defined, above-target group and false-positive in the NCEP-defined, below-target group. Univariate analyses were used to compare the demographic and clinical variables of patients correctly and incorrectly classified in each group. The accuracy of the single LDL-cholesterol threshold was also assessed after exclusion of patients with overt diabetes and those treated with lipid-lowering, antihypertensive, or hypoglycemic drugs, as these are high-risk patients in whom treatment could have affected the measured LDL cholesterol.

RESULTS

On the basis of fasting lipid profiles measured on admission, 101 (28.4%) of the 356 psychiatric patients had above-target LDL cholesterol. In 15 (14.9%) of these 101 patients, the > 130-mg/dL threshold produced false-negative results, i.e., these were high-risk patients with LDL cholesterol lower than 130 mg/dL but higher than the NCEP therapeutic target of < 100 mg/dL. Conversely, the > 130-mg/dL threshold produced false-positive results in 31 (12.2%) of the 255 patients with below-target LDL cholesterol, i.e., these were low-risk patients with LDL cholesterol > 130 mg/dL but still within the NCEP therapeutic target of < 160 mg/dL. Patients with false-negative and false-positive results based on the > 130-mg/dL threshold had a mean ± SD 10-year CHD risk of 23.1% ± 12.2% and 2.1% ± 2.2%, respectively (Table 1).

In the 171 patients with a clinical diagnosis of schizophrenia (which was the focus of the Mount Sinai conference[22]), the single > 130-mg/dL threshold produced

Table 1. Demographic and Clinical Characteristics of High Coronary Heart Disease (CHD)-Risk Patients and Low CHD-Risk Patients Identified by the Single Low-Density Lipoprotein Cholesterol Threshold of > 130 mg/dL

Characteristic	Total (N = 356)	High CHD Risk Identified by the > 130-mg/dL Threshold (N = 86)	High CHD Risk Not Identified by the > 130-mg/dL Threshold (N = 15)	p Value	Low CHD Risk Identified by the > 130-mg/dL Threshold (N = 224)	Low CHD Risk Not Identified by the > 130-mg/dL Threshold (N = 31)	p Value
Demographic and medical variables							
Age, mean ± SD, y	43.0 ± 14.9	45.6 ± 14.5	59.9 ± 17.0	**.0008***	41.0 ± 14.9	42.5 ± 14.9	.60
Sex, male, N (%)	197 (55.3)	54 (62.8)	12 (80.0)	.20	119 (53.1)	12 (38.7)	.13
Race, white, N (%)	236 (67.4)[a]	65 (78.3)[b]	10 (66.7)	.96	141 (63.5)[c]	20 (66.7)[d]	.74
Smoker, N (%)	194 (54.5)	56 (65.1)	8 (53.3)	.38	115 (51.3)	15 (48.4)	.76
History/presence of diabetes, N (%)	50 (14.0)	11 (12.8)	8 (53.3)	**.0002***	30 (13.4)	1 (3.2)	.10
History of coronary artery disease, N (%)	29 (8.1)	6 (7.0)	5 (33.3)	**.0025***	16 (7.1)	2 (6.5)	.89
Body mass index, mean ± SD, kg/m^2	28.9 ± 6.7	29.7 ± 6.0	31.1 ± 6.6	.40	28.4 ± 6.9	29.1 ± 6.7	.62
Waist circumference, mean ± SD, cm[e]	92.5 ± 14.1	92.4 ± 15.1	101.3 ± 11.3	.068	92.1 ± 13.8	91.4 ± 14.4	.89
Primary psychiatric diagnosis, N (%)							
Schizophrenia	171 (48.0)	41 (47.7)	6 (40.0)	.58	111 (49.6)	13 (41.9)	.43
Bipolar disorder	72 (20.2)	16 (18.6)	3 (20.0)	.90	44 (19.6)	9 (29.0)	.23
Depressive disorder	74 (20.8)	22 (25.6)	4 (26.7)	.93	42 (18.8)	6 (19.4)	.94
Substance use disorder	17 (4.8)	2 (2.3)	1 (6.7)	.36	14 (6.3)	0 (0.0)	.15
Dementia	9 (2.5)	5 (5.8)	1 (6.7)	.90	2 (0.9)	1 (3.2)	.26
Other	13 (3.7)	0 (0.0)	0 (0.0)	-	11 (4.9)	2 (6.5)	.71
Antipsychotic treatment, N (%)							
Olanzapine	114 (32.0)	31 (36.0)	7 (46.7)	.43	64 (28.6)	12 (38.7)	.25
Quetiapine	105 (29.5)	29 (33.7)	5 (33.3)	.98	66 (29.5)	5 (16.1)	.12
Risperidone	101 (28.4)	19 (22.1)	2 (13.3)	.44	71 (31.7)	9 (29.0)	.76
Aripiprazole	33 (9.3)	7 (8.1)	0 (0.0)	.25	24 (10.7)	2 (6.5)	.46
Ziprasidone	30 (8.4)	6 (7.0)	2 (13.3)	.40	19 (8.5)	3 (9.7)	.82
Clozapine	27 (7.6)	6 (7.0)	0 (0.0)	.29	16 (7.1)	5 (16.1)	.088
First-generation antipsychotic	18 (5.1)	5 (5.8)	1 (6.7)	.90	10 (4.5)	2 (6.5)	.62
Antipsychotic polytherapy	70 (19.7)	16 (18.6)	2 (13.3)	.62	44 (19.6)	8 (25.8)	.42
Nonantipsychotic treatment, N (%)							
Anxiolytics/hypnotics	182 (51.1)	47 (54.7)	7 (46.7)	.57	112 (50.0)	16 (51.6)	.87
Antidepressants	166 (46.6)	48 (55.8)	7 (46.7)	.51	94 (42.0)	17 (54.8)	.17
Mood stabilizers	129 (36.2)	26 (30.2)	4 (26.7)	.78	90 (40.2)	9 (29.0)	.23
Anticholinergics	30 (8.4)	8 (9.3)	0 (0.0)	.22	18 (8.0)	4 (12.9)	.37
Lipid-lowering drugs	49 (13.8)	11 (12.8)	6 (40.0)	**.0093***	31 (13.8)	1 (3.2)	.094
Hypoglycemic drugs	21 (5.9)	4 (4.7)	3 (20.0)	**.031***	14 (6.3)	0 (0.0)	.15
Antihypertensive drugs	54 (15.2)	13 (15.1)	6 (40.0)	**.023***	34 (15.2)	1 (3.2)	.070
Metabolic parameters							
Presence of metabolic syndrome, N (%)	136 (38.2)	43 (50.0)	14 (93.3)	**.0018***	72 (32.1)	7 (22.6)	.18
No. of metabolic syndrome criteria, mean ± SD	2.0 ± 1.3	2.4 ± 1.3	3.7 ± 0.8	**.0004***	1.8 ± 1.4	1.4 ± 1.1	.28
10-year CHD risk, mean ± SD[e]	5.8 ± 7.1	9.6 ± 9.2	23.1 ± 12.2	**.0006***	3.7 ± 6.2	2.1 ± 2.2	.24

[a]In total, 6 patients were without ethnic/racial information.
[b]In this group, 3 patients were without ethnic/racial information.
[c]In this group, 2 patients were without ethnic/racial information.
[d]In this group, 1 patient was without ethnic/racial information.
[e]p Value was adjusted for sex.
*p Values in boldface are significant at p < .05.

6 (12.8%) of 47 false-negative results and 13 (10.5%) of 124 false-positive results. On the other hand, in the 241 nondiabetic patients who were not receiving antihyperglycemic, lipid-lowering, or antihypertensive treatment, the single > 130-mg/dL threshold produced only 1 (1.6%) of 64 false-negative results but produced 28 (15.8%) of 177 false-positive results for identifying patients with above-target LDL cholesterol.

Comparing misclassified patients with above-target LDL cholesterol (i.e., false-negative) with correctly identified patients in the entire sample in univariate analyses, misclassified patients were more likely than correctly identified patients to have diabetes (p = .0002), more metabolic syndrome criteria (p = .0004), greater 10-year CHD risk (p = .0006), higher age (p = .0008), metabolic syndrome (p = .0018), past CHD events (p = .0025), and treatment with lipid-lowering (p = .0093), antihypertensive (p = .023), or hypoglycemic (p = .031) drugs (Table 1). By contrast, the false-positive patients who were in the below-target group did not differ in any of their demographic and clinical features from those that were classified correctly as being below-target by NCEP standards.

DISCUSSION

This cross-sectional study indicates that following the recommendation to use a single LDL-cholesterol threshold of > 130 mg/dL in psychiatric patients results in infe-

rior performance in the identification of high-risk CHD patients compared to using the national standard set by the NCEP guidelines. The application of this single-threshold method would have deprived 15 of 101 seriously mentally ill patients of therapy to reduce their high risk of CHD because they had LDL-cholesterol levels lower than the > 130-mg/dL threshold but higher than their < 100-mg/dL NCEP target.

Furthermore, following the single-threshold recommendation would have increased the cost of care through unnecessary referrals in 31 of 255 patients who were at low risk for CHD, having NCEP-defined LDL-cholesterol targets of < 160 mg/dL. Performance of the single LDL-cholesterol threshold of > 130 mg/dL was similarly suboptimal in the subgroup of 171 patients with a clinical diagnosis of schizophrenia. Although the false-negative rate of the single > 130-mg/dL LDL-cholesterol threshold was reduced considerably in patients without diabetes and not receiving lipid-lowering, antihypertensive, or antihyperglycemic drugs, the false-positive rate did not improve.

Thus, it is best clinical practice, and the most cost-effective, to follow the NCEP standard for the general population and to calculate individual LDL-cholesterol targets for each patient. This calculation can be achieved by taking a brief history of simple demographic variables (i.e., age and sex) and CHD risk factors (i.e., past medical history for CHD or CHD-equivalent disorders, family history of premature cardiac death, smoking, and arterial hypertension) and routinely reviewing HDL-cholesterol levels in all patients. For calculation of the 10-year CHD risk, a convenient, web-based calculator (NCEP risk assessment tool based on information from the Framingham Heart Study, available at: www.hp2010.nhlbihin.net/atpiii/calculator.asp) can assist in the rapid calculation of LDL-cholesterol patient targets.

Although a simple method for identifying patients at high risk of CHD is clearly desirable given psychiatrists' suboptimal performance in referring or treating at-risk patients,[16,22] our data indicate that the proposed Mount Sinai consensus recommendation does not adequately answer this need, at least in severely mentally ill patients requiring hospitalization. We recently reported that only 32% of psychiatric patients with above-target LDL cholesterol received appropriate interventions during their hospital stays (mean stay = 28 days) and that outpatient referrals to primary care providers or medical subspecialists were not initiated in any of these patients.[17]

Other studies[25,26] also demonstrated suboptimal medical care by primary care providers and medical specialists in a large cohort of mentally ill patients with diabetes or coronary artery disease events. In one study[25] of patients with diabetes, 33.4% of patients with mental health conditions had no LDL-cholesterol test done and 53.5% had poor lipid control. These findings support evidence that the significant excess in mortality observed in psychiatric patients treated for CHD events is largely due to the underutilization of standard therapeutic procedures and targeted drug interventions to reduce CHD mortality rather than to demographic and clinical factors.[26]

In this context, the data presented here highlight the need for the audit and study of recommendations produced by expert consensus in order to test the assumptions and attempt to turn recommendations into evidence-based guidelines or to reject them.[27] The attempt by the Mount Sinai conference at simplifying decision-making meant a departure from the national standard. Moreover, the simplified threshold performed suboptimally compared to the national standard. The departure from established national standards without validation and/or with suboptimal performance runs the risk of creating different standards of provider knowledge and applied management strategies and of reducing the quality of care delivered to the mentally ill. Therefore, we believe that the single > 130-mg/dL threshold does not contribute to the efficient screening of psychiatric patients for CHD risk nor to treatment planning for its reduction.

In view of a greater prevalence of CHD risk factors, insufficient primary and secondary prevention, and premature death from CHD in the severely mentally ill, psychiatric care providers are required to treat psychiatrically ill patients within the framework of an integrated mental and medical health model.[6] This approach is particularly important, as psychotropic treatments can aggravate CHD risk and since all too often primary care is inactive in this vulnerable population.

Research should be conducted to identify the most cost-effective strategies to reduce CHD risk in mentally ill patients as well as in subgroups at greatest risk, in whom preventive strategies may need to be intensified to achieve the desired risk reduction. Efforts to simplify psychiatrists' obligation to provide high-quality preventive care to their patients need to conform to the national standard in order to decrease suboptimal health care of the mentally ill. Comprehensive educational programs to improve psychiatrists' knowledge and skills in assessing and addressing the CHD risk of their patients are required. Performance-improvement projects are needed that engage mental health providers together with primary care physicians in the orchestration of their patients' physical health care in addition to addressing their mental illness needs.

Initiatives should target the dissemination, implementation, and facilitation of efficacious strategies to reduce the CHD risk and mortality in the seriously mentally ill. As in the general population, these strategies should include structured approaches to routine monitoring, interdisciplinary collaborations, therapeutic lifestyle changes (smoking cessation, weight reduction, dietary changes to reduce saturated fats, and increased aerobic activities),

and treatments to control dyslipidemia, obesity, glucose intolerance, and arterial hypertension. Studies should investigate which dissemination, implementation, and facilitation methods are most effective in improving proactive primary and secondary preventive management behaviors in broad-based clinical practice settings.

Drug names: aripiprazole (Abilify), clozapine (FazaClo, Clozaril, and others), olanzapine (Zyprexa), quetiapine (Seroquel), risperidone (Risperdal), ziprasidone (Geodon).

REFERENCES

1. Osby U, Correia N, Brandt L, et al. Time trends in schizophrenia mortality in Stockholm County, Sweden: cohort study. BMJ 2000 Aug;321 (7259):483–484
2. Enger C, Weatherby L, Reynolds RF, et al. Serious cardiovascular events and mortality among patients with schizophrenia. J Nerv Ment Dis 2004; 192:19–27
3. Colton CW, Manderscheid RW. Congruencies in increased mortality rates, years of potential life lost, and causes of death among public mental health clients in eight states. Prev Chronic Dis 2006 Apr;3(2):A42
4. Newcomer JW. Second-generation (atypical) antipsychotics and metabolic effects: a comprehensive literature review. CNS Drugs 2005;19 (suppl 1):1–93
5. Meyer J, Koro CE, L'Italien GJ. The metabolic syndrome and schizophrenia: a review. Int Rev Psychiatry 2005 Jun;17(3):173–180
6. Correll CU. Balancing efficacy and safety in treatment with antipsychotics. CNS Spectr 2007;12(10 suppl 17):12–20,35
7. De Hert M, van Winkel R, Van Eyck D, et al. Prevalence of diabetes, metabolic syndrome and metabolic abnormalities in schizophrenia over the course of the illness: a cross-sectional study. Clin Pract Epidemol Ment Health 2006 Jun;2:14
8. Osborn DP, Levy G, Nazareth I, et al. Relative risk of cardiovascular and cancer mortality in people with severe mental illness from the United Kingdom's General Practice Research Database. Arch Gen Psychiatry 2007 Feb;64(2):242–249. Erratum in: Arch Gen Psychiatry 2007 Jun;64(6):736
9. Henderson DC, Nguyen DD, Copeland PM, et al. Clozapine, diabetes mellitus, hyperlipidemia, and cardiovascular risks and mortality: results of a 10-year naturalistic study. J Clin Psychiatry 2005 Sep;66(9): 1116–1121
10. Cohn T, Prud'homme D, Streiner D, et al. Characterizing coronary heart disease risk in chronic schizophrenia: high prevalence of the metabolic syndrome. Can J Psychiatry 2004;49:753–760
11. Goff DC, Sullivan LM, McEvoy JP, et al. A comparison of ten-year cardiac risk estimates in schizophrenia patients from the CATIE study and matched controls. Schizophr Res 2005 Dec;80(1):45–53
12. Correll CU, Frederickson AM, Kane JM, et al. Metabolic syndrome and the risk of coronary heart disease in 367 patients treated with second-generation antipsychotic drugs. J Clin Psychiatry 2006 Apr;67(4): 575–583
13. Buckley PF, Miller DD, Singer B, et al. Clinicians' recognition of the metabolic adverse effects of antipsychotic medications. Schizophr Res 2005 Nov;79(2–3):281–288
14. Newcomer JW, Nasrallah HA, Loebel AD. The Atypical Antipsychotic Therapy and Metabolic Issues National Survey: practice patterns and knowledge of psychiatrists. J Clin Psychopharmacol 2004 Oct;24 (5 suppl 1):S1–S6
15. Weissman EM, Zhu CW, Schooler NR, et al. Lipid monitoring in patients with schizophrenia prescribed second-generation antipsychotics. J Clin Psychiatry 2006 Sep;67(9):1323–1326
16. Nasrallah HA, Meyer JM, Goff DC, et al. Low rates of treatment for hypertension, dyslipidemia and diabetes in schizophrenia: data from the CATIE schizophrenia trial sample at baseline. Schizophr Res 2006 Sep;86(1–3):15–22
17. Correll CU, Harris JL, Pantaleon Moya RA, et al. Low-density lipoprotein cholesterol in patients treated with atypical antipsychotics: missed targets and lost opportunities. Schizophr Res 2007;92:103–107
18. Cohn TA, Sernyak MJ. Metabolic monitoring for patients treated with antipsychotic medications. Can J Psychiatry 2006 Jul;51(8):492–501
19. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of The Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA 2001;285(19):2486–2497
20. Hennekens CH, Hollar D, Eidelman RS, et al. Update for primary healthcare providers: recent statin trials and revised National Cholesterol Education Program III guidelines. MedGenMed 2006 Feb;8(1):54
21. Grundy SM, Cleeman JI, Merz CN, et al. Coordinating Committee of the National Cholesterol Education Program. Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III Guidelines. J Am Coll Cardiol 2004;44(3):720–732
22. Marder SR, Essock SM, Miller AL, et al. Physical health monitoring of patients with schizophrenia. Am J Psychiatry 2004 Aug;161(8): 1334–1349
23. Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. The Expert Panel. Arch Intern Med 1988 Jan;148(1):36–69
24. Wilson PW, D'Agostino RB, Levy D, et al. Prediction of coronary heart disease using risk factor categories. Circulation 1998;97:1837–1847
25. Frayne SM, Halanych JH, Miller DR, et al. Disparities in diabetes care: impact of mental illness. Arch Intern Med 2005;165(22):2631–2638
26. Druss BG, Bradford WD, Rosenheck RA, et al. Quality of medical care and excess mortality in older patients with mental disorders. Arch Gen Psychiatry 2001;58:565–572
27. Foy R, Eccles MP, Jamtvedt G, et al. What do we know about how to do audit and feedback? pitfalls in applying evidence from a systematic review. BMC Health Serv Res 2005 Jul;5:50