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## Cannabis use and metabolic syndrome among clients with first episode psychosis

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### Abstract

**Aim:** To explore the relationship between cannabis use and metabolic syndrome (MetS) among those who have experienced first episode psychosis (FEP).

**Methods:** A retrospective analysis of 404 participants enrolled in the Recovery After Initial Schizophrenia Episode-Early Treatment Program (RAISE-ETP) was conducted. Using multiple logistic regression, we investigated the correlation between cannabis use and rate of MetS at baseline and across time as well as the specific metabolic derangements among cannabis users and abstainers.

**Results:** Although cannabis users had similar rates of MetS at baseline when compared with abstainers, those who used cannabis at any time during the study period tended to have lower triglycerides and elevated high-density lipoprotein (HDL). Cannabis users were less likely to develop MetS, relative to nonusers.

**Conclusions:** Cannabis use may be associated with lower incidence of MetS in patients who have experienced FEP. Further research is indicated to develop these observations.

### Keywords

BMI; cannabis; first episode psychosis; metabolic syndrome; obesity; RAISE-ETP

## 1 | INTRODUCTION

Individuals diagnosed with a schizophrenia-spectrum disorder are twice as likely to develop metabolic syndrome (MetS). MetS, if left untreated or unmonitored, may progress to

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### DATA AVAILABILITY STATEMENT

Data used in the preparation of this article were obtained and analyzed from the controlled access data sets distributed from the National Database for Clinical Trials (NDCT). NDCT is a collaborative informatics system created and supported by the National Institute of Mental Health (NIMH) to provide a national resource to support and accelerate discovery related to clinical trial research in mental health. Dataset identifier, 2249. This article reflects the views of the authors and may not reflect the opinions or views of the NIMH or of the submitters of original data to NDCT.

cardiovascular disease (CVD) (Vancampfort et al., 2013). Research indicates that most weight gain and metabolic derangement occur within the first 3 years after an initial schizophrenia-spectrum diagnosis representing a critical period of MetS intervention for individuals experiencing their first-episode of psychosis (FEP) (Pérez-Iglesias et al., 2014).

While cannabis use among individuals with schizophrenia is associated with an increased illness severity, worsened positive symptoms and poor functionality the effect it has on MetS and CVD appears mixed (Coutinho et al., 2019; Oluwoye et al., 2018). Two studies describe a lower risk of MetS among those with FEP and cannabis use (Scheffler et al., 2018; Vázquez-Bourgon et al., 2019) while another describes hyperglycemia and increased weight in those with serious mental illness (Isaac, Isaac, & Holloway, 2005). Given the limited research within the context of a wide CVD-related mortality gap, we conducted secondary analyses using data from the Recovery After an Initial Schizophrenia Episode-Early Treatment Program (RAISE-ETP) study to examine the relationship between cannabis use and MetS among treatment seeking individuals with FEP.

## 2 | METHODS

### 2.1 | Data source

Data was obtained from RAISE-ETP study a large clustered randomized controlled trial that randomly assigned 17 community mental health clinics to NAVIGATE (treatment group) and 17 to standard care (control group). NAVIGATE is multidisciplinary team based intervention that includes personalized medication management, family psychoeducation, individual resiliency training and supported education and employment. Additional details on participant characteristics and study procedures (eg, inclusion/exclusion criteria) are discussed elsewhere (Kane et al., 2015).

### 2.2 | Assessments

Participants underwent health assessment and physical screening that included a review of current medications, medication adherence and updates to the medical record at baseline and months 3, 6, 12, 18 and 24. Height, weight, waist circumference and blood pressure were measured in the standard way. Blood samples were also collected to assess fasting serum glucose concentration, high and low-density lipoprotein concentrations. Each month, participants completed the Service Use and Resource Form used to assess cannabis use, participants were asked, 'In the past 30 days how many days have you used marijuana (pot, reefer, hash, cannabis)?' Based on the baseline and monthly responses, participants were coded into cannabis users if they used cannabis greater than or equal to 1 day during the past 30 days (Kane et al., 2015; Rosenheck et al., 2016, 2017).

MetS was defined according to the Adult Treatment III guidelines (Alberti et al., 2009; Correll et al., 2014; Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, 2001; Grundy et al., 2006). Criteria for MetS were met if participants had three or more of the following: waist circumference  $\geq 102$  cm for males or  $\geq 88$  cm for females; triglycerides  $\geq 150$  mg/dl or on drug treatment for hypertriglyceridemia; high-density lipoprotein (HDL) concentration  $<40$  mg/dl in males,  $<50$  mg/dl in females or on a

treatment for reduced HDL; systolic blood pressure (SBP)  $\geq 130$  mm Hg or a diastolic blood pressure (DBP)  $\geq 85$  mm Hg or on an antihypertensive medication; fasting serum glucose  $\geq 100$  mg/dl or on a drug treatment for hyperglycemia.

### 2.3 | Statistical analysis

Baseline descriptive statistics were analysed with *t* tests for continuous and Fischer's exact test for categorical variables. To measure the effect of cannabis across time, multiple logistic regression with generalized estimating equations were used to examine the association between cannabis use and the development of MetS during the 24-month treatment period.

In an effort to assess confounders we first conducted a bivariate logistic regression to estimate the association between cannabis use and MetS (model 1A). We then successively accounted for baseline MetS (model 1B) as well as time, and site (model 1C). Potential confounders were assessed in models two through five. Model 2 investigates the effect of treatment group (multimodal vs standard therapy), baseline MetS and demographics. Models 3, 4 and 5 were added in parallel to model two to investigate the effects that either first generation (model 3), second generation antipsychotics (model 4) or long acting injectables (model 5) may separately have on the development of MetS. Finally, we examined the individual components of MetS against models one through five. Odds ratios (OR) and their 95% confidence intervals (CI) were reported with an alpha level of 0.05. All analyses were conducted in Stata version 15.1 (StataCorp, 2017).

## 3 | RESULTS

From the original sample of 404 participants, 1 participant was excluded due to missing cannabis use data and 132 for missing MetS data. Of the 271 subjects remaining, 96 reported cannabis use during the previous 30-days at baseline. Cannabis users were significantly younger ( $M_{\text{age}} = 17.4$  years) at first psychiatric illness diagnosis compared with abstainers ( $M_{\text{age}} = 19.7$  years,  $P = .002$ ). Cannabis use co-occurred more frequently with cigarette use over abstainers (75.8 vs 50.6%,  $P < .001$ ). There was no significant association between cannabis use and MetS at baseline. Participant demographics and baseline cardiometabolic factors are displayed in Table 1.

Table 2 presents the multivariate association between cannabis use and MetS over the duration of the study period. There was a significant decrease in participants who used cannabis over the study period; 46 at 12 months and 33 at 24 months. However, in all levels of our multivariate analysis, cannabis use was significantly associated with decreased rate of MetS (OR = 0.40;  $P = .003$ ). These results did not differ with consideration of antipsychotic therapy.

Table 3 presents the multivariate associations between cannabis use and the contributing metabolic derangements. Accounting for baseline demographics as covariates in Model 2, cannabis use was associated with lower triglycerides (OR = 0.30,  $P = .001$ ) and higher sex-adjusted HDL (OR = 0.40,  $P = .017$ ). Again, results remained significant after controlling for use of first, second generation and long acting injectable antipsychotic medications.

## 4 | DISCUSSION

Our findings revealed an inverse association between cannabis use and the rate of MetS throughout the study period. MetS component analysis identified lower triglycerides and a higher sex-adjusted HDL as significant contributors. The relationship persisted despite the addition of antipsychotic therapies to multivariate analysis. These findings are consistent with aforementioned investigations, but must be taken in context (Desai et al., 2019).

Individuals who have FEP are more likely than the general population to smoke both cannabis and tobacco together rather than separately (Grossman et al., 2017). However, there is a paucity of cardiometabolic data among individuals experiencing FEP who use cannabis but do not smoke cigarettes. Among university students, previous studies have revealed that cigarette use is associated with poor metabolic outcomes (Barbosa et al., 2016; Cheng et al., 2019). However, the relationship between cigarette use and MetS is known to vary depending by age (Chen et al., 2019).

Previous research suggests that chronic cannabis use in the general population is associated with a decreased BMI (Le Strat & Le Foll, 2011). Rimonabant (Sanofi-Aventis), a cannabinoid receptor 1 inverse agonist, was developed as an antiobesity agent (Sam, Salem, & Ghatei, 2011). Furthermore, Rimonabant has been associated with significant decreases in weight, waist circumference, triglycerides, fasting insulin, leptin and the inflammation marker, C-reactive protein, along with increases in LDL particle size, HDL and adiponectin (Després, Golay, & Sjöström, 2005). Rimonabant demonstrated a possible therapeutic target for weight loss via the endocannabinoid system (Sam et al., 2011). Our findings lend further support for this therapeutic target among those with FEP.

### 4.1 | Limitations

Several limitations should be considered when interpreting our findings. First, cannabis dose and strain were not defined as it has been in previous studies, which limits our ability to ascribe a dose-effect relationship with MetS. Second, there was a significant decrease in cannabis consumption across the study period increasing the possibility of a type 1 error (Christley, 2010). Last, only 271/404 (67.0%) participants had complete information for the determination of MetS. Differential missingness of MetS information will result in biased estimates. Prior studies have already reported differential dropouts based on the treatment (Rosenheck et al., 2017) and based on cannabis use (Alcover, Oluwoye, Kriegel, McPherson, & McDonnell, 2019). Finally, it is notable that even while controlling for the type of antipsychotic medication, which have well known effects on MetS components, the inverse cannabis and MetS relationship persisted.

## 5 | CONCLUSION

To our knowledge this is the first study to analyse the longitudinal effects of cannabis use and MetS in a US based population with FEP, replicating international findings. We have demonstrated an inverse relationship between cannabis use and the rate of MetS. As rates of MetS vary regionally and nationally, future studies need to be conducted with varied populations to assess the effects of geography. Cannabis strain, doses and frequency need to

be defined and assessed in some standardized fashion—a major challenge for cannabis research (Filbey, 2020; Freeman & Lorenzetti, 2020). While it has been well documented that cannabis use is linked to the deleterious effects on the psychological wellbeing of individuals diagnosed with schizophrenia-spectrum disorders, our findings provide preliminary evidence that cannabis may have a preventative effect on MetS. Further research is needed to assess this association prospectively and identify a pathway for this effect.

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## REFERENCES

- Alberti KGMM, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, ... Smith SC (2009). Harmonizing the metabolic syndrome: A joint interim Statement of the international diabetes federation task force on epidemiology and prevention; National Heart, Lung, and Blood Institute; American Heart Association; world heart federation; international atherosclerosis society; and International Association for the Study of obesity. *Circulation*, 120(16), 1640–1645. 10.1161/CIRCULATIONAHA.109.192644 [PubMed: 19805654]
- Alcover KC, Oluwoye O, Kriegel L, McPherson S, & McDonell MG (2019). Impact of first episode psychosis treatment on heavy cannabis use: Secondary analysis on RAISE-ETP study. *Schizophrenia Research*, S0920996419302774, 86–87. 10.1016/j.schres.2019.07.014
- Barbosa JB, dos Santos AM, Barbosa MM, Barbosa MM, de Carvalho CA, Fonseca P. C. d. A., ... Silva A. A. M. d. (2016). Metabolic syndrome, insulin resistance and other cardiovascular risk factors in university students. *Ciência & Saúde Coletiva*, 21(4), 1123–1136. 10.1590/1413-81232015214.10472015 [PubMed: 27076011]
- Chen H-J, Li G-L, Sun A, Peng D-S, Zhang W-X, & Yan Y-E (2019). Age differences in the relationship between secondhand smoke exposure and risk of metabolic syndrome: A meta-analysis. *International Journal of Environmental Research and Public Health*, 16(8), 1409. 10.3390/ijerph16081409
- Cheng E, Burrows R, Correa P, Güichapani CG, Blanco E, & Gahagan S (2019). Light smoking is associated with metabolic syndrome risk factors in Chilean young adults. *Acta Diabetologica*, 56(4), 473–479. 10.1007/s00592-018-1264-2 [PubMed: 30635716]
- Christley RM (2010). Power and error: Increased risk of false positive results in underpowered studies. *The Open Epidemiology Journal*, 3(1), 16–19. 10.2174/1874297101003010016
- Correll CU, Robinson DG, Schooler NR, Brunette MF, Mueser KT, Rosenheck RA, ... Kane JM (2014). Cardiometabolic risk in patients with first-episode schizophrenia spectrum disorders: Baseline results from the RAISE-ETP study. *JAMA Psychiatry*, 71(12), 1350–1363. 10.1001/jamapsychiatry.2014.1314 [PubMed: 25321337]
- Coutinho LS, Honorato H, Higuchi CH, Cavalcante DA, Belangeiro S, Noto M, ... Gadelha A (2019). Cannabis acute use impacts symptoms and functionality in a cohort of antipsychotic naïve first episode of psychosis individuals. *Schizophrenia Research: Cognition*, 16, 12–16. 10.1016/j.scog.2018.10.002 [PubMed: 30581766]
- Desai R, Singh S, Patel K, Goyal H, Shah M, Mansuri Z, ... Qureshi AI (2019). Stroke in young cannabis users (18–49 years): National trends in hospitalizations and outcomes. *International Journal of Stroke: Official Journal of the International Stroke Society*, 15, 539. 10.1177/1747493019895651
- Després J-P, Golay A, & Sjöström L (2005). Effects of rimonabant on metabolic risk factors in overweight patients with dyslipidemia. *The New England Journal of Medicine*, 353(20), 2121–2134. [PubMed: 16291982]
- Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. (2001). 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: The Journal of the American Medical Association*, 285(19), 2486–2497. 10.1001/jama.285.19.2486 [PubMed: 11368702]
- Filbey FM (2020). The viability of a standard THC unit. *Addiction*, 115(7), 1218–1219. 10.1111/add.14961 [PubMed: 32022342]
- Freeman TP, & Lorenzetti V (2020). ‘Standard THC units’: A proposal to standardize dose across all cannabis products and methods of administration. *Addiction*, 115(7), 1207–1216. 10.1111/add.14842 [PubMed: 31606008]
- Grossman M, Bowie CR, Lepage M, Malla AK, Joober R, & Iyer SN (2017). Smoking status and its relationship to demographic and clinical characteristics in first episode psychosis. *Journal of Psychiatric Research*, 85, 83–90. 10.1016/j.jpsychires.2016.10.022 [PubMed: 27863280]
- Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, ... Costa F (2006). Diagnosis and management of the metabolic syndrome: An American Heart Association/National Heart, Lung, and Blood Institute scientific statement. *Yearbook of Endocrinology*, 2006, 113–114. 10.1016/S0084-3741(08)70316-0
- Isaac M, Isaac M, & Holloway F (2005). Is cannabis an anti-antipsychotic? The experience in psychiatric intensive care. *Human Psychopharmacology: Clinical and Experimental*, 20(3), 207–210. 10.1002/hup.674 [PubMed: 15682431]
- Kane JM, Schooler NR, Marcy P, Correll CU, Brunette MF, Mueser KT, ... Robinson DG (2015). The RAISE early treatment program for first-episode psychosis: Background, rationale, and study design. *The Journal of Clinical Psychiatry*, 76(3), 240–246. 10.4088/JCP.14m09289 [PubMed: 25830446]
- Le Strat Y, & Le Foll B (2011). Obesity and cannabis use: results from 2 representative national surveys. *American journal of epidemiology*, 174(8), 929–933. 10.1093/aje/kwr200 [PubMed: 21868374]
- Oluwoye O, Monroe-DeVita M, Burduli E, Chwastiak L, McPherson S, McClellan JM, & McDonell MG (2018). Impact of tobacco, alcohol and cannabis use on treatment outcomes among patients experiencing first episode psychosis: Data from the National RAISE-ETP Study. *Early Intervention in Psychiatry*, 13, 142–146. 10.1111/eip.12542 [PubMed: 29356438]
- Pérez-Iglesias R, Martínez-García O, Pardo-García G, Amado JA, García-Unzueta MT, Tabares-Seisdedos R, & Crespo-Facorro B (2014). Course of weight gain and metabolic abnormalities in first treated episode of psychosis: The first year is a critical period for development of cardiovascular risk factors. *The International Journal of Neuropsychopharmacology*, 17(01), 41–51. 10.1017/S1461145713001053 [PubMed: 24103107]
- Rosenheck R, Leslie D, Sint K, Lin H, Robinson DG, Schooler NR, ... Kane JM (2016). Cost-effectiveness of comprehensive, integrated care for first episode psychosis in the NIMH RAISE Early Treatment Program. *Schizophrenia Bulletin*, 42(4), 896–906. 10.1093/schbul/sbv224 [PubMed: 26834024]
- Rosenheck R, Mueser KT, Sint K, Lin H, Lynde DW, Glynn SM, ... Kane JM (2017). Supported employment and education in comprehensive, integrated care for first episode psychosis: Effects on work, school, and disability income. *Schizophrenia Research*, 182, 120–128. 10.1016/j.schres.2016.09.024 [PubMed: 27667369]
- Sam AH, Salem V, & Ghatei MA (2011). Rimonabant: From RIO to ban. *Journal of Obesity*, 2011, 1–4. 10.1155/2011/432607
- Scheffler F, Kilian S, Chiliza B, Asmal L, Phahladira L, Plessis S, ... Emsley R (2018). Effects of cannabis use on body mass, fasting glucose and lipids during the first 12 months of treatment in schizophrenia spectrum disorders. *Schizophrenia Research*, 199, 90–95. 10.1016/j.schres.2018.02.050 [PubMed: 29519756]
- StataCorp (2017). *Stata statistical software: Release 15*. In StataCorp LP. College Station, TX: Stata Press Publication.
- Vancampfort D, Wampers M, Mitchell AJ, Correll CU, De Herdt A, Probst M, & De Hert M (2013). A meta-analysis of cardio-metabolic abnormalities in drug naïve, first-episode and multi-episode patients with schizophrenia versus general population controls. *World Psychiatry*, 12(3), 240–250. 10.1002/wps.20069 [PubMed: 24096790]

Vázquez-Bourgon J, Setién-Suero E, Pilar-Cuéllar F, Romero-Jiménez R, Ortiz-García de la Foz V, Castro E, & Crespo-Facorro B. (2019). Effect of cannabis on weight and metabolism in first-episode non-affective psychosis: Results from a three-year longitudinal study. *Journal of Psychopharmacology*, 33(3), 284–294. 10.1177/0269881118822173 [PubMed: 30702972]

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**TABLE 1**

Baseline demographic and metabolic characteristics

	Total n = 402	Cannabis use		P-value
		No (n = 306)	Yes (n = 96)	
<b>DEMOGRAPHICS</b>				
Age, years (SD) n = 400	23.6 (5.1)	23.7 (5.2)	23.4 (4.4)	.644
Sex, n (%) n = 400				.009
Male, n (%)	291	212 (72.8)	79 (27.2)	-
Female, n (%)	109	93 (85.3)	16 (14.7)	-
Race (%) n = 402				.105
Non-Hispanic, White, n (%)	173	141 (81.5)	32 (18.5)	-
Non-Hispanic, Black, n (%)	137	96 (70.1)	41 (29.9)	-
Non-Hispanic, Others, n (%)	19	13 (68.4)	6 (31.6)	-
Hispanics, n (%)	73	56 (76.7)	17 (23.3)	-
Duration untreated psychosis, months (SD) n = 401	45.0 (61.0)	43.6 (60.8)	49.3 (61.6)	.428
Age at first psychiatric illness, years (SD) n = 390	19.2 (6.1)	19.7 (6.3)	17.4 (6.2)	.002
BMI, kg/m <sup>2</sup> (SD) n = 389	26.5 (6.6)	26.6 (6.7)	26.2 (6.6)	.624
BMI categories, kg/m <sup>2</sup> n = 389				.793
Underweight, BMI < 18.5, n (%)	9 (2.3)	6 (66.7)	3 (33.3)	-
Normal BMI 18.5, <25, n (%)	188 (48.3)	143 (76.1)	45 (23.9)	-
Overweight: 25, <30, n (%)	111 (28.5)	84 (75.7)	27 (24.3)	-
Obese: 30, <35, n (%)	81 (20.8)	63 (77.8)	18 (22.2)	-
Fat % (SD) n = 374	22.7 (11.5)	23.1 (11.5)	21.6 (11.6)	.274
Cigarette smokers, n (%) n = 401	227 (56.6)	155 (50.6)	72 (75.8)	<.001
<b>CARDIOMETABOLIC RISK FACTORS</b>				
Waist circumference, inches (SD) n = 388	35.9 (6.4)	35.9 (6.4)	35.8 (6.5)	.9162
Triglycerides, mg/dl (SD) n = 308	115.9 (77.5)	113.9 (69.0)	122.8 (101.6)	.402
HDL, mg/dl (SD) n = 308	49.0 (12.5)	48.5 (12.9)	50.9 (11.0)	.156
Systolic BP, mm Hg (SD) n = 389	117.1 (13.4)	116.5 (13.8)	118.8 (12.0)	.148
Diastolic BP, mm Hg (SD) n = 389	75.5 (10.0)	75.5 (9.9)	75.4 (10.2)	.885
Fasting blood glucose, mg/dl (SD) n = 277	87.6 (20.7)	88.0 (22.7)	86.3 (10.6)	.568



	Cannabis use		P-value
	No (n = 306)	Yes (n = 96)	
<b>Total n = 402</b>	<b>n = 271</b>	<b>n = 211</b>	<b>n = 60</b>
METABOLIC SYNDROME <sup>a</sup>	35 (12.9)	29 (13.7)	6(10)
Metabolic syndrome n (%) n = 271			.520

<sup>a</sup>Metabolic syndrome is defined as three or more of the following: waist circumference 102 cm for males or 88 cm for females; triglycerides 150 mg/dl or on drug treatment for hypertriglyceridemia; HDL concentration <40 mg/dl in males, <50 mg/dl in females or on a treatment for reduced HDL; systolic blood pressure 130 mm Hg or a diastolic blood pressure 85 mm Hg or on an antihypertensive medication; fasting serum glucose 100 mg/dl or on a drug treatment for hyperglycemia.

**TABLE 2**

Association between cannabis and metabolic syndrome over time (n = 271)

Model	Model A ( <i>as is</i> )			Model B <i>model A</i> + baseline MS			Model C <i>model B</i> + time + site		
	OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI	P-value
Model 1: cannabis use	0.4	0.2, 0.8	.008	0.4	0.2, 0.8	.004	0.4	0.2, 0.8	.008
Model 2: <i>model 1</i> + treatment group + age + sex + race/ethnicity	0.4	0.2, 0.8	.011	0.4	0.2, 0.7	.003	0.4	0.2, 0.7	.003
Model 3: <i>model 2</i> + FGA	0.5	0.2, 0.8	.018	0.4	0.2, 0.7	.005	0.4	0.2, 0.7	.004
Model 4: <i>model 2</i> + SGA	0.5	0.2, 0.8	.012	0.4	0.2, 0.7	.004	0.4	0.2, 0.7	.004
Model 5: <i>model 2</i> + LAI	0.4	0.2, 0.8	.012	0.4	0.2, 0.7	.003	0.4	0.2, 0.7	.003

Abbreviations: FGA, first generation antipsychotic; LAI, long acting injectable; SGA, second generation antipsychotic.

**TABLE 3**

Relationship between cannabis and metabolic syndrome parameters (n = 271 first-episode psychosis patients)

Outcomes	Model 1: cannabis use		Model 2: <i>model 1</i> + baseline parameter + treatment group + age + sex + race/ethnicity + time + site			Model 3: <i>model 2</i> + FGA			Model 4: <i>model 2</i> + SGA			Model 5: <i>model 2</i> + LAI			
	OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI	P-value
Triglycerides	0.6	0.4, 1.1	.087	0.3	0.1, 0.6	.001	0.3	0.2, 0.6	.002	0.3	0.1, 0.6	.001	0.3	0.1, 0.6	.001
Lower HDL	0.4	0.2, 0.7	.001	0.4	0.2, 0.9	.017	0.4	0.2, 0.9	.019	0.4	0.2, 0.9	.017	0.4	0.2, 0.9	.017
Elevated blood pressure	1.0	0.7, 1.4	.897	1.1	0.7, 1.7	.707	1.1	0.7, 1.7	.693	1.1	0.7, 1.7	.605	1.1	0.7, 1.7	.707
Elevated fasting glucose	1.4	0.9, 2.5	.134	0.8	0.4, 1.7	.573	0.8	0.4, 1.7	.640	0.9	0.4, 1.8	.668	0.8	0.4, 1.7	.573
Waist circumference	0.7	0.4, 1.1	.109	0.6	0.3, 1.3	.240	0.7	0.3, 1.4	.272	0.6	0.3, 1.3	.240	0.6	0.3, 1.3	.240

*Note:* Metabolic syndrome is defined as three or more of the following: waist circumference 102 cm for males or 88 cm for females; triglycerides 150 mg/dl or on drug treatment for hypertriglyceridemia; HDL concentration <40 mg/dl in males, <50 mg/dl in females or on a treatment for reduced HDL; systolic blood pressure 130 mm Hg or a diastolic blood pressure 85 mm Hg or on an antihypertensive medication; fasting serum glucose 100 mg/dl or on a drug treatment for hyperglycemia.

Abbreviations: FGA, first generation antipsychotic; LAI, long acting injectable; SGA, second generation antipsychotic.