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High prevalence of metabolic alterations in Latin American patients at initial stages of psychosis

Barbara Iruretagoyena[1,2] | Carmen P. Castañeda[2] | Juan Undurraga[2,3] | Rubén Nachar[2,4] | Cristian Mena[2] | Carlos Gallardo[2,5] | Nicolas A. Crossley[1,6] | Alfonso Gonzalez-Valderrama[2,4]

[1]Department of Psychiatry, School of Medicine, Pontificia Universidad Católica de Chile, Santiago, Chile

[2]Early Intervention Program, J. Horwitz Psychiatric Institute, Santiago, Chile

[3]Department of Neurology and Psychiatry, Faculty of Medicine, Clínica Alemana Universidad del Desarrollo, Santiago, Chile

[4]School of Medicine, Universidad Finis Terrae, Santiago, Chile

[5]Clínica Psicológica, Universidad Diego Portales, Santiago, Chile

[6]Department of Psychosis Studies, Institute of Psychiatry, Psychology and Neuroscience, King's College, London, UK

Correspondence
Barbara Iruretagoyena, Diagonal Paraguay 362, Oficina 543, Santiago 833077, Chile.
Email: bairuret@uc.cl

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Aim: Studies conducted in the United States have highlighted a higher prevalence of metabolic alterations (MA) in Latino population and Latino psychotic patients. Metabolic risk in psychosis is known to be present from initial stages of the disease. To better characterize this population, we explored the prevalence of MA and metabolic syndrome (MS) in early psychosis patients in a Latin American country.

Methods: Transversal, observational study comparing the prevalence of MA and MS in patients with early psychosis from an outpatient program in Chile (n = 148) with a community representative sample from the 2009-2010 National Health Survey (n = 568). ANOVA and regression analysis were performed obtaining odds ratio for MA and MS.

Results: The prevalence of MS was 44.7% in patients compared to 11.4% in the community sample (odds ratio [OR] 5.28, confidence interval [CI] 95% 3.07-9.08; *P*-value <0.001). There was no effect of gender. Subgroup analyses showed no significant association of MS with clozapine/olanzapine use, treatment duration or tobacco use. There was an association between treatment duration and hypertriglyceridemia (*P* = 0.024; OR 1.02, CI 95% 1.00-1.04) and obesity (*P* = 0.007; OR 5.93, CI 95% 1.82-20.22). Clozapine/olanzapine use was associated with hyperglycaemia (*P* = 0.007; OR 6.04, CI 95% 1.63-22.38) and high low density lipoprotein (*P* = 0.033 ANOVA; OR 5.28, CI 95% 1.14-24.37).

Conclusion: Latino psychotic patients have a high risk of MA and MS at initial stages of the disease which is not entirely explained by the higher risk in the whole Latino population, is irrespective of gender, and does not seem to be entirely a response to atypical antipsychotic use.

KEYWORDS

early psychosis, Latino population, metabolic alterations, metabolic syndrome

1 | INTRODUCTION

People with schizophrenia have approximately two to three times higher mortality rates than the general population (Brown, 2000; Fleischhacker et al., 2008; Suvisaari et al., 2013). While there is a higher rate of suicide that partly explains this increased mortality risk (Suvisaari et al., 2013), it is physical illness which mostly accounts for this association. Patients with schizophrenia have higher rates of tobacco use (Bobes, Arango, Garcia-Garcia, & Rejas, 2010), poor access to healthcare, inadequate management of medical illness (DE Hert et al., 2011; Osby, Correia, Brandt, Ekbom, & Sparén, 2000) and particularly, a significantly higher risk of cardiovascular diseases, with higher prevalence of obesity and metabolic alterations (MA) (DE Hert et al., 2011; Laursen, 2011).

Metabolic syndrome (MS) is more frequently encountered in people with schizophrenia and its prevalence continues rising with age and years of treatment (Correll et al., 2014; Foley & Morley, 2011; Mitchell et al., 2013; Mitchell, Vancampfort, De Herdt, Yu, & De Hert, 2013). Despite different studies have shown that antipsychotic-naïve first-episode psychosis patients do not differ in their baseline rates of MS in comparison with healthy subjects (Fleischhacker et al., 2013; Mitchell, Vancampfort, Sweers, et al., 2013), they rapidly add more

metabolic risk factors during the first year of treatment (Curtis et al., 2011).

Different populations have different risk to MA and MS. INTERHEART and INTERSTROKE studies demonstrated that abdominal obesity (AO) in Latin American countries was the highest cardiovascular risk factor compared with the rest of the world (Lanas et al., 2007; O'Donnell et al., 2010). Studies conducted in the United States show a higher prevalence of MA and MS in the general Latino population, with figures showing around a 50%-60% higher risk of MS (Daviglus et al., 2012; Rodriguez, Naderi, Wang, Johnson, & Foody, 2013; Roger et al., 2011). Echoing these results, studies in psychotic patients show that Latino patients have a significantly higher prevalence of MS than non-Latino ones (Kato, Currier, Gomez, Hall, & Gonzalez-Blanco, 2004). Little is known about the causes of these differences. The higher risk might be related to a sociocultural factor or a genetic predisposition to MA and MS, which in the case of psychotic patients may be accentuated by metabolic adverse effects of atypical antipsychotics (Ellingrod et al., 2008). Others speculate that poor health access and the socioeconomic context of Latino population in the United States could be the main etiological factor (Rodriguez et al., 2013).

We here explored the prevalence of MA and MS in a Latin-American group of patients with early psychosis, comparing the rates with a community representative sample of the same country (participants of the last National Health Survey [Nacional, 2010]). We hypothesized that we will find high rates of MA and MS in this group of patients from a developing country in the early stages of this disorder, highlighting the need for early intervention in this relatively understudied population.

2 | MATERIALS AND METHODS

This study was a cross-sectional, observational study comparing the prevalence of MA and MS in young patients with early psychosis and a community sample. Patients included were aged 15 to 24 years old and followed-up in the Outpatient Clinic from the Early Intervention in Psychosis (EIP) Program of the state Psychiatric Institute "Dr. José Horwitz B." in Santiago, Chile. They all were in their first 5 years since their first episode of psychosis. All of them were receiving antipsychotic treatment, and no treatment naive patients were included. The control sample was age-paired participants of the National Health Survey (HS) 2009-2010 that reported no medication use, which were affiliated with the public health insurance from the Chilean National Health System (FONASA).

Information of EIP patients was obtained from their clinical records between 2016 and 2017. Anthropometric and metabolic evaluations were carried out following the same procedures used in the HS. Weight and height was measured in a standardized calibrated balance, abdominal circumference was measured with a metallic inextensible metric tape during expiration in the middle point between de costal border and the iliac crest following the axillar midline. Arterial pressure was measured during fasting, after 5 minutes rest and with previous vesical emptying. Two measures of arterial pressure were taken, separated by 2 minutes and a mean of systolic and diastolic arterial pressure recorded. Metabolic parameters were evaluated after 9 hours of fasting.

Sociodemographic, anthropometric, metabolic and MS data of HS participants was obtained from a public database, provided by the Chilean Ministry of Health (Ministerio de Salud Chile, Encuesta Nacional de salud 2009-2010) (Available in http://epi.minsal.cl/bases-de-datos/). The HS was a cross-sectional study which took place between 2009 and 2010. Participants from a random sample of houses, with national, regional and rural/urban zone representativeness, were invited to participate. The survey had a response rate of 85%, including 5434 people. Forty two health items were evaluated, including arterial pressure, dyslipidaemia, nutritional status, diabetes mellitus and MS prevalence.

MS was diagnosed following the definition of the "National Cholesterol Education Program" Adult treatment panel III expert panel actualization (Grundy et al. 2006), using a cut point for abdominal circumference determined by a study based on the data from the 2009 to 2010 Chilean National Health Survey data (Gómez Restrepo, Muñoz, Ruiz, & Lanas, 2017; Ministerio de Salud [MINSAL], 2014). MS was defined by at least three of the following criteria: Abdominal circumference ≥90 cm in men and ≥80 cm in women, Arterial Pressure ≥ 130/85 (or in treatment), high density lipoprotein (HDL) cholesterol <40 mg/dL in men and <50 mg/dL in women, triglycerides ≥150 mg/dL (or in treatment) and fasting glycaemia ≥100 mg/dL (or in treatment). The rest of metabolic parameters alterations were defined as follows: being overweight as having a body mass index between 25 and 29.9 kg/m^2 and obesity above 30 kg/m^2; alterations in low density lipoprotein (LDL) cholesterol were defined according to the US task forces (≥130 mg/dL) (Stone et al., 2014).

Subjects with at least one metabolic measure were included, resulting in 148 patients of the EIP program and 568 people from the HS. Subjects with all parameters to calculate MS were 123 EIP patients (90 men; 33 women) and 298 controls from the HS (135 men; 163 women). The study was approved by the Ethical Committee of the North Metropolitan Health Service.

2.1 | Statistical analysis

Descriptive statistics and corresponding measures of variability were calculated for both groups, testing for normality of their distribution using Kolmorov-Smirnov test. For the univariate analysis, *t*-student or Mann-Whitney tests were made for numerical variables and χ^2 test for categorical ones. Logistic regression analysis was made obtaining Odds Ratio (0R) adjusted for age and gender. ANOVA testing for interactions for gender and psychosis was applied. All statistical analyses used two-tailed tests and a P value <0.05 is considered statistically significant. SPSS version 21.0 statistical package was used.

3 | RESULTS

3.1 | Clinical and demographic characterization

One hundred and forty eight patients of the EIP program and 568 people from the HS were included. Demographic data and clinical

characteristics are presented in Table 1. The HS sample was younger and had more women. All subsequent analyses control for these factors. 93.2% (138 subjects) of EIP patients were diagnosed with a non-affective psychosis and 6.8% (10 subjects) with an affective psychosis. Regarding their illness course, the mean number of hospitalizations was 1.33 (SD: 1.2) with a median duration of treatment of 26 (SD: 25.81) months. 63% of the patients used antipsychotics with high metabolic risk (olanzapine or clozapine). There was no difference in tobacco use between the 80 EIP patients and 413 HS subjects with information on tobacco current use (EIP: 46.3% (37 subjects); HS: 38.5% (159 subjects); *P*-value: 0.194).

3.2 | Prevalence of MA in both groups

Univariate analyses comparing metabolic parameters showed obesity, fasting glucose, hypertriglyceridemia, abdominal circumference, diastolic and systolic hypertension as significantly higher in the EIP group (Table 1).

Prevalence of MA is shown in Table 2. Abdominal obesity (AO) was the most prevalent MA in both groups. All MA were more prevalent in the EIP group (age and gender adjusted analysis), except for LDL ≥130 and overweight. Hyperglycaemia (odds ratio [OR] 14.43, confidence interval [CI] 95% 6.48-32.12), diastolic hypertension (OR 7.43, CI 95% 4.25-12.99) and (OR 4.64, CI 95% 2.98-7.22) were the MA with more risk to be altered in the EIP group (Table 2).

TABLE 1 Clinical and demographic characteristics of EIP and HS samples

Variables	EIP (N = 148)	HS (N = 568)	*P*-value
Age; mean (SD)[a]	21.06 (2.01)	19.53 (2.78)	<0.0001
Female; n (%)[b]	33 (22.3)	331 (58.3)	<0.0001
Height (centimetres); mean (SD)[a]	168 (9.01)	163.4 (8.05)	<0.0001
BMI 25–29.9; n (%)[b]	48 (32.4)	147 (25.9)	0.082
BMI ≥ 30; n (%)[b]	51 (34.5)	78 (13.7)	<0.0001
Glucose (mg/dL); mean (SD)[a]	93.1 (16.54)	84.76 (9.37)	<0.000
TG (mg/dL); mean (SD)[a]	143.9 (91.46)	106.21 (88.28)	<0.000
HDL (mg/dL); mean (SD)[a]	45.59 (12.84)	46.21 (10.12)	0.396
LDL (mg/dL); mean (SD)[a]	93.83 (30.24)	92.72 (24.94)	0.564
AC (centimetres); mean (SD)[a]	95.04 (14.02)	81.47 (12.41)	<0.000
SAP (mm Hg); mean (SD)[a]	122 (14.72)	113.7 (39.08)	<0.000
DAP (mm Hg); mean (SD)[a]	79.84 (12.79)	68.31 (9.2)	<0.000
Tobacco use (current smokers); n (%)[c]	37 (46.3)[c]	159 (38.5)[c]	0.194
Number of hospitalizations; mean (SD)	1.34 (1.21)		
Treatment duration (months); median (SD)	26 (25.81)		
Ola/Clz use; n (%)	94 (63.5)		
Diagnoses			
Non-affective psychosis; n (%)	138 (93.2)		
Affective psychosis; n (%)	10 (6.8)		

Abbreviations: AC, abdominal circumference; BMI, body mass index; Clz, clozapine; DAP, diastolic arterial pressure; EIP, Early Intervention Program; HDL, high density lipoprotein; HS, National Health Survey; LDL, low density lipoprotein; Ola, olanzapine; SAP, systolic arterial pressure; TG, triglyceridemia.

[a] *t*-Student or Mann–Whitney *U* test.

[b] χ^2.

[c] Data from 80 EIP patients and from 413 HS subjects.

3.3 | Prevalence of MA stratified by gender in both groups

The HS sample had a high prevalence of AO and overweight in both genders (AO: 26.6%, men HS; 47.4%, women HS. Overweight: 25.7%, men HS; 26%, women HS) and of HDL cholesterol alteration in women (32.6%) compared to other international populations (Table 2). Abdominal obesity was the most prevalent MA in both genders in EIP patients (69.6%, men EIP; 75.8%, women EIP) (Figure 1).

We found male patients with psychosis had a higher risk of diastolic hypertension (OR 7.07, CI 95% 3.52-14.21), hyperglycaemia (OR 6.56, CI 95% 2.53-17.01) and AO (OR 5.05, CI 95% 3.03-8.41) (gender and age adjusted analysis). Female patients with psychosis had a higher risk of hyperglycaemia (OR 47.93, CI 95% 12.04-190.68) and diastolic hypertension (OR 8.06, CI 95% 3.22-20.17) (gender and age adjusted analysis). (Table 2).

ANOVA testing for interactions between gender and diagnosis (controlling for age) for all metabolic abnormalities was significant only for hyperglycaemia ($P < 0.001$). Hyperglycaemia was higher in women with a psychotic episode, and not in men.

3.4 | MS prevalence

MS prevalence in EIP patients was 44.7% and 11.4% in HS (OR 5.28, CI 95% 3.07-9.08; *P*-value <0.001, gender and age adjusted). ANOVA testing for interactions for gender and psychosis in MS was not significant ($P = 0.3$) (Table 2).

3.5 | High metabolic risk antipsychotic use and MA/MS in EIP

ANOVA analysis showed no significant association of MS prevalence with use of high metabolic risk antipsychotics (olanzapine/clozapine) ($P = 0.321$), with no gender interaction ($P = 0.271$). Olanzapine/clozapine showed a significant association with glycaemic alterations ($P = 0.032$ ANOVA; OR 6.04, CI 95% 1.63-22.38, gender and age adjusted), and high LDL above 130 mg/dL, ($P = 0.033$ ANOVA; OR 5.28, CI 95% 1.14-24.37, gender and age adjusted). There was no significant gender interaction in any of them (glycaemic alterations: $P = 0.077$; LDL ≥ 130: $P = 0.12$). There was no effect in other MA.

3.6 | Treatment duration and MA/MS in EIP

There was no significant association of MS prevalence with antipsychotic treatment duration. Subjects with higher triglycerides had longer median treatment duration (hypertriglyceridemia [HTG], 35.5 (SD 31.79) months; non HTG, 21 (SD 22.13); $P = 0.024$; OR 1.02, CI 95% 1.00-1.04). Similarly, obese patients had longer median treatment duration (obese, 38 (SD 32.3) months; non obese, 23 (SD 20.7) months; $P = 0.007$; OR 5.93, CI 95% 1.82-20.22). There was no association with other MA.

TABLE 2 Metabolic alterations and metabolic syndrome prevalence stratified by gender

Variables n (%)	Total			Men			Women		
	EIP (N = 148)	HS (N = 568)	OR EIP/HS (CI 95%)[a]	EIP (N = 115)	HS (N = 237)	OR EIP/HS (CI 95%)[b]	EIP (N = 33)	HS (N = 331)	OR EIP/HS (CI 95%)[b]
BMI 25–29.9	48 (33.1)	147 (25.9)	1.17 (0.76-1.8)	39 (33.9)	61 (25.7)	1.22 (0.73-2.04)	9 (27.3)	86 (26)	1.04 (0.46-2.3)
BMI ≥ 30	51 (34.5)	78 (13.7)	3.28 (2.07-5.22)*	38 (33)	27 (11.4)	3.43 (1.9-6.21) *	13 (39.4)	51 (15.4)	1.11 (1-1.24) **
SAH	43 (29.7)	53 (9.3)	2.45 (1.48-4.04) *	40 (32.5)	41 (17.3)	2.05 (1.18-3.56) **	6 (19.4)	12 (3.6)	5.72 (1.95-16.8) **
DAH	50 (34.5)	29 (5.1)	7.43 (4.25–12.99)*	40 (35.1)	13 (5.5)	7.07 (3.52–14.21) *	10 (30.3)	16 (4.8)	8.06 (3.22–20.17) *
AO	105 (71.4)	220 (38.7)	4.64 (2.98–7.22) *	80 (69.6)	63 (26.6)	5.05 (3.03–8.41) *	25 (78.1)	157 (47.4)	3.43 (1.43-8.22) **
HTG	45 (35.2)	46 (14.9)	2.22 (1.32-3.73)**	39 (40.6)	21 (15.6)	2.96 (1.53-5.639)**	6 (18.8)	25 (14.4)	1.17 (0.43-3.18)
HG	28 (21.9)	12 (2.2)	14.43 (6.48–32.12)*	18 (18.8)	7 (3.1)	6.56 (2.53–17.01) *	10 (31.3)	5 (1.6)	47.93 (12.04–190.68) *
Low HDL	52 (35.2)	146 (25.7)	2.2 (1.42-3.41) *	37 (33.6)	38 (16)	2.79 (1.58-4.93) *	15 (46.9)	108 (32.6)	1.67 (0.79-3.5)
LDL ≥ 130	16 (12.5)	44 (10.1)	1.1 (0.54-2.23)	12 (12.5)	14 (10.4)	1.07 (0.45-2.5)	4 (12.5)	14 (8.1)	0.67 (0.2-2.22)
Variables n (%)	EIP (N = 123)	HS (N = 298)	OR EIP/HS (CI 95%)[a]	EIP (N = 90)	HS (N = 135)	OR EIP/HS (CI 95%)[b]	EIP (N = 33)	HS (N = 163)	OR EIP/HS (CI 95%)[b]
MS	55 (44.7)	34 (11.4)	5.28 (3.07–9.08) *	44 (47.3)	13 (9.6)	6.69 (3.26-13.73) *	11 (36.7)	21 (13)	3.56 (1.47-8.61) **

Abbreviations: AO, abdominal obesity; BMI, body mass index; CI, confidence interval; DAH, diastolic arterial hypertension; EIP, Early Intervention Program; HDL, high density lipoprotein; HG, hyperglycaemia; HS, National Health Survey; HTG, hypertriglyceridemia; LDL, low density lipoprotein; MS, metabolic syndrome; OR, odds ratio; SAH, systolic arterial hypertension.

[a] Logistic regression adjusted by sex and age.

[b] Logistic regression adjusted by age.

*$P < 0.001$.; **$P < 0.05$.

3.7 | Diagnoses and MA/MS in EIP

There was no difference observed in MS prevalence between affective or non-affective patients ($P = 0.157$) or other MA (abdominal circumference $P = 0.53$, diastolic arterial pressure $P = 0.853$, systolic arterial pressure $P = 0.195$, hyperglycaemia $P = 0.5$, hypertriglyceridemia $P = 0.23$, low HDL $P = 0.1$, LDL ≥ 130 $P = 0.18$, overweight $P = 0.56$, obesity $P = 0.12$).

3.8 | Tobacco use and MA/MS in EIP

Tobacco use was not associated with MS ($P = 0.526$) or other MA (abdominal circumference $P = 0.12$, systolic arterial pressure $P = 0.11$, hyperglycaemia $P = 0.77$, hypertriglyceridemia $P = 0.81$, low HDL $P = 0.66$, LDL ≥ 130 $P = 0.65$, overweight $P = 0.21$, obesity $P = 0.12$).

4 | DISCUSSION

The main result of our study is that Latin American patients during the first 5 years after their first episode of psychosis already had a very high prevalence of MAs and MS compared with a representative sample of the general population. Four out of five patients had abdominal obesity, one out of three had arterial hypertension, low HDL, overweight, obesity and hypertriglyceridemia, one in five had hyperglycaemia and one in ten high LDL. Patients have a 44.7% prevalence of MS, 5.28 times higher than their age peers in the general population.

4.1 | Where do we stand compared to other countries?

A previous meta-analysis describes a 2-4-fold increase in MS in patients compared to the healthy population (Vancampfort et al., 2013). Mitchell et al. conducted a global multicentric meta-analysis including 25 692 patients, with a mean duration of illness of 10.4 years, and found a prevalence of 32.5% (Mitchell, Vancampfort, Sweers, et al., 2013). This percentage varies among studies: 35.4% in the Netherlands (Schorr, Slooff, Bruggeman, & Taxis, 2009), 30.2% in Spain (Mitchell, Vancampfort, Sweers, et al., 2013), 40.9% in United States (McEvoy et al., 2005) and 27.5% in Japan (Sugawara et al., 2010) among others. Studies in Latin America are scarce, with reports coming mainly from Brazil, describing prevalence of MS in schizophrenia ranging from 28.7% (Gordon, Xavier, & Louzã, 2012) to 31.8% (Teixeira & Rocha, 2007). One study in Brazilian patients with a first episode of psychosis described a prevalence of 19.5% (Benseñor et al., 2012).

Considering these results, Chile has a high prevalence of MS in patients with early psychosis, higher than the level reported in other countries and similar to the Latino population in the United States. At the same time, our patients have a higher risk of MS compared to the risk reported for patients in Vancamfort et al previous meta-analysis (OR 5.28 vs 2-4). Direct comparison of the risk between international cohorts is difficult considering the heterogeneity among studies regarding definitions of MS used, AO criteria cut points and differences between the samples included, (such as gender, age, illness

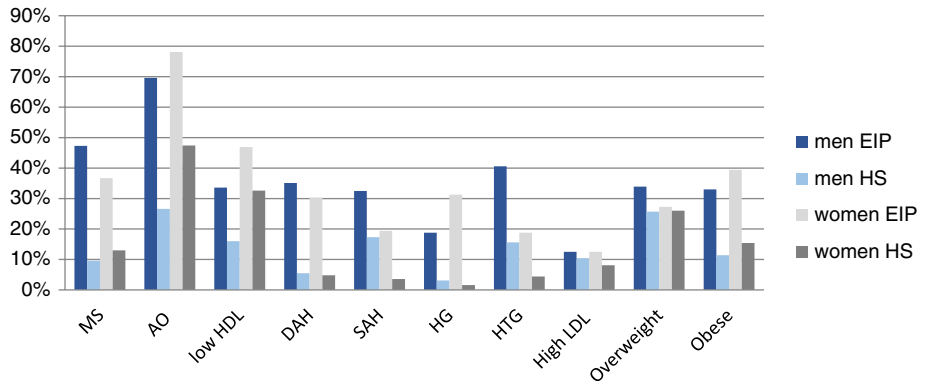

FIGURE 1 Metabolic alterations and metabolic syndrome in EIP patients vs HS stratified by gender. AO, abdominal obesity; DAH, diastolic arterial hypertension; EIP, Early Intervention Program; HDL, high density lipoprotein; HG, hyperglycaemia; HTG, hypertriglyceridemia; high LDL, low density lipoprotein ≥130; HS, National Health Survey; MS, metabolic syndrome; Obese: body mass index ≥30 kg/m^2; Overweight: body mass index 25-29.9 kg/m^2; SAH, systolic arterial hypertension

stage and treatment). However, our individual rates for each criterion seem to be high for international standards even though our patient group was composed of young people with early psychosis, characteristics one would expect would decrease the risk of MA and MS.

Over the last few decades Latin American countries have undergone an epidemiological transition in terms of nutrition (PAHO, 2012) with a rapid dietary change rich in energy, fat and proteins (Corvalán et al., 2017). More than 20% of Latin American children and adolescent are overweight or obese (Rivera et al., 2014). However, we here show that higher rates of MS in psychotic Latino patients cannot be fully accounted by the effect of a shift to the right in the distribution of the general population's risk to MS. This implies that populational interventions, such as general promotion of healthy lifestyles in the community, would be helpful but not enough to decrease this risk. Latino population with psychosis seem to have a specific higher risk for developing a MS and other cardiovascular complications, compared to other international psychotic populations, which is not shared with the Latino population in the community. Whether this risk comes from a cultural factor related to illness or a genetic predisposition to metabolic adverse effects of obesogenic antipsychotics highly prescribed in this studied population ((Mena, Gonzalez-Valderrama, Iruretagoyena, Undurraga, & Crossley, 2018), is a question that needs to be addressed.

This highlights the need to intervene early in this population with initiatives such as Iphys's HeAL (healthy active lives) statement. This initiative aims to reverse the trend of people with severe mental illness dying early by diminishing risks for future physical illnesses pro-actively and earlier (available in https://www.iphys.org.au/what-is-heal).

4.2 | Use of high metabolic risk antipsychotics

The use of clozapine/olanzapine was significantly associated with hyperglycaemia and LDL alteration. Several studies have shown a higher prevalence of MS, weight gain and diabetes in patients treated with atypical antipsychotics, especially olanzapine and clozapine (Chadda, Ramshankar, Deb, & Sood, 2013; De Hert et al., 2008; Meyer & Koro, 2004). The median treatment duration in the EIP group was of 26 months, which could be a short exposition time to obesogenic antipsychotics for the MS and other MA to develop.

We conducted the analysis of obesogenic antipsychotics effect grouping olanzapine and clozapine. One could question that though they have a similar metabolic profile, their use in first episode patients is different. Patients taking clozapine may have treatment resistant psychosis, more severe and longer illness and higher exposure to other antipsychotics. This could have influenced our result. In next studies it would be interesting to consider the effect of these drugs in separate, considering their time of exposure and doses used.

4.3 | Gender differences

We found that women with psychosis had a higher risk of hyperglycaemia. There are reports that recognize a greater sensibility of woman in developing metabolic adverse effects: higher prevalence of elevated body mass index (Atmaca, Kuloglu, Tezcan, & Ustundag, 2003; Eder et al., 2001; Russell & Mackell, 2001) and higher risk of diabetes, hypertension and dyslipidaemia (McEvoy et al., 2005; Ollendorf, Joyce, & Rucker, 2004). This could explain the interaction of gender and psychosis with higher prevalence of hyperglycaemia in female psychotic patients.

4.4 | Treatment duration

Treatment duration, independent of gender and age, was associated with higher prevalence of hypertriglyceridemia and obesity. Treatment duration is composed of two important elements that are difficult to differentiate: illness duration and antipsychotic drug exposure. This finding is consistent with other studies, which show a strong association with higher cardiovascular risk with illness duration (Mitchell, Vancampfort, Sweers, et al., 2013). The median treatment duration in this study was of 26 months, and such a short period could explain why we couldn't see the association with other metabolic parameters and MS.

4.5 | Limitations

One of the limitations of our study is that patients with affective psychosis (n = 10) and women in EIP program were sub represented (n = 33) diminishing the power of results. On the other hand, we

didn't include treatment naive patients, so we could not evaluate the differential effect of illness exposure and treatment factors in MS.

Regarding our control group, our proxy for healthy individual was that they were not taking any medication. This could have left a percentage of individuals with untreated mental illness in the control group.

Future studies must considerate a prospective model with long follow up, with samples more balanced by gender and diagnoses. It would have been interesting to explore other risk factors for MA and MS, such as sedentary lifestyles, socioeconomic status and number of psychotic episodes.

4.6 | Conclusions

Latin American patients with psychosis have a very high risk of MA and MS already at the early stages of this disorder. Future studies will address possible genetic and cultural factors explaining this higher vulnerability. There is a need to intervene early in this population.

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ORCID

Barbara Iruretagoyena https://orcid.org/0000-0001-6975-380X
Juan Undurraga https://orcid.org/0000-0001-6958-2369
Alfonso Gonzalez-Valderrama https://orcid.org/0000-0003-4716-4021

REFERENCES

Atmaca, M., Kuloglu, M., Tezcan, E., & Ustundag, B. (2003). Serum leptin and triglyceride levels in patients on treatment with atypical antipsychotics. *The Journal of Clinical Psychiatry*, *64*(5), 598–604. Retrieved from. http://www.ncbi.nlm.nih.gov/pubmed/12755665

Benseñor, I. M., Brunoni, A. R., Pilan, L. A., Goulart, A. C., Busatto, G. F., Lotufo, P. A., … Menezes, P. R. (2012). Cardiovascular risk factors in patients with first-episode psychosis in São Paulo, Brazil. *General Hospital Psychiatry*, *34*(3), 268–275. https://doi.org/10.1016/j.genhosppsych.2011.12.010

Bobes, J., Arango, C., Garcia-Garcia, M., & Rejas, J. (2010). Healthy lifestyle habits and 10-year cardiovascular risk in schizophrenia spectrum disorders: An analysis of the impact of smoking tobacco in the CLAMORS schizophrenia cohort. *Schizophrenia Research*, *119*(1–3), 101–109. https://doi.org/10.1016/j.schres.2010.02.1030

Brown, S. (2000). Causes of the excess mortality of schizophrenia. *The British Journal of Psychiatry*, *177*, 212–217. https://doi.org/10.1192/bjp.177.3.212

Chadda, R., Ramshankar, P., Deb, K., & Sood, M. (2013). Metabolic syndrome in schizophrenia: Differences between antipsychotic-naïve and treated patients. *Journal of Pharmacology and Pharmacotherapeutics*, *4*(3), 176–186. https://doi.org/10.4103/0976-500X.114596

Correll, C. U., Robinson, D. G., Schooler, N. R., Brunette, M. F., Mueser, K. T., Rosenheck, R. A., … Kane, J. M. (2014). Cardiometabolic risk in patients with first-episode schizophrenia spectrum disorders baseline results from the RAISE-ETP study. *JAMA Psychiatry*, *71*(12), 1350–1363. https://doi.org/10.1001/jamapsychiatry.2014.1314

Corvalán, C., Garmendia, M. L., Jones-Smith, J., Lutter, C. K., Miranda, J. J., Pedraza, L. S., … Stein, A. D. (2017). Nutrition status of children in Latin America. *Obesity Reviews*, *18*, 7–18. https://doi.org/10.1111/obr.12571

Curtis, J., Henry, C., Watkins, A., Newall, H., Samaras, K., & Ward, P. B. (2011). Metabolic abnormalities in an early psychosis service: A retrospective, naturalistic cross-sectional study. *Early Intervention in Psychiatry*, *5*(2), 108–114. https://doi.org/10.1111/j.1751-7893.2011.00262.x

Daviglus, M. L., Talavera, G. A., Avilés-Santa, M. L., Allison, M., Cai, J., Criqui, M. H., … Stamler, J. (2012). Prevalence of major cardiovascular risk factors and cardiovascular diseases among Hispanic/Latino individuals of diverse backgrounds in the United States. *Journal of the American Medical Association*, *308*, 1775–1784. https://doi.org/10.1001/jama.2012.14517

DE Hert, M., Correll, C. U., Bobes, J., Cetkovich-Bakmas, M., Cohen, D., Asai, I., … Leucht, S. (2011). Physical illness in patients with severe mental disorders. I. Prevalence, impact of medications and disparities in health care. *World Psychiatry : Official Journal of the World Psychiatric Association (WPA)*, *10*(1), 52–77. https://doi.org/10.1002/j.2051-5545.2011.tb00014.x

De Hert, M., Schreurs, V., Sweers, K., Van Eyck, D., Hanssens, L., Šinko, S., … van Winkel, R. (2008). Typical and atypical antipsychotics differentially affect long-term incidence rates of the metabolic syndrome in first-episode patients with schizophrenia: A retrospective chart review. *Schizophrenia Research*, *101*(1–3), 295–303. https://doi.org/10.1016/j.schres.2008.01.028

Eder, U., Mangweth, B., Ebenbichler, C., Weiss, E., Hofer, A., Hummer, M., … Fleischhacker, W. W. (2001). Association of olanzapine-induced weight gain with an increase in body fat. *American Journal of Psychiatry*, *158*(10), 1719–1722. https://doi.org/10.1176/appi.ajp.158.10.1719

Ellingrod, V. L., Miller, D. D., Taylor, S. F., Moline, J., Holman, T., & Kerr, J. (2008). Metabolic syndrome and insulin resistance in schizophrenia patients receiving antipsychotics genotyped for the methylenetetrahydrofolate reductase (MTHFR) 677C/T and 1298A/C variants. *Schizophrenia Research*, *98*(1–3), 47–54. https://doi.org/10.1016/j.schres.2007.09.030

Fleischhacker, W. W., Cetkovich-Bakmas, M., De Hert, M., Hennekens, C. H., Lambert, M., Leucht, S., … Lieberman, J. A. (2008). Comorbid somatic illnesses in patients with severe mental disorders: Clinical, policy, and research challenges. *The Journal of Clinical Psychiatry*, *69*(4), 514–519. https://doi.org/10.4088/JCP.V69N0401

Fleischhacker, W. W., Siu, C. O., Bodén, R., Pappadopulos, E., Karayal, O. N., & Kahn, R. S. (2013). Metabolic risk factors in first-episode schizophrenia: Baseline prevalence and course analysed from the European First-Episode Schizophrenia Trial. *International Journal of Neuropsychopharmacology*, *16*, 987–995. https://doi.org/10.1017/S1461145712001241

Foley, D. L., & Morley, K. I. (2011). Systematic review of early cardiometabolic outcomes of the first treated episode of psychosis. *Archives of General Psychiatry*, *68*(6), 609–616. https://doi.org/10.1001/archgenpsychiatry.2011.2

Gómez Restrepo, C., Muñoz, N. S., Ruiz, A. J., & Lanas, F. (2017). Latin American Clinical Epidemiology Network Series – Paper 1: The Latin American Clinical Epidemiology Network "LatinCLEN". *Journal of Clinical Epidemiology*, *86*, 71–74. https://doi.org/10.1016/j.jclinepi.2016.10.002

Gordon, P. C., Xavier, J. C., & Louză, M. R. (2012). Weight gain, metabolic disturbances, and physical health care in a Brazilian sample of outpatients with schizophrenia. *Neuropsychiatric Disease and Treatment*, *9*(1), 133–138. https://doi.org/10.2147/NDT.S37019

Grundy, S. M., Cleeman, J. I., Daniels, S. R., Donato, K. A., Eckel, R. H., Franklin, B. A., … Costa, F. (2006). Diagnosis and management of the metabolic syndrome An American Heart Association/National Heart, Lung, and Blood Institute scientific statement. *Current Opinion in Cardiology*. https://doi.org/10.1113/jphysiol.2006.113472

Kato, M. M., Currier, M. B., Gomez, C. M., Hall, L., & Gonzalez-Blanco, M. (2004). Prevalence of metabolic syndrome in Hispanic and non-

Hispanic patients with schizophrenia. *Primary Care Companion to The Journal of Clinical Psychiatry*, *6*(2), 74–77.

Lanas, F., Avezum, A., Bautista, L. E., Diaz, R., Luna, M., Islam, S., & Yusuf, S. (2007). Risk factors for acute myocardial infarction in Latin America: The INTERHEART Latin American study. *Circulation*, *115*, 1067–1074. https://doi.org/10.1161/CIRCULATIONAHA.106.633552

Laursen, T. M. (2011). Life expectancy among persons with schizophrenia or bipolar affective disorder. *Schizophrenia Research*, *131*(1–3), 101–104. https://doi.org/10.1016/j.schres.2011.06.008

McEvoy, J. P., Meyer, J. M., Goff, D. C., Nasrallah, H. A., Davis, S. M., Sullivan, L., … Lieberman, J. A. (2005). Prevalence of the metabolic syndrome in patients with schizophrenia: Baseline results from the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) schizophrenia trial and comparison with national estimates from NHANES III. *Schizophrenia Research*, *80*(1), 19–32. https://doi.org/10.1016/j.schres.2005.07.014

Mena, C., Gonzalez-Valderrama, A., Iruretagoyena, B., Undurraga, J., & Crossley, N. A. (2018). Early treatment resistance in a Latin-American cohort of patients with schizophrenia. *Schizophrenia Research*, *199*, 380–385. https://doi.org/10.1016/j.schres.2018.02.056

Meyer, J. M., & Koro, C. E. (2004). The effects of antipsychotic therapy on serum lipids: A comprehensive review. *Schizophrenia Research*, *70*, 1–17. https://doi.org/10.1016/j.schres.2004.01.014

Ministerio de Salud (MINSAL). (2014). Enfoque de riesgo para la prevención de enfermedades cardiovasculares, 1–63. Retrieved from http://www.compuerta.cl/joomla/documentos/Consenso_2014_prevencion_enfermedades_cardiovasculares.pdf

Mitchell, A. J., Vancampfort, D., De Herdt, A., Yu, W., & De Hert, M. (2013). Is the prevalence of metabolic syndrome and metabolic abnormalities increased in early schizophrenia? A comparative meta-analysis of first episode, untreated and treated patients. *Schizophrenia Bulletin*, *39*(2), 295–305. https://doi.org/10.1093/schbul/sbs082

Mitchell, A. J., Vancampfort, D., Sweers, K., Van Winkel, R., Yu, W., & De Hert, M. (2013). Prevalence of metabolic syndrome and metabolic abnormalities in schizophrenia and related disorders—A systematic review and meta-analysis. *Schizophrenia Bulletin*, *39*(2), 306–318. https://doi.org/10.1093/schbul/sbr148

Nacional, E. (2010). Encuesta nacional de salud. chile 2009–2010 1.

O'Donnell, M. J., Denis, X., Liu, L., Zhang, H., Chin, S. L., Rao-Melacini, P., … Yusuf, S. (2010). Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): A case-control study. *The Lancet*, *376*, 112–123. https://doi.org/10.1016/S0140-6736(10)60834-3

Ollendorf, D. a., Joyce, A. T., & Rucker, M. (2004). Rate of new-onset diabetes among patients treated with atypical or conventional antipsychotic medications for schizophrenia. *MedGenMed : Medscape General Medicine*, *6*(1), 5. Retrieved from. http://www.ncbi.nlm.nih.gov/pubmed/15208518

Osby, U., Correia, N., Brandt, L., Ekbom, A., & Sparén, P. (2000). Time trends in schizophrenia mortality in Stockholm County, Sweden. *British Medical Journal*. https://doi.org/10.1177/0143034304046906

PAHO. (2012). *Health in the Americas: Ecuador. Health in the Americas*. Washington, DC: Pan American Health Organization. World Health Organization regional office for the Americas. https://doi.org/10.1126/science.179.4077.1022-a

Rivera, J. Á., de Cossío, T. G., Pedraza, L. S., Aburto, T. C., Sánchez, T. G., & Martorell, R. (2014). Childhood and adolescent overweight and obesity in Latin America: A systematic review. *The Lancet Diabetes & Endocrinology*, *2*, 321–332. https://doi.org/10.1016/S2213-8587(13)70173-6

Rodriguez, F., Naderi, S., Wang, Y., Johnson, C. E., & Foody, J. M. (2013). High prevalence of metabolic syndrome in young Hispanic women: Findings from the National sister to sister campaign. *Metabolic Syndrome and Related Disorders*, *11*(2), 81–86. https://doi.org/10.1089/met.2012.0109

Roger, V. L., Go, A. S., Lloyd-Jones, D. M., Adams, R. J., Berry, J. D., Brown, T. M., … Wylie-Rosett, J. (2011). Heart disease and stroke statistics-2011 update: A report from the American Heart Association. *Circulation*, *123*, e18–e209. https://doi.org/10.1161/CIR.0b013e3182009701

Russell, J. M., & Mackell, J. A. (2001). Bodyweight gain associated with atypical antipsychotics: Epidemiology and therapeutic implications. *CNS Drugs*, *15*(7), 537–551. https://doi.org/10.2165/00023210-200115070-00004

Schorr, S. G., Slooff, C. J., Bruggeman, R., & Taxis, K. (2009). The incidence of metabolic syndrome and its reversal in a cohort of schizophrenic patients followed for one year. *Journal of Psychiatric Research*, *43*(13), 1106–1111. https://doi.org/10.1016/j.jpsychires.2009.03.002

Stone, N. J., Robinson, J. G., Lichtenstein, A. H., Bairey Merz, C. N., Blum, C. B., Eckel, R. H., … Wilson, P. W. F. (2014). 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. *Journal of the American College of Cardiology*, *63*, 2889–2934. https://doi.org/10.1016/j.jacc.2013.11.002

Sugawara, N., Yasui-Furukori, N., Sato, Y., Umeda, T., Kishida, I., Yamashita, H., … Kaneko, S. (2010). Prevalence of metabolic syndrome among patients with schizophrenia in Japan. *Schizophrenia Research*, *123*(2–3), 244–250. https://doi.org/10.1016/j.schres.2010.08.030

Suvisaari, J., Partti, K., Perälä, J., Viertiö, S., Saarni, S. E., Lönnqvist, J., … Härkänen, T. (2013). Mortality and its determinants in people with psychotic disorder. *Psychosomatic Medicine*, *75*(1), 60–67. https://doi.org/10.1097/PSY.0b013e31827ad512

Teixeira, P. J. R., & Rocha, F. L. (2007). The prevalence of metabolic syndrome among psychiatric inpatients in Brazil. *Revista Brasileira de Psiquiatria (Sao Paulo, Brazil : 1999)*, *29*(4), 330–336.

Vancampfort, D., Wampers, M., Mitchell, A. J., Correll, C. U., 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. https://doi.org/10.1002/wps.20069

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