



Research paper

Determinants and geographical variation in the distribution of depression in the Southern cone of Latin America: A population-based survey in four cities in Argentina, Chile and Uruguay



F.M. Daray^{a,b}, A.L. Rubinstein^c, L. Gutierrez^c, F. Lanas^d, N. Mores^e, M. Calandrelli^f, R. Poggio^c, J. Ponzo^g, V.E. Irazola^{c,*}

^a University of Buenos Aires, School of Medicine, Institute of Pharmacology, Argentina

^b National Council of Scientific and Technical Research (CONICET), Argentina

^c South American Center of Excellence in Cardiovascular Health (CESCAS), Institute for Clinical Effectiveness and Health Policy (IECS), Buenos Aires, Argentina

^d CIGES, Universidad de La Frontera (UFRO), Temuco, Chile

^e Municipalidad de Marcos Paz, Pcia de Buenos Aires, Argentina

^f Sanatorio San Carlos, Bariloche, Pcia de Río Negro, Argentina

^g Facultad de Medicina, Universidad de la República, Uruguay

ARTICLE INFO

Keywords:

Depression
Prevalence
Stressful life events
Latin America
Risk factors

ABSTRACT

Background: Depression is one of the major contributors to the global burden of diseases; however, population-based data in South America are limited.

Methods: We conducted a population-based cross sectional study with 7524 participants, aged 35–74 years old, recruited between February 2010 and December 2011 from randomly selected samples in 4 cities (Bariloche and Marcos Paz, Argentina; Temuco, Chile; and Pando-Barros Blancos, Uruguay). Major Depressive Episode (MDE) was assessed using the Patient Health Questionnaire (PHQ) – 9.

Results: The overall prevalence of MDE was 14.6% (95% CI: 13.6, 15.6). However, there was a geographical variability of up to 3.7 folds between different cities being 5.6% (95% CI: 4.6, 6.7) in Marcos Paz, Argentina; 9.5% (95% CI: 8.2, 10.9) in Bariloche, Argentina; 18.1% (95% CI: 16.3, 20.0) in Temuco, Chile, and 18.2 (95% CI: 16.3, 20.2) in Pando-Barros Blancos, Uruguay. The multivariate model showed that, adjusted by location, being female, being between 35 and 44 years old, having experienced at least one stressful life event, currently smoking, and having a history of chronic medical diseases were independently associated with an increased risk of MDE, while having higher education and being married or living with a partner reduced the risk of MDE.

Limitations: These results are representative of the selected cities included in the study. As such extrapolation to the general populations of Argentina, Chile, and Uruguay should be done with caution

Conclusions: This study showed a high prevalence and variability of MDE in the Southern Cone of Latin America.

1. Introduction

Mental and substance use disorders are major contributors to the global burden of disease and their impact has been rising in the recent years (Whiteford et al., 2013). Five types of mental illness appear within the top 20 causes of global burden of disease (GBD), with major depression being the mental disorder associated with the greatest burden (Global burden of disease, 2015). According to the World Health Organization (WHO) over 350 million people have depression and on average about 1 in 20 people reported having a depressive episode the previous year (Marcus et al., 2012).

Prevalence of depression varies according to the region and

methodology employed in each study. With regards to regional differences, a study employing the same methodology and conducted to determine the rate of major depression in 10 countries, found that depression prevalence is extremely variable with higher values found in Western compared to Eastern countries (Weissman et al., 1996). Regarding methodology, a systematic review of the epidemiological literature including studies from 53 countries found that when depression prevalence was assessed with structure interviews based on either the Diagnostic and Statistical Manual of Mental Disorders (DSM) or the International Classification of Diseases (ICD), the pooled point prevalence was 3.8% (95% CI = 3.1; 4.6), while when using symptom scale instruments, it was 12.1% (95% CI = 9.3; 15.7) (Ferrari et al.,

* Corresponding author.

E-mail address: virazola@iecs.org.ar (V.E. Irazola).

2013).

There are different symptoms scale instruments available to assess depressive symptoms. The Patient Health Questionnaire-9 (PHQ-9) is one of the most commonly used instruments not only to detect patients with Major Depressive Episode (MDE) but also to assess the severity of depression in clinical (12) and population based studies (13–16). There is an adapted version of the PHQ-9 in Spanish for Latin America that has been recently validated and calibrated in Argentina by our research team to determine the appropriate cut-off points for assessing diagnosis and degrees of the severity of MDE in the adult population (Urtasun et al., 2017).

Several studies have consistently found some risk factors related to depression, such as sex (more females than males are affected) and age (depression is more frequently found in middle-aged people) (Paykel et al., 2005). However, the variability observed in the prevalence rates for major depression across countries suggests that some cultural differences or environmental risk factors may affect the expression of the disorder (Weissman et al., 1996). Unfortunately, almost two-thirds of the epidemiological studies on depression were conducted in North America or Western Europe (Ferrari et al., 2013) while information from developing regions such as South America is scarce. Since the epidemiology of depression has only been reported for two countries in the region: Brazil (Andrade et al., 2003, 2002; Munhoz et al., 2016; Simon et al., 2002) and Chile (Andrade et al., 2003; Araya et al., 2001) there is an urgent need to conduct more population-based epidemiological studies on depression across countries in Latin America.

In order to reduce this knowledge gap, the aim of the present study was to estimate the prevalence and geographical variability of MDE in the general adult populations in four cities in the Southern Cone of Latin America (Argentina, Uruguay and Chile). We also aimed to evaluate the independent associations of MDE with sociodemographic, behavioral factors, chronic medical illness and stressful life events (SLEs). These results would be beneficial to the development of policies that aim at reducing the mental health burden in the region.

2. Materials and methods

2.1. Study participants

The details of the study design and sampling methods of the CESCAS I study have been published previously (Rubinstein et al., 2011). Briefly, 7524 women and men aged 35–74 years old, were recruited between February 2010 and December 2011 from randomly selected samples in 4 mid-sized cities in the Southern Cone of Latin America: two cities located in Argentina (Bariloche and Marcos Paz), one in Chile (Temuco), and one in Uruguay (Pando-Barros Blancos). Marcos Paz and Pando-Barros Blancos are small cities with 54,000 and 58,000 residents, respectively, according to the latest census data. Bariloche (Argentina) and Temuco (Chile) are larger cities with 134,000 and 245,000 residents, respectively, according to the latest census data. Only the urban populations were included from these sites. These study locations were selected based on population characteristics reflecting country averages. In addition, all four locations have demonstrated stable populations with migration rates below 10% over the past 10 years. A four-stage stratified sampling method was used to select a representative sample from the general population of the Southern Cone of Latin America (Levy and Lemeshow, 2008). In the first stage, census radii were randomly selected from each of the four locations, stratified by socio-economic level. In the second stage, a number of blocks proportional to the radius size were randomly selected. In the third stage, households within each block were selected by systematic random sampling. All members between the ages of 35 and 74 in the selected households were listed to create the study sampling frame. In the final stage of sampling, one listed member per household was randomly selected to be included in the study.

Of the 10,254 individuals randomly selected, 550 were never found

at their homes and 1,394 refused to participate. Of those 8310 who completed the home surveys, 786 did not attend the clinical examination. Thus, the final sample for this analysis includes 7,524 participants (3,165 men and 4,359 women). The overall response rate was 73.4%, and the response rates were similar in men and women and across different locations.

The study complies with the Declaration of Helsinki. The study protocol was approved by IRBs in all participating institutes in Argentina, Chile, Uruguay and the US and written informed consent was obtained from all study participants.

2.2. Data collection

Study data were collected during a home visit and a clinical visit. Depression was measured during the home visits, using the PHQ-9. The PHQ-9 is a nine-item self-reported scale, developed to diagnose MDE as well as assess the severity of depressive symptoms during the two weeks prior to data collection in primary care settings and the community. The definition of an MDE according to the PHQ-9 is based on the DSM-IV diagnostic criteria, which considers at least 2 weeks of persistent depressed mood or anhedonia, accompanied by a total of at least 5 or more of the 9 DSM-IV symptoms of major depression during the episode (significant weight change [5%] or change in appetite; change in sleep [insomnia or hypersomnia]; change in activity [psychomotor agitation or retardation]; fatigue or loss of energy; feelings of worthlessness or excessive or inappropriate guilt; diminished ability to think or concentrate or more indecisiveness; and thoughts of death or suicide) (Kroenke et al., 2001). Each question in the PHQ-9 has four response choices: “not at all”, “several days”, “more than half the days”, and “nearly every day”. This instrument has been validated and calibrated in Argentina (Urtasun et al., 2017). Two scoring systems have been proposed for the PHQ-9 (Kroenke et al., 2001) in the present study, the continuous score was employed by adding up the responses to the nine questions. This way of using the PHQ-9 allowed for the assessment not only of the diagnosis but also of the severity of depressive symptoms, the score ranging from 0 to 27. The cut-off point of ≥ 8 used to determine MDE was based on the calibration of this instrument by our group (Urtasun et al., 2017). Regarding the severity, the cut-off points for depressive symptoms were 6–8 for mild, 9–14 for moderate and ≥ 15 for severe depression (Urtasun et al., 2017).

During the home survey, other information on demographic characteristics, including age, sex, education, occupation, and lifestyle risk factors, including cigarette smoking, alcohol consumption, and physical activity was obtained using standard questionnaires. Religious practice was defined as attending religious services at least once a week. Stressful life events (SLEs) were determined by asking participants whether they had experienced stressful life events in the past year such as marital separation or divorce, loss of job or retirement, loss of crop or business failure, violence, major intra-family conflict, major personal injury or illness, death or major illness of a close family member, death of a spouse, or other major stress (Rosengren et al., 2004, 2015). Quality of life was assessed by Mental Health and Physical Composite Scale scores derived from the locally validated version of the SF-12 (Augustovski et al., 2008).

During the clinical examination, blood pressure (BP) and anthropometric measurements were obtained by trained and certified observers using the standard protocols and techniques described previously (Pickering et al., 2005). Hypertension was defined as mean systolic BP ≥ 140 mm Hg, and/or diastolic BP ≥ 90 mm Hg, and/or current use of antihypertensive medications. Obesity was defined as a body-mass index (BMI) ≥ 30 kg/m², and overweight as BMI ≥ 25 kg/m² (Grundy et al., 2005). Diabetes was defined as fasting glucose ≥ 126 mg/dL or self-reported history of Diabetes (2014).

Table 1
General characteristics of the study population in the Southern Cone of Latin America.

	No. of study participants	Unemployed	Married or living with partner	Regular religious practice	Stressful life events		Current cigarette smoking	Alcohol abuse	High Physical Activity	PCSC ^a	MCSC ^a
					No events	1 event					
Overall	7524	6.0 (5.3, 6.7)	69.8 (68.5, 71.1)	30.1 (28.8, 31.4)	47.1 (45.7, 48.5)	29.9 (28.7, 31.2)	29.7 (28.4, 31.0)	4.2 (3.6, 4.7)	64.8 (63.5, 66.2)	49.3 (49.1, 49.5)	51.8 (51.4, 52.1)
Sex											
Men	3165	5.1 (4.2, 6.1)	77.9 (76.2, 79.7)	24.0 (22.2, 25.9)	48.6 (46.5, 50.7)	30.6 (28.7, 32.5)	33.3 (31.3, 35.3)	6.2 (5.3, 7.2)	71.7 (69.8, 73.6)	49.8 (49.5, 50.1)	54.1 (53.6, 54.5)
Women	4359	6.8 (5.7, 7.8)	62.5 (60.7, 64.3)	35.5 (33.7, 37.3)	45.8 (44.0, 47.7)	29.3 (27.6, 31.0)	26.5 (24.8, 28.3)	2.3 (1.8, 2.8)	58.7 (56.9, 60.6)	48.8 (48.6, 49.1)	49.7 (49.2, 50.2)
Age groups, years											
35–44	1716	8.7 (7.2, 10.3)	72.5 (70.1, 75.0)	26.5 (24.0, 29.0)	50.2 (47.5, 53.0)	27.3 (24.8, 29.7)	33.9 (31.2, 36.5)	3.6 (2.6, 4.6)	67.7 (65.1, 70.4)	50.6 (50.3, 51.0)	51.4 (50.7, 52.0)
45–54	2072	6.4 (5.2, 7.6)	70.9 (68.7, 73.1)	29.1 (26.8, 31.4)	46.2 (43.8, 48.7)	31.0 (28.7, 33.3)	35.8 (33.4, 38.1)	4.4 (3.5, 5.4)	65.5 (63.2, 67.9)	49.5 (49.1, 49.8)	51.6 (51.0, 52.1)
55–64	2114	3.8 (2.9, 4.8)	67.6 (65.3, 69.9)	32.6 (30.3, 34.9)	43.7 (41.3, 46.0)	32.2 (29.9, 34.4)	24.2 (22.2, 26.3)	4.7 (3.7, 5.6)	64.4 (62.1, 66.7)	48.5 (48.1, 48.9)	51.8 (51.2, 52.4)
65–74	1622	0.5 (0.1, 0.8)	62.8 (60.1, 65.4)	38.8 (36.1, 41.5)	45.6 (42.9, 48.3)	31.6 (29.0, 34.1)	12.6 (10.9, 14.4)	4.2 (3.2, 5.2)	55.4 (52.7, 58.1)	46.2 (45.8, 46.7)	53.4 (52.7, 54.0)
Education level											
Primary School	3409	5.2 (4.3, 6.2)	66.8 (64.8, 68.7)	29.6 (27.7, 31.6)	48.3 (46.3, 50.4)	29.5 (27.6, 31.4)	26.4 (24.5, 28.2)	4.4 (3.5, 5.3)	66.7 (64.8, 68.6)	48.3 (47.9, 48.6)	52.7 (52.2, 53.2)
Secondary School	2790	6.3 (5.1, 7.4)	73.3 (71.4, 75.2)	30.4 (28.3, 32.5)	47.4 (45.2, 49.7)	30.8 (28.7, 32.8)	31.2 (29.1, 33.3)	3.8 (3.0, 4.6)	65.1 (63.0, 67.3)	49.8 (49.5, 50.1)	51.5 (51.0, 52.1)
University	1318	6.7 (4.9, 8.5)	67.9 (65.0, 70.9)	30.0 (27.0, 33.0)	44.8 (41.6, 48.0)	29.1 (26.2, 32.0)	32.0 (28.9, 35.0)	4.5 (3.3, 5.7)	61.6 (58.4, 64.7)	49.8 (49.4, 50.3)	50.8 (50.1, 51.6)
Location											
Marcos Paz, Argentina	1991	8.5 (7.1, 9.9)	72.7 (70.6, 74.7)	14.1 (12.5, 15.6)	61.4 (59.0, 63.7)	24.2 (22.1, 26.2)	28.7 (26.5, 31.0)	2.0 (1.3, 2.7)	75.7 (73.7, 77.6)	48.6 (48.3, 48.9)	56.0 (55.6, 56.5)
Bariloche, Argentina	1999	3.4 (2.5, 4.3)	68.9 (66.7, 71.0)	28.9 (26.9, 31.0)	44.4 (42.0, 46.8)	34.3 (32.1, 36.6)	28.2 (26.0, 30.4)	7.5 (6.3, 8.8)	72.2 (70.2, 74.3)	49.7 (49.3, 50.0)	53.8 (53.2, 54.3)
Temuco, Chile	1950	7.3 (5.9, 8.6)	70.0 (67.8, 72.2)	39.3 (37.0, 41.7)	45.3 (42.9, 47.7)	28.4 (26.2, 30.5)	30.9 (28.6, 33.2)	1.9 (1.2, 2.6)	58.0 (55.6, 60.4)	49.4 (49.1, 49.8)	49.7 (49.2, 50.3)
Barros Blancos, Uruguay	1584	5.1 (3.9, 6.3)	69.1 (66.7, 71.4)	13.9 (12.1, 15.6)	48.7 (46.1, 51.3)	30.5 (28.1, 32.9)	29.5 (27.1, 32.0)	6.5 (5.2, 7.7)	65.7 (63.2, 68.1)	48.6 (48.2, 49.0)	51.8 (51.2, 52.5)

	Hypertension	Diabetes	Obesity	History of Cardiovascular Disease		History of Respiratory Disease		History of Cancer
				No events	1 event	No events	1 event	
Overall	40.8 (39.4, 42.1)	12.4 (11.5, 13.3)	35.7 (34.4, 37.0)	8.6 (7.9, 9.3)	7.9 (7.2, 8.7)	3.8 (3.3, 4.3)		
Sex								
Men	44.7 (42.6, 46.7)	10.6 (9.4, 11.7)	31.9 (30.0, 33.8)	9.2 (8.1, 10.2)	6.7 (5.7, 7.7)	1.6 (1.2, 2.0)		
Women	37.3 (35.5, 39.0)	14.0 (12.8, 15.3)	39.1 (37.3, 40.9)	8.1 (7.2, 9.1)	9.0 (8.0, 10.1)	5.8 (5.0, 6.7)		
Age groups, years								
35–44	22.5 (20.2, 24.8)	6.1 (4.7, 7.4)	32.4 (29.8, 35.0)	4.6 (3.5, 5.8)	5.5 (4.3, 6.8)	2.0 (1.2, 2.8)		
45–54	38.8 (36.4, 41.2)	11.1 (9.5, 12.7)	35.3 (33.0, 37.7)	6.7 (5.5, 7.9)	8.0 (6.7, 9.3)	3.8 (2.8, 4.7)		
55–64	57.2 (54.8, 59.6)	18.4 (16.5, 20.3)	39.3 (37.0, 41.7)	12.4 (10.8, 14.0)	10.1 (8.6, 11.7)	5.2 (4.0, 6.3)		
65–74	72.4 (69.9, 74.8)	24.1 (21.7, 26.4)	40.6 (37.9, 43.2)	18.7 (16.6, 20.8)	11.3 (9.6, 13.0)	7.2 (5.8, 8.6)		
Education level								
Primary School	50.6 (48.5, 52.6)	15.6 (14.1, 17.0)	40.9 (38.9, 42.9)	11.4 (10.1, 12.7)	9.3 (8.1, 10.5)	3.8 (3.0, 4.5)		
Secondary School	38.3 (36.1, 40.4)	11.7 (10.3, 13.0)	35.1 (33.0, 37.3)	8.1 (7.0, 9.3)	6.9 (5.9, 7.9)	3.9 (3.1, 4.7)		
University	31.1 (28.3, 33.9)	9.1 (7.3, 10.9)	29.4 (26.4, 32.3)	5.5 (4.2, 6.7)	7.8 (6.0, 9.5)	3.8 (2.6, 5.0)		
Location								
Marcos Paz, Argentina	41.0 (38.7, 43.4)	11.9 (10.4, 13.4)	44.7 (42.3, 47.2)	7.6 (6.4, 8.8)	6.9 (5.7, 8.2)	1.6 (1.1, 2.1)		
Bariloche, Argentina	45.3 (42.9, 47.6)	8.4 (7.2, 9.6)	32.2 (30.0, 34.4)	6.6 (5.5, 7.7)	6.4 (5.3, 7.5)	3.6 (2.8, 4.4)		

(continued on next page)

Table 1 (continued)

	Hypertension	Diabetes	Obesity	History of Cardiovascular Disease	History of Respiratory Disease	History of Cancer
Temuco, Chile	36.9 (34.6, 39.1)	14.3 (12.7, 15.8)	35.6 (33.3, 37.9)	8.7 (7.5, 9.9)	8.5 (7.2, 9.8)	4.3 (3.4, 5.2)
Barros Blancos, Uruguay	44.5 (41.9, 47.0)	14.2 (12.5, 15.9)	36.7 (34.2, 39.2)	12.5 (10.9, 14.1)	9.6 (8.1, 11.0)	4.2 (3.2, 5.1)

Hypertension: systolic blood pressure \geq 140 mm Hg and/or diastolic blood pressure \geq 90 mm Hg and/or use of antihypertensive medication; Diabetes: fasting glucose \geq 126 mg/dL or self-reported history of diabetes; Obesity: body-mass index \geq 30 kg/m²; History of Cardiovascular disease: self-report any of the following conditions diagnosed by a physician: acute myocardial infarction, angina, heart failure, cerebrovascular events, peripheral vascular disease or coronary or peripheral revascularization; Cancer by self-report; History of Respiratory disease: COPD, asthma and TB by self-report.

* Data are weighted percentages (95% confidence intervals).
^a Data are weighted means (95% confidence intervals). Regular religious practice was defined as \geq 1 religious practices per week; Alcohol Abuse: \geq 15 drinks per week in men or \geq 8 drinks per week in women; High physical activity: \geq 600 MET-minutes/week; PCSc: Physical Health Composite Scale scores derived from the SF-12; MCSc: Mental Health Composite Scale scores derived from the SF-12.

2.3. Statistical analysis

All calculations were weighted to represent the general adult population aged 35–74 years in the study sites, according to the study sampling design. Prevalence of MDE and Depressive Symptoms were calculated for the overall population, by sex and four age groups: 35–44, 45–54, 55–64 and 65–74 years old. Standard errors were calculated by a technique appropriate for the complex survey design (Levy and Lemeshow, 2013; Rubinstein et al., 2011). Odds ratios (OR) and 95% CI for the association between MDE and selected risk factors were obtained using multivariable-adjusted logistic regression models. All data analyses were done with SAS 9.3 (SAS Institute, Cary NC).

3. Results

3.1. General characteristics

The demographics and behavioral risk factors in the study population are shown in Table 1. A total of 7524 subjects were included, 3165 (42.1%) men and 4359 (57.9%) women. Approximately, 52.3% did not complete high school (52.4% of men and 52.2% of women), 6.0% were unemployed (5.1% of men and 6.8% of women) and 69.8% were married or lived with a partner (77.9% of men and 62.5% of women).

About 30.1% of adults (24.0% men and 35.5% women) reported maintaining a regular religious practice with variations across the sites, being higher in Temuco, Chile (39.3%) and lower in Pando-Barros Blancos, Uruguay (13.9%).

Almost 52.9% of adults (51.4% men and 54.2% women) reported at least one SLE in the year previous to the assessment. These values were consistent across sex and age groups, however, differed between cities, being lower in Marcos Paz, Argentina (38.6%). Overall, 29.7% of adults (33.3% men and 26.5% women) were current cigarette smokers and 4.2% (6.2% men and 2.3% women) were heavy drinkers. While the prevalence of cigarette smoking was consistent among the four study locations, alcohol excess varied significantly, with higher values in Temuco (39.3%) and lower values in Marcos Paz (14.1%).

The mean value of the Physical Health Composite Scale (PCSc) score derived from the SF-12 was 49.3 (95% CI: 49.1, 49.5), while the mean Mental Health Composite Scale score (MCSc) was 51.8 (95% CI: 51.4, 52.1). These values were higher in men than in women. PCSc values decreased with age.

3.2. Prevalence of MDE and severity of depressive symptoms

Overall prevalence of MDE in adults aged 35–74 years in the Southern Cone was 14.6% (95% CI: 13.6, 15.6) (Table 2) with variation according to sex and age, being almost double in women than in men (9.9% in men and 18.8% in women), and decreasing in adults older than 65 years old (14.3% 35–44 of age, 15.8% 45–54 of age, 14.5% 55–64 of age and 12.9% 65–74 of age). With the increase of educational level there was a decreasing trend in the prevalence of MDE (16.3% primary school, 13.9% secondary school and 13.3% university level) this being observed among both men and women (Table 2).

There was a geographical variability in the prevalence of MDE: 5.6% (95% CI: 4.6, 6.7) in Marcos Paz, Argentina; 9.5% (95% CI: 8.2, 10.9) in Bariloche, Argentina; 18.1% (95% CI: 16.3, 20.0) in Temuco, Chile, and 18.2 (95% CI: 16.3, 20.2) in Pando-Barros Blancos, Uruguay (Table 2).

We observed a prevalence of 10.7% (95% CI: 9.8, 11.6) for mild depressive symptoms, 8.0% (95% CI: 7.2, 8.8) for moderate depressive symptoms and 3.5% (95% CI: 3.0, 4.1) for severe depressive symptoms (Fig. 1). As observed for MDE prevalence, when analyzing the prevalence of depressive symptoms by sex we observed higher rates for women in comparison to men for all severity categories. In men, 7.9% reported mild depressive symptoms, 5.7% reported moderate depressive symptoms, and 1.9% reported severe depressive symptoms.

Table 2
Estimated prevalence and 95% confidence intervals of Mayor Depressive Episode among study population in the Southern Cone of Latin America.

	Overall	Men	Women
<i>Total</i>	14.6 (13.6, 15.6)	9.9 (8.5, 11.2)	18.8 (17.3, 20.3)
<i>Age groups, years</i>			
35–44	14.3 (12.3, 16.3)	9.8 (7.2, 12.4)	18.5 (15.5, 21.6)
45–54	15.8 (13.9, 17.7)	9.7 (7.5, 12.0)	21.3 (18.4, 24.1)
55–64	14.5 (12.8, 16.3)	10.7 (8.4, 12.9)	18.0 (15.3, 20.6)
65–74	12.6 (10.8, 14.4)	9.0 (6.7, 11.2)	15.4 (12.8, 18.1)
<i>Education Level</i>			
Primary	16.3 (14.7, 18.0)	11.6 (9.4, 13.8)	20.3 (18.0, 22.6)
Secondary	13.9 (12.3, 15.5)	9.2 (7.2, 11.2)	18.2 (15.8, 20.6)
University	13.3 (11.1, 15.6)	8.7 (6.0, 11.5)	17.6 (14.2, 21.1)
<i>Location</i>			
Marcos Paz, Argentina	5.6 (4.6, 6.7)	4.2 (2.7, 5.7)	7.0 (5.5, 8.5)
Bariloche, Argentina	9.5 (8.2, 10.9)	5.1 (3.6, 6.7)	13.6 (11.5, 15.7)
Temuco, Chile	18.1 (16.3, 20.0)	13.0 (10.6, 15.5)	22.5 (19.7, 25.3)
Barros Blancos, Uruguay	18.2 (16.3, 20.2)	12.6 (9.9, 15.2)	23.6 (20.7, 26.4)

Data are weighted percentages (95% confidence intervals).

In women, 13.1% reported mild depressive symptoms, 10.1% moderate depressive symptoms, and 5.0% severe depressive symptoms (Fig. 1). The prevalence distribution of mild, moderate and severe symptoms was the same in all locations.

3.3. Factors associates with MDE

The crude and adjusted odds ratios (ORs) for the association of MDE with locations, sociodemographic characteristics, behavioral factors, and health status are presented in Table 3. After adjusting for covariates, MDE prevalence was significantly different between locations, being lower in Marcos Paz (reference), increasing in Bariloche (OR = 1.5; 95% CI: 1.2, 2.0), and being higher in Temuco (OR = 3.7;

95% CI: 2.9, 4.8) and Pando-Barros Blancos (OR = 3.7; 95% CI: 2.8, 4.7).

In the adjusted model, the prevalence of MDE was more than double in women when compared to men (OR = 2.1; 95% CI: 1.7, 2.6). Regarding age, a higher chance of having a MDE was observed within the group of 35–44 years old, decreasing across older age-groups: 45–54 years old (OR = 1.0; 95% CI: 0.8, 1.2); 55–64 years old (OR = 0.8; 95% CI: 0.6, 1.0); 65–74 years old (OR = 0.6; 95% CI: 0.4, 0.8). There were no differences across locations regarding these associations.

The probability of having an MDE showed an inverse relationship with the educational level, being higher in people with a primary school-level education (reference) and decreasing in the secondary school-level (OR = 0.7; 95% CI: 0.6, 0.8) and the university-level group (OR = 0.5; 95% CI: 0.4, 0.7), across all locations. The association between MDE and employment status was no longer statistically significant after adjustment. Being married or living with a partner reduced the risk of an MDE (OR = 0.8; 95% CI: 0.6, 0.9) in all the sites.

Having an SLE in the past year increased the likelihood of MDE. This effect was dose-dependent, the risk being lower when having one SLE (OR = 2.4; 95% CI: 1.9, 3.0) compared to two or more SLE (OR = 5.2; 95% CI: 4.1, 6.5). The chance of MDE was higher in current smokers (OR = 1.5; 95% CI: 1.2, 1.8) but not in heavy drinkers. After adjusting, the association between high physical activity and MDE was no longer statistically significant.

Finally, the probability of MDE was increased in approximately 50% in individuals with chronic medical illness such as history of cardiovascular disease (OR = 1.5, 95% CI: 1.1, 2.0), or cancer (OR = 1.6; 95% CI: 1.1, 2.3), while the associations between MDE and CV risk factors (hypertension, diabetes and obesity) were lost after adjustment. These findings were the same across all sites.

4. Discussion

The major finding of the present study was that the prevalence of MDE in adults aged 35–74 years in a representative sample of the general populations of four cities in the Southern Cone of Latin-America was 14.6% (95% CI 13.6; 15.6). The MDE prevalence showed a significant variability of up to 3.7 folds between different cities. Interestingly, across all the locations, being female, being between the ages of 35–44, having experienced at least one SLE, current smoking, and history of chronic disease (cardiovascular disease, respiratory disease, or cancer) were associated with an increased risk

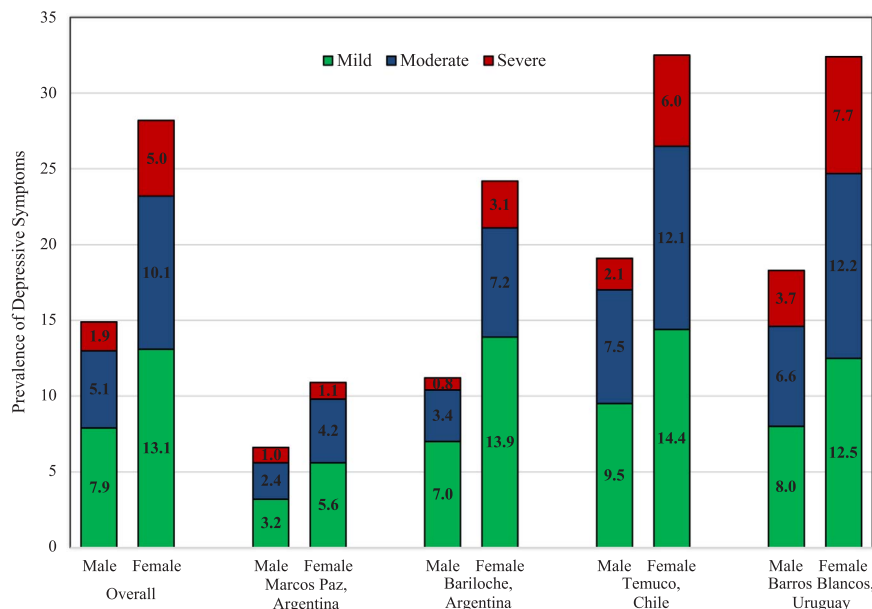


Fig. 1. Prevalence of Depressive Symptoms among study population in the Southern Cone of Latin America.

Table 3

Unadjusted and adjusted odds ratios (ORs) and 95% confidence intervals (95% CIs) for the association of risk factors with Mayor Depressive Episode among study population in the Southern Cone of Latin America.

Risk factors		Unadjusted ¹ OR (95% CI)	Adjusted ¹ OR (95% CI)	Adjusted ² OR (95% CI)
Location	Marcos Paz, Argentina	1.0	1.0	1.0
	Bariloche, Argentina	1.8 (1.4, 2.3)	1.6 (1.2, 2.1)	1.5 (1.2, 2.0)
	Temuco, Chile	3.7 (2.9, 4.7)	3.9 (2.9, 5.1)	3.7 (2.9, 4.8)
	Barros Blancos, Uruguay	3.7 (3.1, 4.8)	3.6 (2.8, 4.7)	3.7 (2.8, 4.7)
Sex	Men	1.0	1.0	1.0
	Women	2.1 (1.8, 2.5)	2.09 (1.7, 2.6)	2.07 (1.7, 2.5)
Age, yrs	35–44	1.0	1.0	1.0
	45–54	1.1 (0.9, 1.4)	1.0 (0.8, 1.2)	0.9 (0.7, 1.2)
	55–64	1.0 (0.8, 1.3)	0.8 (0.6, 1.0)	0.8 (0.6, 1.0)
	65–74	0.9 (0.7, 1.1)	0.6 (0.4, 0.8)	0.6 (0.4, 0.7)
Education level	Primary	1.0	1.0	1.0
	Secondary	0.8 (0.7, 1.0)	0.7 (0.6, 0.8)	0.7 (0.6, 0.9)
	University	0.8 (0.6, 1.0)	0.5 (0.4, 0.7)	0.5 (0.4, 0.7)
Unemployed	No	1.0	1.0	
	Yes	1.7 (1.2, 2.3)	1.2 (0.9, 1.7)	
Married or living with partner	No	1.0	1.0	1.0
	Yes	0.6 (0.5, 0.7)	0.8 (0.7, 1.0)	0.8 (0.6, 0.9)
Regular religious practice	No	1.0	1.0	
	Yes	0.9 (0.8, 1.1)	0.8 (0.7, 1.0)	
Stressful life events	Without events	1.0	1.0	1.0
	One event	2.5 (2.0, 3.1)	2.4 (1.9, 3)	2.4 (1.9, 3.0)
	Two or more events	5.8 (4.7, 7.2)	5.15 (4.1, 6.5)	5.24 (4.2, 6.6)
Current cigarette smoking	No	1.0	1.0	1.0
	Yes	1.6 (1.3, 1.9)	1.5 (1.2, 1.8)	1.6 (1.3, 2.0)
Alcohol abuse	No	1.0	1.0	
	Yes	1.1 (0.8, 1.7)	1.2 (0.8, 1.8)	
High physical activity	No	1.0	1.0	
	Yes	0.8 (0.7, 0.9)	0.9 (0.8, 1.1)	
Physical Health Composite Score (cont., change 1 point)	0.9 (0.9, 1.0)	1.0 (1.0, 0.1.0)	1.0 (1.0, 1.0)	1.0 (1.0, 1.0)
Hypertension	No	1.0	1.0	
	Yes	0.8 (0.7, 0.9)	0.9 (0.7, 1.1)	
Diabetes	No	1.0	1.0	
	Yes	1.3 (1.1, 1.6)	1.1 (0.9, 1.4)	
Obesity	No	1.0	1.0	
	Yes	1.0 (0.8, 1.2)	0.9 (0.7, 1.1)	
History of CV disease	No	1.0	1.0	1.0
	Yes	2.0 (1.6, 2.5)	1.5 (1.2, 2.0)	1.5 (1.1, 1.9)
History of respiratory disease	No	1.0	1.0	1.0
	Yes	1.9 (1.5, 2.4)	1.5 (1.1, 2.0)	1.5 (1.1, 2.0)
History of cancer	No	1.0	1.0	1.0
	Yes	2.1 (1.5, 2.9)	1.6 (1.1, 2.3)	1.6 (1.1, 2.3)

Adjusted¹ for all variables.

Adjusted² for all significant variables.

of MDE, while having higher education and being married or living with a partner reduced the risk of MDE. Of note, despite the differences observed in the prevalence of MDE by city, factors associated with this condition were consistent across sites.

Depression is one of the leading causes of worldwide disease burden (Vigo et al., 2016; Whiteford et al., 2013). Taking into account that epidemiological studies which have measured the prevalence of depression across several countries consistently detected large cross-national variations with almost 15-fold variation between the highest and lowest rates (Simon et al., 2002), regional studies are urgently needed to plan local intervention strategies. However, most of the epidemiological studies of depression are from high-income countries and there are few studies from low-and middle-income countries (Ferrari et al., 2013). Particularly in South America, information regarding the prevalence of depression is scarce. Epidemiological studies have been reported only in two countries, Chile (Andrade et al., 2003; Araya et al., 2001) and Brazil (Andrade et al., 2003; Munhoz et al., 2016). In Chile, depression has been measured in Santiago de Chile, the capital city, using the Clinical Interview Schedule-Revised (CIS-R), reporting a point prevalence of 5.5 (4.5; 6.7) for MDE (Araya et al., 2001). In this country depression has also been assessed in four different cities by the International Consortium of Psychiatric Epidemiology (ICPE), with the Composite International

Diagnostic Interview (CIDI) reporting an average point prevalence of 3.3 (0.4) for MDE (Andrade et al., 2003). The ICPE also measured depression in São Paulo, Brazil, reporting a point prevalence of 3.9 (0.6) (Andrade et al., 2003). The prevalence reported in the present study is higher than those previously described in Chile and Brazil. This may be related to the different instruments employed to measure depression. In the present study, we used the PHQ-9, which is a self-reported depressive symptoms scale, while the Chilean and Brazilian studies used clinical structured interviews such as the CIS-R or the CIDI. It has been recognized that symptoms scales yield higher values of MDE prevalence when compared with clinical structural interviews (Ferrari et al., 2013). However, their use has been accepted, especially for large-scale epidemiological studies, where clinical interviews would not be feasible (Hollifield et al., 2002). Recently, a systematic review summarizing the epidemiology of major depressive disorder across 53 countries found, using symptom scale instruments, that point prevalence of depression worldwide was 12.1% (9.3; 15.7) (Ferrari et al., 2013), which is similar to our findings.

Several epidemiological studies comparing the prevalence of MDE across different countries consistently found large cross-national variability (Weissman et al., 1996). Some of the proposed explanations for this variability include using different sampling methods, diagnostic tools, and analytical approaches (Ferrari et al., 2013). In the present

study, we were able to establish a direct comparison of MDE prevalence across 4 representative cities of 3 different countries in the Southern Cone of Latin America (Argentina, Chile and Uruguay) with the same method, diagnostic tool, and statistical analysis. We found a wide range of variability ranging from 5.6% (4.6, 6.7) to 18.2% (16.3, 20.2), suggesting that these methodological aspects would not be an explanation for the variation found. The results of our study confirms and expands the observation of the WHO International Consortium in Psychiatry Epidemiology (ICPE), which conducted an epidemiological study comparing the rates of depression in 37,000 respondents from 10 different countries using the same methodology and observing a substantial cross-national variation (Andrade et al., 2003). Other studies suggested that cross-national variation in MDE prevalence might be due, at least in part, to cultural differences in the threshold for reporting depressive symptoms (Andrade et al., 2002). However, the present study investigated 4 cities in the 3 culturally-related countries of Argentina, Chile, and Uruguay, observing a variability of up to 3.7 folds. Likewise, an epidemiological study carried out with 2509 adults in 4 cities in Mexico also found that prevalence of MDE varied by location (Slone et al., 2006), speculating that variability depends on the characteristics of these cities, with the highest prevalence of depression in those cities with higher levels of poverty (Slone et al., 2006). However, our findings contradict this hypothesis, since the smallest city with the highest level of poverty, Marcos Paz, showed the lowest MDE prevalence. This observation is in line with a cross-national epidemiological study of MDE in 18 countries, which observed that the highest prevalence of depression was found in the world's wealthiest countries (Bromet et al., 2011). Therefore, other characteristics of these cities, such as welfare or optimism, which we have not quantified in the present study, might explain these differences.

The large cross-sectional differences in the prevalence of depression contrast with the relatively uniform prevalence of other major psychiatric disorders like bipolar disorder (Weissman et al., 1996) or schizophrenia (Sartorius et al., 1986), which may suggest that depression is strongly influenced by social or environmental factors. In this study, we explored whether social (e.g. education) or environmental factors (e.g. STLEs) could explain variations in MDE prevalence; however, none of these factors could explain the observed differences. Therefore, differences in MDE prevalence may be due to unidentified sources that we were unable to capture in the present study. More cross-national research is needed to explore and interpret the impact of other determinants of depression across cities and regions.

Regarding measurement tools, there are several symptom scales available to assess depressive symptoms, however most of them have been developed in high-income countries and have not been adapted cross-culturally or validated for their use in Latin America. The PHQ-9, one of these symptoms scales, is a short self-administered questionnaire (Kroenke et al., 2010), widely used for the screening of depression in primary care settings (Kung et al., 2013) and in large epidemiological studies (Tracy et al., 2014; van Dooren et al., 2016). The PHQ-9 is based on DSM IV criteria and can be used to diagnose patients with MDE, and also for severity assessment of depression (Kroenke et al., 2010). There are two possibilities for the scoring of PHQ-9: one is a scoring algorithm, based on DSM-IV criteria (Lotrakul et al., 2008) and the other a score that is based on a continuous measurement composed of the responses to the nine questions, which range from 0 to 27 (the higher the score, the more severe the depression) (Chagas et al., 2013). Recently, Munhoz et al. (Munhoz et al., 2016) used the PHQ-9 in a population-based study of depression in Brazil and reported that 13.2% of the individuals presented mild depression, 4.8% moderate depression, 2.1% moderately-severe depression, and 1.0% severe depression. However, one of the main limitations of this study was that the Brazilian version of the PHQ-9 had not been previously calibrated in Brazil, meaning they employed the cut-off points reported by Kroenke et al. for the U.S. population (Kroenke et al., 2001). We have recently validated and calibrated, at a local level, the adapted version of the

PHQ-9 in Spanish for Latin America, to determine the appropriate cut-off points for the diagnosis of MDE and assessment of the severity of depression symptoms in the adult population (Urtasun et al., 2017). Interestingly, we reported differences in the cut-off points when comparing them with the ones obtained by Kroenke for the US population (Urtasun et al., 2017). When evaluating the severity of depressive symptoms in the Southern Cone of Latin-America, we found a prevalence of 10.7% (95% CI: 9.8, 11.6) for mild depressive symptoms, 8.0% (95% CI: 7.2, 8.8) for moderate depressive symptoms and 3.5% (95% CI: 3.0, 4.1) for severe depressive symptoms. Information regarding the severity of depressive symptoms is highly relevant for planning intervention strategies, considering that interventions vary according to depression severity, e.g. mild depression can be treated with either psychotherapy or pharmacotherapy while severe depression requires pharmacological treatments or the combination of both pharmacological treatments with psychotherapy (Gelenberg et al., 2010). To our knowledge, the present study is the first epidemiological study to report the severity categories of depression after using a calibrated instrument in the Southern Cone of Latin America.

Consistent with the epidemiological literature (Ferrari et al., 2013), prevalence of depression in the Southern Cone of Latin America is higher in women than in men, with an overall gender ratio of 2:1. The present study also demonstrates that this ratio was even larger (3:1) for severe depression. The explanations for this difference are not clear, but are likely due to combined factors related to biology and social determinants (Paykel, 1991). It has been reported that age and depression are related in a curvilinear manner (Jorm, 1987). The prevalence of depression starts to rise in adolescence, reaching a pick at middle age and then declining subsequently. In the present study we observed that the prevalence of depression decreases as age increases. It is worth mentioning that the present study includes patients ranging from 35 to 74 years old, therefore, we could only analyzed the descending part of the age curve. The association between MDE and being married or living with a partner was not surprising, since most epidemiological studies on depression have reported not living alone as a protective factor (Andrade et al., 2003; Paykel et al., 2005; Weissman et al., 1996).

Previous studies have also shown an association between depression and variables representing less privileged social position (Fryers et al., 2003). Accordingly, we observed that a low educational level was associated with a higher prevalence of depression; however, the relation between depression and unemployment was not found in the multivariable adjusted model.

Different theories have been proposed to explain the etiology of affective disorders, with some of them based on biological variables while others refer to psychological or cultural factors (Akiskal et al., 2006; Kessing et al., 2004). Nowadays it is accepted that the occurrence of affective disorders cannot be understood by focusing on factors from a single domain and most theories are based on the stress-diathesis model (Ghaemi, 2004; Monroe and Simons, 1991; Perris, 1991). Based on this model, affective symptoms result from an interaction between both environmental and biological factors. Thus, we explored the association of MDE with different environmental factors. Although we failed to observe a protective effect of regular religious practice and high physical activity; we found a strong and dose-related association with recent SLE. Stressful life events in depressed subjects showed ORs in the range of 6–7 (Paykel, 1978), which are higher than the values found in other psychiatric illnesses like schizophrenia. This suggests an associated effect of moderate magnitude while leaving room for other biological factors, indicating a multifactorial causation (Paykel, 2002). The present study has a cross-sectional design and, therefore, cannot establish causality. However, both the strength of the association and the dose-dependence relationship make the SLE relevant for exploration in further longitudinal studies. Although the association between the MDE and SLE has been demonstrated previously (Paykel et al., 2005), the present study is the first report for a Latin American population.

Previous studies have shown an association between depression and addictive behaviors such as smoking or alcohol abuse (Chaiton et al., 2009). Here we observed an association between MDE and smoking, however, no association with alcohol abuse was found.

Several studies have shown a relationship between depression and physical illness (Fryers et al., 2003; Yanzon de la Torre et al., 2016). Here, we observed that the probability of having an MDE among chronically ill patients with histories of cancer, cardiovascular diseases or respiratory diseases was almost 50% higher than those without chronically illness.

4.1. Study strength and limitations

The main strengths of the current study are: 1-the random multi-stage sampling design, which allowed a direct estimation of the prevalence of MDE and depressive symptoms in adults, and which supported representativeness of the target population; 2-the high response rate (73.4%), which minimized selection bias; and 3-the use of a rigorous methodology, standardized measurements, and trained interviewers.

Some limitations of the present study should be underscored. Although the PHQ-9 has been validated and calibrated in Argentina, it was not calibrated in Chile and Uruguay. However, we consider that Argentina is culturally much closer to Chile and Uruguay than other countries and therefore the local cut-off points are more suitable than other alternatives. Finally, these results are representative of the selected cities included in the study. As such extrapolation to the general populations of Argentina, Chile, and Uruguay should be done with caution.

5. Conclusions

The present study showed that the prevalence of MDE in adults in a representative sample of the general population of four cities in the Southern Cone of Latin America was 14.6% (95% CI 13.6; 15.6). MDE prevalence showed a significant geographical variability between different cities. After adjusting by location, being female, being between 35 and 44 years old, having experienced at least one SLE, smoking currently and having a history of chronic disease (cardiovascular disease, respiratory disease, or cancer) were associated with an increased risk of MDE, while having higher education and being married or living with a partner reduced the risk of MDE. Altogether, these results will be useful for the design and implementation of country-specific policies to reduce the mental health burden in the region.

Funding

This project has been funded in whole with Federal funds from the United States National Heart, Lung, and Blood Institute (U01 HD40477), National Institutes of Health, Department of Health and Human Services, under Contract No. 268200900029C.

Acknowledgment

The authors want to gratefully acknowledge the study participants for their collaboration, and the field teams in each city.

References

2014. Diagnosis and classification of diabetes mellitus. *Diabetes Care*, 37, Suppl. 1, S81–S90.
2015. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet*, 386, pp. 743–800.
- Akiskal, H.S., Kilzieh, N., Maser, J.D., Clayton, P.J., Schettler, P.J., Traci Shea, M., Endicott, J., Scheftner, W., Hirschfeld, R.M., Keller, M.B., 2006. The distinct temperament profiles of bipolar I, bipolar II and unipolar patients. *J. Affect. Disord.* 92, 19–33.
- Andrade, L., Walters, E.E., Gentil, V., Laurenti, R., 2002. Prevalence of ICD-10 mental disorders in a catchment area in the city of Sao Paulo, Brazil. *Soc. Psychiatry Psychiatr. Epidemiol.* 37, 316–325.
- Andrade, L., Caraveo-Anduaga, J.J., Berglund, P., Bijl, R.V., De Graaf, R., Vollebergh, W., Dragomirecka, E., Kohn, R., Keller, M., Kessler, R.C., Kawakami, N., Kilic, C., Offord, D., Ustun, T.B., Wittchen, H.U., 2003. The epidemiology of major depressive episodes: results from the International Consortium of Psychiatric Epidemiology (ICPE) Surveys. *Int. J. Methods Psychiatr. Res.* 12, 3–21.
- Araya, R., Rojas, G., Fritsch, R., Acuna, J., Lewis, G., 2001. Common mental disorders in Santiago, Chile: prevalence and socio-demographic correlates. *Br. J. Psychiatry* 178, 228–233.
- Augustovski, F.A., Lewin, G., Elorrio, E.G., Rubinstein, A., 2008. The Argentine-Spanish SF-36 Health Survey was successfully validated for local outcome research. *J. Clin. Epidemiol.* 61, 1279–1284.
- Bromet, E., Andrade, L.H., Hwang, I., Sampson, N.A., Alonso, J., de Girolamo, G., de Graaf, R., Demyttenaere, K., Hu, C., Iwata, N., Karam, A.N., Kaur, J., Kostyuchenko, S., Lepine, J.P., Levinson, D., Matschinger, H., Mora, M.E., Browne, M.O., Posada-Villa, J., Viana, M.C., Williams, D.R., Kessler, R.C., 2011. Cross-national epidemiology of DSM-IV major depressive episode. *BMC Med.* 9, 90.
- Chagas, M.H., Tumas, V., Rodrigues, G.R., Machado-de-Sousa, J.P., Filho, A.S., Hallak, J.E., Crippa, J.A., 2013. Validation and internal consistency of Patient Health Questionnaire-9 for major depression in Parkinson's disease. *Age Ageing* 42, 645–649.
- Chaiton, M.O., Cohen, J.E., O'Loughlin, J., Rehm, J., 2009. A systematic review of longitudinal studies on the association between depression and smoking in adolescents. *BMC Public Health* 9, 356.
- Ferrari, A.J., Somerville, A.J., Baxter, A.J., Norman, R., Patten, S.B., Vos, T., Whiteford, H.A., 2013. Global variation in the prevalence and incidence of major depressive disorder: a systematic review of the epidemiological literature. *Psychol. Med.* 43, 471–481.
- Fryers, T., Melzer, D., Jenkins, R., 2003. Social inequalities and the common mental disorders: a systematic review of the evidence. *Soc. Psychiatry Psychiatr. Epidemiol.* 38, 229–237.
- Gelenberg, A.J., Freeman, M.P., Markowitz, J.C., Rosenbaum, J.F., Thase, M.E., Trivedi, M.H., Van Rhoads, R.S., Reus, V.I., J Raymond DePaulo Jr., M., Fawcett, J.A., 2010. Practice guideline for the treatment of patients with major depressive disorder. *Am. J. Psychiatry* 167, 1 third edition.
- Ghaemi, S.N., 2004. *The Concepts of Psychiatry: A Pluralistic Approach to the Mind and Mental Illness*. JHU Press, Baltimore, Mariland, U.S.
- Grundy, S.M., Cleeman, J.I., Daniels, S.R., Donato, K.A., Eckel, R.H., Franklin, B.A., Gordon, D.J., Krauss, R.M., Savage, P.J., Smith Jr., S.C., Spertus, J.A., Costa, F., 2005. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation* 112, 2735–2752.
- Hollifield, M., Warner, T.D., Lian, N., Krakow, B., Jenkins, J.H., Kesler, J., Stevenson, J., Westermeyer, J., 2002. Measuring trauma and health status in refugees: a critical review. *J. Am. Med. Assoc.* 288, 611–621.
- Jorm, A.F., 1987. Sex and age differences in depression: a quantitative synthesis of published research. *Aust. N. Z. J. Psychiatry* 21, 46–53.
- Kessing, L.V., Agerbo, E., Mortensen, P.B., 2004. Major stressful life events and other risk factors for first admission with mania. *Bipolar Disord.* 6, 122–129.
- Kroenke, K., Spitzer, R.L., Williams, J.B., 2001. The PHQ-9: validity of a brief depression severity measure. *J. Gen. Intern. Med.* 16, 606–613.
- Kroenke, K., Spitzer, R.L., Williams, J.B., Lowe, B., 2010. The patient health questionnaire somatic, anxiety, and depressive symptom scales: a systematic review. *Gen. Hosp. Psychiatry* 32, 345–359.
- Kung, S., Alarcon, R.D., Williams, M.D., Poppe, K.A., Jo Moore, M., Frye, M.A., 2013. Comparing the Beck Depression Inventory-II (BDI-II) and Patient Health Questionnaire (PHQ-9) depression measures in an integrated mood disorders practice. *J. Affect. Disord.* 145, 341–343.
- Levy, P., Lemeshow, S., 2008. *Sampling of Populations: Methods and Applications*, 4th ed. John Wiley & Sons, NY.
- Levy, P.S., Lemeshow, S., 2013. *Sampling of Populations: Methods and Applications*. John Wiley & Sons.
- Lotrakul, M., Sumrithe, S., Saipanish, R., 2008. Reliability and validity of the Thai version of the PHQ-9. *BMC Psychiatry* 8, 46.
- Marcus, M., Yasamy, M., van Ommeren, M., Chisholm, D., Saxena, S., 2012. Depression: a global public health concern. *WHO Dep. Ment. Health Subst. Abuse*.
- Monroe, S.M., Simons, A.D., 1991. Diathesis-stress theories in the context of life stress research: implications for the depressive disorders. *Psychol. Bull.* 110, 406–425.
- Munhoz, T.N., Nunes, B.P., Wehrmeister, F.C., Santos, I.S., Matijasevich, A., 2016. A nationwide population-based study of depression in Brazil. *J. Affect. Disord.* 192, 226–233.
- Paykel, E.S., 1978. Contribution of life events to causation of psychiatric illness. *Psychol. Med.* 8, 245–253.
- Paykel, E.S., 1991. Depression in women. *Br. J. Psychiatry Suppl.* 22–29.
- Paykel, E.S., 2002. Which depressions are related to life stress? *Acta Neuropsychiatr.* 14, 167–172.
- Paykel, E.S., Brugha, T., Fryers, T., 2005. Size and burden of depressive disorders in Europe. *Eur. Neuropsychopharmacol.* 15, 411–423.
- Perris, C., 1991. An interactionistic integrating view of depressive disorders and their treatment. *Acta Psychiatr. Scand.* 84, 413–423.
- Pickering, T.G., Hall, J.E., Appel, L.J., Falkner, B.E., Graves, J., Hill, M.N., Jones, D.W.,

- Kurtz, T., Sheps, S.G., Roccella, E.J., 2005. Recommendations for blood pressure measurement in humans and experimental animals: part 1: blood pressure measurement in humans: a statement for professionals from the subcommittee of professional and public education of the American Heart Association Council on High Blood Pressure Research. *Circulation* 111, 697–716.
- Rosengren, A., Hawken, S., Ounpuu, S., Sliwa, K., Zubaid, M., Almahmeed, W.A., Blackett, K.N., Sitthi-amorn, C., Sato, H., Yusuf, S., 2004. Association of psychosocial risk factors with risk of acute myocardial infarction in 11119 cases and 13648 controls from 52 countries (the INTERHEART study): case-control study. *Lancet* 364, 953–962.
- Rosengren, A., Teo, K., Rangarajan, S., Kabali, C., Khumalo, I., Kutty, V.R., Gupta, R., Yusuf, R., Iqbal, R., Ismail, N., Altuntas, Y., Kelishadi, R., Diaz, R., Avezum, A., Chifamba, J., Zatonska, K., Wei, L., Liao, X., Lopez-Jaramillo, P., Yusufali, A., Seron, P., Lear, S.A., Yusuf, S., 2015. Psychosocial factors and obesity in 17 high-, middle- and low-income countries: the Prospective Urban Rural Epidemiologic study. *Int. J. Obes.* 39, 1217–1223.
- Rubinstein, A.L., Irazola, V.E., Poggio, R., Bazzano, L., Calandrelli, M., Lanús Zanetti, F.T., Manfredi, J.A., Olivera, H., Seron, P., Ponzio, J., He, J., 2011. Detection and follow-up of cardiovascular disease and risk factors in the Southern Cone of Latin America: the CESCAS I study. *BMJ Open* 1, e000126.
- Sartorius, N., Jablensky, A., Korten, A., Ernberg, G., Anker, M., Cooper, J.E., Day, R., 1986. Early manifestations and first-contact incidence of schizophrenia in different cultures. A preliminary report on the initial evaluation phase of the WHO Collaborative Study on determinants of outcome of severe mental disorders. *Psychol. Med.* 16, 909–928.
- Simon, G.E., Goldberg, D.P., Von Korff, M., Ustun, T.B., 2002. Understanding cross-national differences in depression prevalence. *Psychol. Med.* 32, 585–594.
- Slone, L.B., Norris, F.H., Murphy, A.D., Baker, C.K., Perilla, J.L., Diaz, D., Rodriguez, F.G., Gutierrez Rodriguez Jde, J., 2006. Epidemiology of major depression in four cities in Mexico. *Depress Anxiety* 23, 158–167.
- Tracy, M., Morgenstern, H., Zivin, K., Aiello, A.E., Galea, S., 2014. Traumatic event exposure and depression severity over time: results from a prospective cohort study in an urban area. *Soc. Psychiatry Psychiatr. Epidemiol.* 49, 1769–1782.
- Urtasun, M., Daray, F.M., Teti, G.L., Coppolillo, F., Herlax, G., Saba, G., Rubinstein, A., Araya, R., Irazola, V., 2017. Validation and calibration of the Patient Health Questionnaire (PHQ-9) in Argentina. *BMC Psychiatry* Submitted for publication.
- van Dooren, F.E., Denollet, J., Verhey, F.R., Stehouwer, C.D., Sep, S.J., Henry, R.M., Kremers, S.P., Dagnelie, P.C., Schaper, N.C., van der Kallen, C.J., Koster, A., Pouwer, F., Schram, M.T., 2016. Psychological and personality factors in type 2 diabetes mellitus, presenting the rationale and exploratory results from The Maastricht Study, a population-based cohort study. *BMC Psychiatry* 16, 17.
- Vigo, D., Thornicroft, G., Atun, R., 2016. Estimating the true global burden of mental illness. *Lancet Psychiatry* 3, 171–178.
- Weissman, M.M., Bland, R.C., Canino, G.J., Faravelli, C., Greenwald, S., Hwu, H.G., Joyce, P.R., Karam, E.G., Lee, C.K., Lellouch, J., Lepine, J.P., Newman, S.C., Rubio-Stipec, M., Wells, J.E., Wickramaratne, P.J., Wittchen, H., Yeh, E.K., 1996. Cross-national epidemiology of major depression and bipolar disorder. *J. Am. Med. Assoc.* 276, 293–299.
- Whiteford, H.A., Degenhardt, L., Rehm, J., Baxter, A.J., Ferrari, A.J., Erskine, H.E., Charlson, F.J., Norman, R.E., Flaxman, A.D., Johns, N., Burstein, R., Murray, C.J., Vos, T., 2013. Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010. *Lancet* 382, 1575–1586.
- Yanzon de la Torre, A., Oliva, N., Echevarrieta, P.L., Perez, B.G., Caporusso, G.B., Titaro, A.J., Todaro Kicyla, A., Cuatz, M., Locatelli, M., Nelson, L.M., Mac Mullen, M., Baldessarini, R.J., Daray, F.M., 2016. Major depression in hospitalized Argentine general medical patients: prevalence and risk factors. *J. Affect. Disord.* 197, 36–42.