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SUPPLEMENT

Impact of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Study on Clinical Practice

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Metabolic Findings From the CATIE Trial and Their Relation to Tolerability

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ABSTRACT

The overall effectiveness of antipsychotics for the management of schizophrenia is restricted by their side-effect profiles, particularly over an extended treatment period. Intolerable side effects can reduce patient adherence to medication and often lead to treatment discontinuation. Some side effects that result from antipsychotic use are precursors to the metabolic syndrome, which is prevalent among individuals with schizophrenia and represents a significant source of cardiovascular risk. The Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) schizophrenia study assessed the efficacy of the atypical antipsychotics olanzapine, quetiapine, risperidone, and ziprasidone relative to the conventional drug perphenazine. Additional assessments included the metabolic effects of these agents in patients with schizophrenia and the incidence of negative side effects. No significant differences were found between treatment groups for time to discontinuation due to intolerability, but the rates of side effects significantly differed ($P=.04$). For metabolic parameters, olanzapine was associated with greater and significant adverse effects on weight, lipids, and glucose metabolism versus the other antipsychotics tested. The CATIE results show that important distinctions exist among currently available atypical antipsychotics. Physicians should be aware of the propensity of these drugs to increase the risks of cardiovascular disease and diabetes in treated patients and tailor individual treatment decisions accordingly. This article highlights the metabolic findings from the CATIE schizophrenia study, and explores the differences shown by atypical antipsychotics, with regard to metabolic side effects that increase cardiovascular risk.

FOCUS POINTS

- Patients with schizophrenia are at higher risk for the metabolic syndrome, diabetes, and cardiac disease than the general population.
- Atypical antipsychotics have metabolic side effects that increase cardiovascular risk in treated patients.
- Results of the CATIE trial demonstrated that olanzapine was associated with a greater number of significant adverse metabolic effects than the other antipsychotics.
- Significant differences exist among atypical antipsychotics with respect to metabolic effects.
- Patients with schizophrenia are undertreated for dyslipidemia, hypertension, and impaired glucose functioning. Baseline data from the CATIE trial reveals many subjects were not receiving medication for their metabolic disorders, including 45% of those with diabetes, 62% of those with hypertension, and 89% of those with dyslipidemia.

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INTRODUCTION

The metabolic syndrome (also known as Syndrome X, the insulin resistance syndrome, or dysmetabolic syndrome)[1,2] is a clustering of physical abnormalities related to body weight, glucose intolerance, dyslipidemia, and hypertension, and is a notable risk factor for coronary heart disease (CHD) and diabetes mellitus (DM).[1-3] According to the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III), the metabolic syndrome can be identified by the presence of at least three abnormal values for the following risk factors: abdominal or visceral obesity, as measured by waist circumference; triglycerides; high-density lipoprotein (HDL) cholesterol; blood pressure; and/or fasting blood glucose level (Table 1).[4] The World Health Organization (WHO)[5] and the American Association of Clinical Endocrinologists (AACE)[6] have also developed clinical criteria for diagnosis which are similar to those outlined by NCEP but differ mainly in their stance on the criterion of insulin resistance.[1,3] For example, ATP III guidelines do not require a diagnosis of insulin resistance, although most patients meeting their metabolic syndrome diagnosis will be insulin resistant. Alternatively, WHO guidelines require insulin resistance in the diagnosis of metabolic syndrome. The AACE guidelines incorporate both WHO and ATP III criteria, but do not have a defined number of risk factors, and defer to clinical judgment for a diagnosis of metabolic syndrome.[1]

In addition to differences in the requirements for diagnosing the metabolic syndrome, there is even disagreement over the name itself. A joint report of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes, points to the lack of consensus between practitioners in diagnosing the condition, as well as a lack of usefulness in defining the cluster of conditions as a syndrome.[5] They state that until there is better justification for the criteria to be used in diagnosis, the separate components should continue to be considered as strong risk factors for cardiovascular disease (CVD) and diabetes, and as such, treated individually.[5]

NCEP ATP III criteria for the diagnosis of metabolic syndrome are considered practical for physicians, as a diagnosis can be made during the course of a routine clinical assessment and the definition is the one most often used by US prevalence studies. WHO and AACE include impaired glucose tolerance, as detected by glucose tolerance test or 2-hour post-glucose challenge, as a risk factor for metabolic syndrome. This was not required by ATP III because of added cost and inconvenience in clinical practice.[1]

Recently, the definition for the metabolic syndrome has been revised. According to the International Diabetes Federation (IDF), the definition is similar to NCEP ATP III with two exceptions. IDF criteria now require a high waist circumference and lower ethnic-specific waist circumference cut points.[7] The American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI) recently modified the ATP III metabolic syndrome diagnostic criteria.[3] As in ATP III, three of five risk factors are required for diagnosis. The AHA/NHLBI modifications include a lowering of waist circumference cutpoints in ethnic groups or individuals at risk for insulin resistance; adding the criteria of drug treatment for abnormal triglyceride, HDL-C, or blood pressure levels; clarification of the definition of high blood pressure; and a reduction in threshold for fasting glucose from 110 mg/dL to 100 mg/dL.[3]

TABLE 1.
Clinical Identification of the Metabolic Syndrome

Risk Factor	*Defining Level*
Abdominal obesity	Waist circumference*
Men	>102 cm (>40 in)
Women	>88 cm (>35 in)
Triglycerides	≥150 mg/dL
HDL cholesterol	
Men	<40 mg/dL
Women	<50 mg/dL
Blood pressure	≥130/≥85 mm Hg
Fasting glucose	≥100 mg/dL

* The ATP III panel did not find adequate evidence to recommend routine measurement of insulin resistance (eg, plasma insulin), proinflammatory state (eg, high-sensitivity C-reactive protein), or prothrombotic state (eg, fibrinogen or PAI-1) in the diagnosis of the metabolic syndrome.

1 Some male persons can develop multiple metabolic risk factors when the waist circumference is only marginally increased, eg, 94-102 cm (37-39 in). Such persons may have a strong genetic contribution to insulin resistance. They should benefit from changes in life habits, similarly to men with categorical increases in waist circumference.

HDL=high-density lipoprotein; ATP III=Adult Treatment Panel III; PAI-1=plasminogen activator inhibitor type 1

Reprinted with permission from: Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation*. 2005;112(17):2735-2752.

Although the medical community has not agreed upon the precise pathophysiology of the metabolic syndrome, it is generally understood that the primary clinical outcome is CVD,[1,8] the risk of which is increased when DM is also present.[1] However, some recent studies indicate that the metabolic syndrome is a stronger predictor of type 2 diabetes then of CVD.[9]

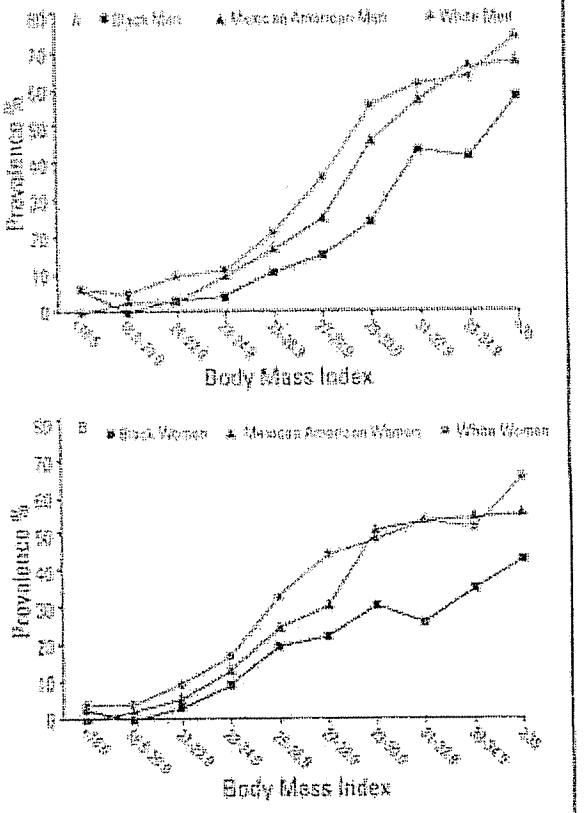
A recently published retrospective analysis of data from the United States National Health and Nutrition Examination Survey 1999–2002 (NHANES 1999–2002) found an overall metabolic syndrome prevalence of 34.5% in adults based on the NCEP definition and an overall prevalence of 39% based on the IDF definition.[10] In addition, the prevalence of the metabolic syndrome increases with increasing age using both of these diagnostic guidelines.[10] In men 60–69 years of age the age-adjusted prevalence using the NCEP and IDF definitions, respectively, were 52% and 58%; corresponding prevalences for women 60–69 years of age were 61% and 69%.[10] Notably, when the IDF criteria for waist circumference were combined with the NCEP definition, the resultant values were similar to those using the IDF definition alone.[10]

The metabolic syndrome was also more common in those with higher body mass index (BMI) in this analysis, with the prevalence increasing significantly ($P<.001$) with increasing BMI (Figure).[10] As rates of obesity in the US continue to soar, the prevalence of metabolic syndrome is expected to substantially increase as well.[10]

THE METABOLIC SYNDROME IN INDIVIDUALS WITH SCHIZOPHRENIA

The prevalence's of metabolic disturbances and CVD in patients with schizophrenia have been reported to be higher than those in the general population.[13,14] A recent comparison of subset data from the Canadian Heart Study with published crude rates in the US adult population reported a prevalence of the metabolic syndrome (NCEP criteria) in 42.6% of men and 48.5% of women with schizophrenia or schizoaffective disorder.[15] Some have suggested that negative symptoms of schizophrenia can contribute to poor lifestyle habits, such as limited physical activity or unhealthy diet, that promote weight gain,[16] which itself has been linked to increased risks of DM, dyslipidemia, and CHD.[13,14] In addition to the possibility that symptoms of schizophrenia might contribute to an increased risk for metabolic disorders, it has also been hypothesized that schizophrenia and other psychiatric disorders might carry an inherent risk for elevated lipid levels, DM, and CHD. In an extensive meta-analysis, Newcomer[13] points to studies, some performed in drug-naïve patients with schizophrenia, others in psychiatric patients with age, ethnicity, and sex-matched controls from the general population, whose outcome suggests a link between mental disorders such as schizophrenia and DM, dyslipidemia, and other metabolic disturbances. Further research is needed, however, in order to determine whether

FIGURE.
Prevalence of the Metabolic Syndrome by Body Mass in Men and Women



The prevalence of the metabolic syndrome by body mass index is calculated as weight in kilograms divided by the square of height in meters) in men (A) and women (B).

Reprinted with permission from: Park Y-W, Zhu S, Palaniappan L, Heshka S, Carnethon MR, Heymsfield SB. The metabolic syndrome: prevalence and associated risk factor findings in the US population from the Third National Health and Nutrition Examination Survey, 1988–1994. *Arch Intern Med.* 2003;163(4):427–436.

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this increased risk is a result of the symptoms of the disease, the disease itself, or possibly an underlying genetic factor.[13]

Atypical antipsychotics, the mainstay of schizophrenia treatment, have metabolic effects that are of particular concern.[3,15,16,23] Although the side-effect profiles of the atypicals are generally better than those of conventional antipsychotics, some atypical antipsychotics have been associated with weight gain and obesity, DM, increased triglycerides, and decreased HDL cholesterol.[13] Alarm about the association between antipsychotics and these CVD risk factors is growing as evidence accumulates.[24] In addition to the potential harmful impact of these medications on a patient's physical health, adverse effects such as weight gain may cause nonadherence and treatment discontinuation.[22]

Metabolic side-effect profiles and tolerability differ among the atypicals currently available in the US: clozapine, risperidone, olanzapine, quetiapine, ziprasidone, and aripiprazole. As mentioned, the primary side effects seen with atypical antipsychotic use are metabolic abnormalities (eg, weight gain, dyslipidemia, diabetes). Clozapine and olanzapine have relatively high risks for these side effects, whereas quetiapine and risperidone have a moderate association, and ziprasidone and aripiprazole a low risk.[15,25,26] Clozapine and olanzapine are generally associated with the greatest risk of DM and the largest changes in cholesterol and triglyceride levels.[26] Both clozapine and olanzapine are associated with significant weight gain, particularly at high dosages.[26] One large retrospective analysis reported a ≥7% increase in weight over baseline for olanzapine within 6 weeks in patients with schizophrenia.[27] A small case series of olanzapine in patients with schizophrenia or schizoaffective disorder reported a mean weight gain of 9.2 kg (20.24 lbs) over a mean duration of 22 months.[28] A large meta-analysis that examined weight gain associated with antipsychotic use, found that using pair-wise comparisons to adjust for differences in the studies, yielded a random-effects model of mean weight change at 10 weeks at the midpoint of the recommended dose.[26] The reported results showed a fixed effects model mean weight gain of 4.17 kg (9.2 lbs) for olanzapine, 3.77 kg (12.7 lbs) for perphenazine, 2.49 kg (5.5 lbs) for quetiapine, 1.67 kg (3.7 lbs) for risperidone, and 0.28 kg (0.6 lbs) for ziprasidone (perphenazine and quetiapine were not included in the 10-week data due to small n).[26] While some of the studies included in this meta-analysis were very small, the results show that many antipsychotic treatments induce clinically significant weight gain.

METABOLIC SYNDROME PREVALENCE IN THE CATIE STUDY

The Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study, a multisite clinical study sponsored by the National Institute of Mental Health, assessed the efficacy and safety/tolerability of olanzapine, quetiapine, risperidone, and ziprasidone compared with the conventional antipsychotic perphenazine in 1,460 patients diagnosed with chronic schizophrenia. The trial was designed so that participants were representative of individuals likely to be encountered in everyday clinical practice and the results thus relevant to a broad patient population.

Data from the baseline CATIE schizophrenia sample confirm previous reports that patients with schizophrenia are at significantly higher metabolic and cardiac risk than the general population. For instance, a considerable percentage of patients enrolled in the CATIE study presented with diagnoses of diabetes (11%), dyslipidemia (14%), or hypertension (20%) at baseline.[29]

A subset consisting of 689 CATIE participants, for which specific baseline data were available (eg, antihypertensive, hypoglycemic medication, or insulin use; fasting glucose and lipid values), were assessed for CHD risk and metabolic syndrome prevalence and compared with a randomly selected sample from the NHANES III database, matched for age, gender, and race/ethnicity.[21,29] Based on predictors from the Framingham Heart Study, CATIE patients with schizophrenia showed a significantly higher 10-year risk for CHD than matched controls (9.4% versus 7.0% for males, 6.3% vs. 4.2% for females; $P=.0001$) that remained elevated after controlling for BMI ($P=.0001$).[21] Compared with controls, significantly greater proportions of a subset of CATIE subjects had diabetes (13% versus 3%), high blood pressure (27% vs. 17%), or were smokers (65% versus 35%) (all $P<.0001$).[21] Using the NCEP ATP III criteria as well as the AHA modified criteria (ie, impaired fasting glucose threshold of 100 mg/dL)[1] for diagnosis of metabolic syndrome, respective unadjusted prevalences in the CATIE study were 40.9% and 42.7%.[21] A significantly greater proportion of females were

diagnosed than males using the NCEP and AHA criteria—respective rates were 51.6% and 54.2% (P=.0002) for females and 36.0% and 36.6% for males.[23] Using waist circumference measurements only from the NCEP ATP III criteria, 73.4% of females and 36.6% of males met the criteria for the metabolic syndrome (P=.0003). After controlling for age and race/ethnicity as covariates using a logistic regression model, CATIE participants were significantly more likely to have the metabolic syndrome than those in the NHANES III matched sample, 138% for males and 251% for females (P<.001).[23] Further, after controlling for differences in BMI logistic regression modeling, CATIE males were 85% and females 137% more likely to have the metabolic syndrome than NHANES participants.[23]

In another baseline data analysis using ATP III-derived diagnostic criteria with lower impaired fasting glucose threshold,[24] 35.8% of evaluated fasting and nonfasting patients (n=1,231) had the metabolic syndrome.[18] Those with the syndrome were more likely to be female, older, and white (Table 2).[18] After adjustment for age, gender, race, ethnicity and site variance, significant distinctions between those with and without the metabolic syndrome in variables of interest were found in Short Form-12 (SF-12) physical scores (P<.001) and a subscore of the Positive and Negative Syndrome Scale (PANSS) that measured the first of the 16 general psychopathology items (ie, the PANSS rating of somatic concern; P=.03).[18] The two patient groups showed no significant differences with respect to neurocognition, quality-of-life, symptom severity, self-rated mental health, or depression. Logistic regression modeling showed that years of antipsychotic exposure and self-reported alcohol use were not predictors of metabolic syndrome; however age, race, and ethnicity were significant predictors.[18]

The baseline CATIE results confirm other reports that patients with schizophrenia are at increased risk for DM and CVD.[8,9] Thus, in addition to bearing a psychiatric burden, the general health of patients with schizophrenia is compromised. More troublesome is further analysis of the baseline phase 1 CATIE results highlighting that a high proportion of individuals at risk for a metabolic condition were not receiving treatment for hypertension (62%), dyslipidemia (89%), or diabetes (45%).[24]

TABLE 2.
Comparison of Baseline CATIE Subjects on the Basis of Metabolic Syndrome Classification

Parameter	Metabolic syndrome	No metabolic syndrome (n=790)	P
Age (years)	43.5±12.2	38.5±11.5	<.0001
Gender (% male)	58.2%	78.4%	<.0001
Race (% white)	56.2%	54.0%	<.0001
Ethnicity (% Hispanic)	11.5%	11.0%	.678
Systolic BP (mm Hg)	123.5±14.5	120.6±13.6	<.0001
Diastolic BP (mm Hg)	83.8±10.4	76.4±10.5	<.0001
Waist circumference	44.1±5.8	35.1±4.8	<.0001
BMI (kg/m²)	34.4±6.9	28.6±5.5	<.0001
HDL (mg/dl)	35.4±9.0	42.3±14.8	<.0001
Glucose (mg/dl)	118.4±56.9	93.6±27.4	<.0001
Triglycerides (mg/dl)	276.6±192.4	151.6±93.2	<.0001

BP=blood pressure; BMI=body mass index; HDL=high density lipoprotein.

Reprinted with permission from Meyer JM, Nasrallah HA, McEvoy JP, et al. The Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) schizophrenia trial: clinical comparison of subgroups with and without the metabolic syndrome. *Schizophr Res.* 2005;80(1):9-18.

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METABOLIC RESULTS FROM THE CATIE TRIAL

Overall, only a quarter of patients in the CATIE study remained on the originally assigned antipsychotic medication for the entire 18-months' duration of the first phase of the trial.[25] The primary reasons for discontinuation included efficacy, intolerability, safety, and patient's decision. The time to discontinuation for any cause, the primary outcome measure, was significantly longer for patients receiving olanzapine than those receiving quetiapine (P<.001) or risperidone (P=.002).[25] The differences between olanzapine, and either the perphenazine or ziprasidone groups, were not significant after adjustment for multiple comparisons.[25] Although there was a separation between olanzapine and ziprasidone, the numerical difference did not reach statistical significance. This may have been partially due to inadequate sample size. It should be pointed out that the olanzapine efficacy advantage in the CATIE study may be due to (A) a more adequate mean dose than the other antipsychotics, and (B) a larger proportion of subjects were receiving olanzapine at enrollment of the CATIE study, and thus were more likely to stay on olanzapine rather than switching to another antipsychotic. A

substantial proportion of patients in each treatment group discontinued medication due to patient decision (range, 24% to 34%), with the time to discontinuation being similar to that for treatment discontinuation for any cause.[32]

Although the time to treatment discontinuation owing to intolerability was comparable among the treatment groups,[32] the proportion of patients who stopped because of intolerable side effects did differ significantly among the treatment groups (P=.04).[32] The rate was lowest for risperidone (10%), highest for olanzapine (19%), and the same for the other three drugs (15%).[32] The rate for discontinuation due to extrapyramidal symptoms was significantly greater for perphenazine (5% vs. 2% to 4%, P=.002).[32] The rate of discontinuation due to weight or metabolic effects was more than twice as great for olanzapine than for any other study medication (9% vs. 1% to 4%, P<.001).[32]

Adverse-event profiles differed among the study medications. Anticholinergic side effects of urinary hesitancy, dry mouth, and constipation occurred significantly more frequently in patients receiving quetiapine (31% vs. 20% to 25%, P<.001),[32] whereas rates of incontinence and nocturia were highest in the risperidone group (7% vs. 2% to 5%, P=.04).[32] Lower rates of insomnia were observed in patients treated with olanzapine or quetiapine than other study drugs (16% and 18%, respectively, vs. 24% to 30%; P<.001).[32]

Significant differences were also seen among the metabolic side-effect profiles of the drugs. Olanzapine caused significantly more weight gain (9–10 times greater) than any other medication, averaging a 9.4-lb gain, compared with gains of only 1.1 lbs and 0.8 lbs with quetiapine and risperidone, respectively, and losses of 1.6 lbs and 2.0 lbs with ziprasidone and perphenazine, respectively (P<.001).[32] Adjusted for treatment duration, the average weight gain with olanzapine was 2.0 lbs (0.9 kg)/month, significantly greater than with the other medications studied (P<.001).[32] More patients in the olanzapine group also reported gains of >7% of their baseline body weight (30% vs. 7% to 16%, P<.001).[32]

Treatment with olanzapine was associated with significantly elevated levels of cholesterol and triglycerides (P<.001) and glycosylated hemoglobin (P=.01), even after adjusting for greater duration of drug exposure.[32] Increases in these laboratory parameters were significant but small for perphenazine (P≤.01). Notably, both risperidone and ziprasidone significantly decreased cholesterol, and ziprasidone also produced reductions in triglycerides (P<.001) and glycosylated hemoglobin (P=.01). Risperidone produced small significant increases in triglycerides and glycosylated hemoglobin (P=.01),[32] however, there were no significant differences among treatment groups in the rates of oral glucose-lowering drugs/insulin or statins added during the study period.[32] Data on these metabolic measures for each treatment group are detailed in Table 3. Fasting measurements were requested for these laboratory tests; however, non-fasting results were not excluded from the analysis. Risperidone was associated with significant increase in prolactin levels compared with the other medications, exposure-adjusted mean 13.8 ng/dL vs. -1.2 to -10.6 (P<.001).[32]

That olanzapine-treated patients gained significantly more weight and displayed more indicators of metabolic dysfunction corroborates other reports.[11,31,33] Atypical antipsychotic-related weight gain, dyslipidemia, and glucose intolerance are primary indicators of possible development of the metabolic syndrome and cardiac disease, for which this patient population is already at elevated risk.[15,31,32] Patients taking antipsychotics should therefore be routinely monitored for changes in weight, BMI, waist circumference, blood pressure, fasting glucose, and fasting lipids, as recommended by a consensus of the ADA, the American Psychiatric

TABLE 3.
Summary of Metabolic Data From CATIE Phase 1

Agent	Weight (lb)	TG (mg/dl)	Chol (mg/dl)	HgbA1c
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Perphenazine	12*	-8.3	+0.5	+0.1%
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Risperidone	[illegible]	2.6	-5.6	+0.08%
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

*Weight=percentage of individuals who gained >7% of their baseline body weight; TG=mean change in triglyceride level; Cholesterol=mean change in total cholesterol levels; HgbA1c=mean change in glycosylated hemoglobin

Adapted from: Lieberman JA, Stroup TS, McEvoy JP, et al, for the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Investigators. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. *N Engl J Med* 2005;353(12):1209-1223

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Association, the AACE, and the North American Association for the Study of Obesity (Table 4).[25] Any significant changes may signal the need to switch medications.

CONCLUSION

The baseline CATIE data confirm previous findings that individuals with schizophrenia are at high risk for metabolic syndrome, and that this ultimately increases their risk for CVD. Metabolic results from phase 1 of the trial confirm that long-term maintenance treatment with antipsychotics, particularly the atypical olanzapine, as well as quetiapine and risperidone, can add to this risk. Therefore, despite the superior adverse-events profiles of atypical antipsychotics compared with conventionals in many cases, undesirable side effects continue to be a factor with these medications. It is therefore important that patients receiving antipsychotics be initially and subsequently checked at regular intervals for changes in BMI, blood glucose, and lipid levels. In addition, a worrisome trend noted in the CATIE study was that many patients with metabolic problems were not receiving standard treatment for their metabolic conditions, including 45% of those with diabetes, 62% with hypertension, and 89% of those with dyslipidemia.

Another point underscored by the results of the first phase of the CATIE study is that the choice of antipsychotic medication can have a significant impact on a patient's metabolic, cardiovascular, and overall general health. A noticeable compromise in physical condition due to medication side effects may be distressing enough as to cause a patient to stop taking the drug altogether, regardless of antipsychotic efficacy. The propensity of the atypical antipsychotics to produce metabolic effects varies among them, and should be an important consideration in drug selection and other treatment decisions. Thus, optimal dosing of each medication (ie, maximizing antipsychotic benefits while minimizing side effects), should, as always, be determined empirically for every patient. Future novel antipsychotic agents should be designed to avoid metabolic side effects, in order to have better effectiveness and more favorable long-term outcomes in patients with schizophrenia. **CNS**

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TABLE 4.
Monitering Protocol for Patients on Atypical Antipsychotics*

	Baseline	4 Weeks	8 Weeks	12 Weeks	Quarterly	Annually	Every 5 Years
Personal/family history	X					X	
Weight (BMI)	X	X	X	X	X		
Waist circumference	X					X	
Blood Pressure	X			X		X	
Fasting plasma glucose	X			X		X	
Fasting lipid profile	X			X			X

* More frequent assessments may be warranted based on clinical status.

BMI=body mass index.

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