

Depression Symptoms among Patients with Multiple Chronic Conditions

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Abstract

Aim: To identify depressive symptoms and biological psychosocial risk factors associated among patients with multiple chronic conditions (MCC).

Methods: The study was conducted in a center for the treatment of hypertension, diabetes, and chronic kidney disease in Brazil. During three months a structured interview was conducted among patients waiting for routine visits. In the univariate analysis, descriptive statistics were performed to characterize the sample and in the bivariate analysis were used the chi-square. The risk of depression was calculated in a Prevalence Ratio with 95% confidence interval, as association measure. Variables with $p < 0.10$ were selected for inclusion in the multivariate model, except in the case of self reported chronic disease and the elderly (60 years old or more).

Results: The study population included 1.558 patients with MCC. The mean age of participants was 61.4 years (SD = 12.4), most were women (57.5%) and had low levels of education (87.3%). The most prevalent disease was hypertension (88.6%), over half of the sample (55.9%) had 2 chronic diseases, 12% were smokers, and 3.5% were heavy alcohol users. The prevalence of depressive symptoms was 33.3% and was associated with female gender, diabetes and tobacco use.

Conclusion: There is a high prevalence of depressive symptoms in this population and it is associated with a number of health conditions and health behaviors, confirming the complex relationship between depressive symptoms and MCC. These data reinforce the need for screening, early diagnosis and management of depression among patients with MCC.

Keywords: Depression; Multiple chronic conditions; Diabetes; Hypertension; Smoking; Public health

Introduction

Depression is defined by the DSM-IV [1] as a disease and also in terms of depressive symptoms. The boundary between each of these conditions is unclear, showing the difficulties and controversies that persist in relation to depressive mood, the validity of the diagnosis and the implications of traumatic events for diagnosis and treatment of psychiatric disorders [2].

A complicating aspect in this scenario refers to the underdiagnoses of depression. Fleck et al. [3] and Molina et al. [4] identified that in primary care and other health care, a prevalence of 30-50% and 50-60% of cases of depression, respectively, are not diagnosed [3,4]. Moreover, it is often the co-occurrence between depression with others chronic diseases, for example, diabetes mellitus (DM) [5,6], arterial hypertension (AH) [7,8] and chronic kidney disease (CKD) [9,10] and it increase up to five times the likelihood of disability, outpatient visits and hospitalizations [11]. Allied, the presence of depression has important role in the increased risk of non-adherence to medical recommendations [12-15].

As for the Secondary Health Service there are lack of rigorous research study design within the Brazilian universal health care system about the association between chronic disease and depressive symptoms. Silva and cols. [7] found a 30.2% of depression symptom in elderly people with hypertension assisted by the Family Health Strategy in South of Minas Gerais, while Pereira and cols [16] in the Hiperdia Program of North of Brazil (Pará) detected 61.5% of depressive symptoms [7,16]. More studies must be development whit this population.

Routine screening is a useful tool to minimize depression's negative impact on quality life and general healthy. Identification of individual

factors is central to understanding treatment outcomes and advancing treatment among patients. The aim of this study is to describe the prevalence of depressive symptoms and factors associated with them in patients with MCC who are being treated at Centro Hiperdia Minas, in Juiz de Fora (CHDM-JF). The present study also adds to the literature the monitoring mental health of patients with chronic disease attending by the Health Secondary Care Center in Brazil. Results from this study should guide the therapeutic attention to depression in the context of ambulatory care of patients with multiple chronic diseases.

Methods

This study was conducted in the secondary or specialty care for chronic illness which is part of the tiered-care system throughout Brazil (Centro Hiperdia Minas de Juiz de Fora – CHDM-JF), that is the link in the universal health care system in Brazil, which consists of primary, secondary, and tertiary (hospital) care facilities [17]. Some health care centers within the Brazilian Universal Health Care system are linked to public academic institutions and research programs, offering a unique opportunity to test interventions and develop programs to eliminate health disparities, therefore called “Centers of Excellence”. CHDM-JF is operated by the Department of Health of Minas Gerais,

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within the Integrated Development Plan of Minas Gerais - 2007-2023 as Resolution SES No. 26/06/2010. The CHDM-JF was designed for patients with multiple chronic conditions: AH, DM, and CKD and has the objective to reduce health care costs and hospitalization. Brazil's health system provides universal coverage relying on secondary level of care for chronic diseases (asthma, chronic obstructive pulmonary disease, smoking and obesity). The public attended in the CHDM is characterized by having low socioeconomic and educational level and high cardiovascular risk.

All patients with scheduled appointments over a period of three months (September-December 2012), older than 18 years, were recruited at the central reception area of the institution [17]. Eligible participants were referred to study staff. Trained research assistants identified participants, explained the objectives of the study, screened for eligibility, and invited eligible patients to participate. Those who accepted signed the free and informed consent form (ICF) and responded to the questionnaire. Survey was administered by research assistants and lasted approximately 10 minutes. To protect user privacy, the team did not collect personally identifiable information. No compensation was provided to study participants. The data were double-date entered into the study database and analyzed [17]. The study was funded by the National Institutes of Health, Fogarty Center (NIH-FC), through a grant to the Kansas University Medical Center. Ethical procedures were approved by the Institutional Review Board of the Kansas University Medical Center (Protocol 12787) and the Ethics Committee of the University Federal of Juiz de Fora (protocol No 283/2011).

Participants

Participants' eligibility was based on the WHO definition of chronic health conditions that is a disease that lasted a year or more, which required continuous medical attention and / or affected the ability to perform the activities of daily living [18]. Patients matching in these criteria at the Primary Health Care were referred to CHDM-JF. Multiple chronic conditions (MCC) were defined as "conditions that last a year or more and require ongoing medical attention and/or limit activities of daily living [19,20].

Measures

Sociodemographic variables (age, education, gender), type and number of chronic diseases (hypertension, diabetes mellitus, CKD) were obtained by self-report via the survey instrument. Individuals aged 60 years old or more are considered elderly by Brazil's Senior Citizens' Statute [21]. To screen for depression were used the PHQ-2 population screening tool (the two-item Patient Health Questionnaire), validated for Brazil by Meneses-Gaya [22]. Both items (Little interest or pleasure in doing things and Feeling down, depressed or hopeless) are rated on a Likert scale of 0-3 points (0 = not at all; 1= several days; 2= more than half the days; 3= nearly every day), with 3 or more indicating the presence of depressive symptoms.

Tobacco-related measures were derived from the Brazillian epidemiological survey PETab, including the current use of tobacco [23]. Alcohol was measured by the AUDIT-C, a brief three-item scale that assesses hazardous/harmful drinking. The maximum AUDIT-C's score is 12 points and the cutoff point for risky consumption is five points [24,25].

Data analysis

Data were recorded by the study team on paper forms and later

double-entered into REDcap [26]. Statistical data extracted from REDcap were analyzed using Stata11 [27].

Statistical analysis was carried out in three steps: univariate, bivariate and multivariate analysis. In univariate analysis, descriptive statistics were performed to characterize the sample, using the mean and standard deviation (quantitative variables) and the absolute and relative frequencies (qualitative variables). In the bivariate analysis, we used the chi-square test (χ^2) to test the association between each of the independent variables (risk factors) with the dependent variable (depression), and we calculated the Prevalence Ratio with 95% confidence interval, as association measure. At this stage, variables with $p < 0.10$ were selected for inclusion in the multivariate model, with the exception of self reported chronic disease and elderly status. These variables were included in the final model to account for the multiple comorbidities, adjusting one effect accounting for the presence of others, a general characteristic of this population.

Poisson regression was used in multivariate analysis if its exponentiated coefficients provide the prevalence ratios. Model adjustment was verified by Likelihood Ratio test and graphic diagnosis on residuals (not shown).

Results

Sample comprised 1558 subjects. Table 1 describes the general characteristics of these health care service users. The study population had an average age of 61.4 ± 12.4 years, with age ranging from 30 to 96 years. Most of them were women (57.5%) and elderly (56.9%). Most had little education (10.9% illiterate, 76.4% incomplete/complete elementary school). The number of chronic diseases ranged from 1 to 3; most of the subjects had two diseases (55.9%); hypertension was the most prevalent (88.6%). About 20% of participants reported drinking alcohol, but only 3.5% were heavy users; 12% were smokers. The prevalence of depression was 33.3% ($n = 498$).

Table 2 shows the association between categorical variables with the outcome (depressive symptoms), by using prevalence ratios (PR) as a measure of association. Women, patients with diabetes and smokers had a higher prevalence of depression than men, non smokers and those without diabetes. On the other hand, the elderly, patients with CKD and those who consumed alcohol were less likely to have depressive symptoms compared to the non-elderly, patients who did not have CKD and those who did not consume alcohol. There was no significant difference in age ($p = 0.06$) and the number of chronic diseases ($p = 0.40$).

Variables		N	%
Sociodemographics	Female	904	58.0
	Elderly	864	55.5
	Educational level (\leq primary school)	1343	86.2
Self-reported chronic conditions	Hypertension	1357	87.1
	Diabetes	987	63.4
	Chronic kidney disease	612	39.4
Number of chronic conditions	1	415	26.6
	2	851	54.6
	3	292	18.7
Comorbidities associated	Smoking	187	12.0
	Alcohol consumption	81	5.2
	Depressive Symptoms	515	33.1

Table 1: Variables from CHDM-JF users (N=1558).

Variable	Category	Depression Cases		P-value	PR	CI 95%
		N	%			
Gender	Male	145	22.17	-	-	-
	Female	370	40.93	<0.001*	1.85	1.52 – 2.24
Elderly	Not elderly	251	36.17	-	-	-
	Elderly	264	30.56	0.019*	0.85	0.71 – 1.00
Low education	≤ Primary school	442	32.91	-	-	-
	>Primary school	73	33.95	0.763	0.97	0.76 – 1.24
Hypertension	No	57	28.36	-	-	-
	Yes	458	33.75	0.129	1.19	0.90 – 1.57
Diabetes	No	159	27.85	-	-	-
	Yes	356	36.07	0.001*	1.30	1.07 – 1.56
Chronic kidney disease	No	326	34.61	-	-	-
	Yes	187	30.56	0.097*	0.88	0.31 – 0.38
Tobacco use	No	431	31.44	-	-	-
	Yes	84	44.92	<0.001*	1.43	1.13 – 1.81
Alcohol consumption	No	494	33.45	-	-	-
	Yes	21	25.93	0.161	0.78	0.50 – 1.20
Number of chronic conditions	1	127	4.60	1.000	-	-
	2	284	5.20	1.100	0.42	0.88 – 1.3
	3	104	20.20	1.200	0.25	40.89 – 1.51

Note: * = significant differences through χ^2 (p<0.05).

Table 2: Odds ratios for depressive symptoms among patients with MCC.

Variable	Prevalence Ratio	p-value	95% CI
Female	1.8	<0.001	(1.5; 2.1)
Elderly	0.9	0.216	(0.7; 1.1)
Diabetic	1.3	0.016	(1.1; 1.5)
Hypertension	1.1	0.290	(0.9; 1.5)
CKD	1.0	0.720	(0.9; 1.2)
Smoker	1.4	0.001	(1.2; 1.9)

Table 3: Multivariate Poisson model for depression symptom associated factors.

Table 3 summarizes the Poisson regression coefficients and their significance in the model. In the final model, the combination of gender, DM and tobacco use significantly associated with patient's depression symptoms. The chance of being classified as depressed increases 80% if the patient is female compared to male; 40% if smokers, compared to non-smokers; and 30% for patients with diabetes compared those without diabetes.

Discussion

Consistent with the literature, our study identified that approximately one third of patients with multiple chronic disease report depressive symptoms [8,28-30] even though our study relied on a brief population screening tool while other studies rely on the DSM-IV depression diagnosis to guide therapeutic treatment. These results are particularly relevant in Brazilian's secondary care level context of "Centers of Excellence" for treatment of patients with MCC, as population screening tools can be easily integrated in the care routine by different members of the health care team. In clinical practice, comorbidity is underrecognized, underdiagnosed, underestimated, and undertreated [2,12,31,32]. A Center of Excellence for treatment of MCC offers a unique opportunity to integrate the assessment of depressive symptoms as routine of care.

Patients with chronic conditions, like hypertension, may experience many negative emotions which increase their risk of developing of mental health disorders, particularly anxiety (56%) and depression (4%). These symptoms among patients increased their likelihood of non-adherence to medication [33] although we did not access the use of depressive medication in our study.

We found that being female, smoker and having diabetes were the factors associated with depressive symptoms, even when controlling for age and schooling. More than half of women with chronic disease are depressed. It is alarming that this number might be an underestimated prevalence considering that depression is underdiagnosed and often minimized by the health professionals, independent of gender. Previous studies offer some reasons that may explain the association between being female and depressive symptoms. These include the social role of women, cultural norms, the different ways women react to adverse events, hormonal rates and changes in the course of life, and genetics [34-36].

Similar to prior studies, we found the association between depressive symptoms and smoking to be significant [37-41]. About 70% of cigarettes are consumed by depressed people, which tend to have higher degree of nicotine dependence, to smoke more cigarettes per day and to have higher risk of relapse compared with smokers without depression. The assumptions underpinning the association of tobacco with depression include non-nicotinic factors (genetic and environmental) and nicotinic factors (nicotine used as self-medication or its consumption generating physical dependence) [42]. Our study identifies the need to better understand the reason why depression is related to tobacco use among patients with multiple comorbidities. Our results highlight the relevance of tailored smoking cessation treatment approaches within the Center of Excellence for multiple chronic conditions throughout Brazil's universal health care system.

Patients with Diabetes mellitus were significantly more depressed, which accords with the literature. Depression is a recognized risk factor for DM but can also be triggered by it [43-46]. The association of depressive symptoms and DM has an adverse impact on both the risk of developing the disease and in the glycemic control. In turn, the loss of glycemic control may accelerate the onset of secondary complications of DM, worsening quality of life, increasing morbidity and mortality, and contributing to depression [46]. Current guidelines recommend the systematic screening of depression among diabetics and referral of those with depression to mental health professionals and specialized treatment [47].

Although the association between depressive symptoms and alcohol use is common in clinical practice [48], our study identified low prevalence of excessive alcohol consumption (3.5%) and a protective effect of alcohol use. One explanation for that is the fact that low doses of alcohol sharply decreases psychiatric symptoms [49,50]. Regarding age, being old was a protective factor for the onset and development of depressive symptoms. In the literature this association is controversial with age sometimes portrayed as a risk factor and sometimes as a protective factor [51-54].

One limitation of this study is the cross-sectional design and use of epidemiological screening scales rather than clinical diagnostic tools. In addition, all patients referred to CHDM-JF already had chronic diseases, limiting our ability to understand the causal effect of MCC on depression (and vice versa). There were also a lack of additional socio-demographic variables to better characterize the sample is an additional limitation of the study. Another limitation is that we did not collect

information about the use of depressive pharmacotherapy treatment that could influence results (e.g. alcohol use is very low in this sample).

The results demonstrate that the fact of depression symptoms being often underdiagnosed and undertreated is common among patients with MCC, especially among female, patients with diabetes and smokers. Encouraging screening, diagnosis, treatment and follow-up of these patients, as well as increasing training of health professionals in the management of these chronic conditions, should be mandatory, in order to better facilitate health service policies.

References

1. American Psychological Association (2003) DSM-IV. Manual Diagnóstico e Estatístico de Transtornos Mentais (4th edn). Porto Alegre: ArtMed 335.
2. Furlanetto LM, Brasil MA (2006) Diagnosticando e tratando depressão no paciente com doença clínica. *J Bras Psiquiatr* 55: 8-19.
3. Fleck MP de A, Lafer B, Sougey EB, Del Porto JA, et al. (2003) Diretrizes da Associação Médica Brasileira para o tratamento da depressão (versão integral). *Rev Bras Psiquiatr* 25: 114-122.
4. Molina MRAL, Wiener CD, Branco JC, Jansen K, D'Souza LDM, et al. (2012) Prevalência de depressão em usuários de unidades de atenção primária. *Rev Psiquiatr Clínica. Faculdade de Medicina da Universidade de São Paulo* 39: 194-197.
5. de Groot M, Anderson R, Freedland K, Clouse R, Lustman P (2001) Association of depression and diabetes complications: a meta-analysis. *Psychosom Med* 63: 619-630.
6. Lustman PJ, Clouse RE (2005) Depression in diabetic patients: the relationship between mood and glycemic control. *J Diabetes Complication* 19: 113-122.
7. D'Silva PCDS, Monteiro LA, Graciano ADDS, Terra FDS, Veiga EV (2014) Assessment of depression in elderly with systemic hypertension. *Rev da Rede Enferm do Nord* 15: 151-157.
8. Pereira SP (2005) Prevalência de depressão na população idosa de Itajaí (SC): relação com variáveis biopsicossociais. Universidade do Vale do Itajaí.
9. <http://kidney.org.au/cms/uploads/docs/ckd-management-in-gp-handbook-3rd-edition.pdf>
10. Bautovich A, Katz I, Smith M, Loo CK, Harvey SB (2014) Depression and chronic kidney disease: A review for clinicians. *Aust New Zeal J Psychiatry* 48: 530-541.
11. De Moura AAG, De Carvalho EF, Da Silva NJC (2007) Repercussão das doenças crônicas não-transmissíveis na concessão de benefícios pela previdência social. *Cien Saude Colet* 12: 1661-1672.
12. Teng CT, De Castro Humes E, Navas Demetrio F (2005) Depressão e comorbidades clínicas. *Rev Psiquiatr Clin* 32: 149-159.
13. Cooper JK, Harris Y, McGready J (2002) Sadness predicts death in older people. *J Aging Health* 14: 509-256.
14. Unützer J, Patrick DL, Marmon T, Simon GE, Katon WJ (2002) Depressive symptoms and mortality in a prospective study of 2,558 older adults. *Am J Geriatr Psychiatry* 10: 521-530.
15. Dimatteo MR, Lepper HS, Croghan TW (2000) Depression is a risk factor for noncompliance with medical treatment: meta-analysis of the effects of anxiety and depression on patient adherence. *Arch Intern Med* 160: 2101-2107.
16. Pereira MM, Rufino MH, Nascimento LC, Macêdo RC, Oliveira RK, et al. (2015) Depression and nutritional status of elderly participants of the Hiperdia Program. *Rev da Rede Enferm do Nord* 16: 731-737.
17. da Campos TS, Richter KP, Cupertino AP, Galil AGS, Banhato EFC, et al. (2014) Cigarette smoking among patients with chronic diseases. *Int J Cardiol* 174: 808-810.
18. Parekh AK, Goodman RA, Gordon C, Koh HK (2011) Managing multiple chronic conditions: a strategic framework for improving health outcomes and quality of life. *Public Health Rep [Internet]*. 126: 460-471.
19. Hwang W, Weller W, Ireys H, Anderson G (2001) Out-of-pocket medical spending for care of chronic conditions. *Health Aff (Millwood)* 20: 267-278.
20. Warshaw G (2006) Introduction: Advances and challenges in care of older people with chronic illness. generations [Internet]. American Society on Aging 30: 5.
21. http://www.planalto.gov.br/ccivil_03/leis/2003/L10.741.htm
22. Meneses-Gaya C de (2011) Estudo de validação de instrumentos de rastreamento para transtornos depressivos, abuso e dependência de álcool e tabaco. Universidade de São Paulo, Brazil.
23. http://www1.inca.gov.br/inca/Arquivos/comunicacao/pesquisa_especial_tabagismo.pdf
24. Bush K, Kivlahan DR, McDonell MB, Fihn SD, Bradley KA (1998) AUDIT alcohol consumption questions (AUDIT-C). *Arch Intern Med* 158: 1789-1795.
25. Bradley KA, De Benedetti AF, Volk RJ, Williams EC, Frank D, et al. (2007) AUDIT-C as a brief screen for alcohol misuse in primary care. *Alcohol Clin Exp Res* 31: 1208-1217.
26. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, et al. (2009) Research electronic data capture (REDCap)-A metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* 42: 377-381.
27. StataCorp (2009) Stata statistical software: Release 11. College Station, TX: StataCorp LP.
28. Sass A, Gravena AAF, Pilger C, De Freitas Mathias TA, Marcon SS (2012) Depression in elderly enrolled in a control program for hypertension and diabetes mellitus. *ACTA Paul Enferm* 25: 80-85.
29. Moussavi S, Chatterji S, Verdes E, Tandon A, Patel V, et al. (2007) Depression, chronic diseases, and decrements in health: results from the World Health Surveys. *Lancet* 370: 851-858.
30. Coelho FMDC, Pinheiro RT, Horta BL, Magalhães PVDS, Garcias CMM, et al. (2009) Common mental disorders and chronic non-communicable diseases in adults: a population-based study. *Cad Saúde Pública, Rio Janeiro* 25: 59-67.
31. Rennó J Jr, Fernandes CE, Mantese JC, Valadares GC, Fonseca ÂM, et al. (2012) Saúde mental da mulher no Brasil: desafios clínicos e perspectivas em pesquisa. *Rev Bras Psiquiatr* 27: S73-S76.
32. Topic R, Milicic D, Stimac Z, Loncar M, Velagic V, et al. (2013) Somatic comorbidity, metabolic syndrome, cardiovascular risk, and CRP in patients with recurrent depressive disorders. *Croat Med J* 54: 453-459.
33. Kretchy IA, Owusu-Daaku FT, Danquah SA (2014) Mental health in hypertension: assessing symptoms of anxiety, depression and stress on anti-hypertensive medication adherence. *Int J Ment Health Syst* 8: 25.
34. Coutinho M, Giovanni M, Pavini L, Ventura M, Elias R, et al. (2015) Aspectos biológicos e psicossociais da depressão relacionado ao gênero feminino. *Rev Bras Neurol e Psiquiatr* 19: 49-57.
35. Gonçalves M (2010) Psiquiatria na Prática Médica: Hipertensão Arterial e Transtornos Psiquiátricos. *Int J Psychiatry* 15.
36. Rombaldi AJ, Da Silva MC, Gazalle FK, Azevedo MR, Hallal PC (2010) Prevalência e fatores associados a sintomas depressivos em adultos do sul do Brasil: estudo transversal de base populacional. *Rev Bras Epidemiol* 13: 620-629.
37. Thorndike AN, Rigotti NA (2009) A tragic triad: coronary artery disease, nicotine addiction, and depression. *Curr Opin Cardiol* 24: 447-453.
38. Boden JM, Fergusson DM, Horwood LJ (2010) Cigarette smoking and depression: Tests of causal linkages using a longitudinal birth cohort. *Br J Psychiatry* 196: 440-446.
39. Sung HY, Prochaska JJ, Ong MK, Shi Y, Max W (2011) Cigarette smoking and serious psychological distress: a population-based study of California adults. *Nicotine Tob Res* 13: 1183-1192.
40. Payne TJ, Ma JZ, Crews KM, Li MD (2013) Depressive symptoms among heavy cigarette smokers: The influence of daily rate, gender, and race. *Nicotine Tob Res* 15: 1714-1721.
41. Haro R, Drucker-Colín R (2004) A two-year study on the effects of nicotine and its withdrawal on mood and sleep. *Pharmacopsychiatry* 37: 221-227.
42. DiFranza JR, Savageau JA, Fletcher K, Ockene JK, Rigotti NA, et al. (2002) Measuring the loss of autonomy over nicotine use in adolescents. *Arch Pediatr Adolesc Med* 156: 397.
43. Nina-e-silva CH, Monteiro AM, Sbroggio Júnior AL, Silva WJ da, D'Affonsico

- GBC, et al. (2015) Revisão Sistemática Da Prevalência De Depressão Na Diabetes Mellitus Tipo 2. *Rev da Univ Val de Rio Verde* 13: 136-141.
44. Fisher L, Gonzalez JS, Polonsky WH. The confusing tale of depression and distress in patients with diabetes: a call for greater clarity and precision. *Diabet Med* 31: 764-772.
45. Eren I, Erdi O, Sahin M (2008) The effect of depression on quality of life of patients with type II diabetes mellitus. *Depress Anxiety* 25: 98-106.
46. Moreira RO, Papelbaum M, Appolinario JC, Matos AG, Coutinho WF, et al. (2003) Diabetes mellitus e depressão: uma revisão sistemática. *Arq Bras Endocrinol Metabol* 47: 19-29.
47. OHTAC OCDM Collaborative (2013) Optimizing Chronic Disease Management in the Community (outpatient) Setting (OCDM): an evidentiary framework. *Ont Health Technol Assess Ser* 13: 1-78.
48. Merchán-Hamann E, Leal EM, Basso Musso L, García Estrada M, Reid P, et al. (2012) Comorbilidad entre abuso/dependencia de drogas y el estrés psicológico en siete países de Latinoamérica y uno del Caribe. *Texto Context - Enferm* 21: 87-95.
49. Munhoz TN, Santos IS, Matijasevich A (2013) Major depressive episode among Brazilian adults: a cross-sectional population-based study. *J Affect Disord* 150: 401-407.
50. Ribeiro M, Laranjeira R, Cividanes G (2005) Transtorno bipolar do humor e uso indevido de substâncias psicoativas. *Rev Psiquiatr Clin* 32: 78-88.
51. Vorcaro CMR, Lima e Costa MFF, Barreto SM, Uchoa E (2008) Unexpected high prevalence of 1-month depression in a small Brazilian community: the Bambuí Study. *Acta Psychiatr Scand* 104: 257-263.
52. Munhoz TN (2012) Prevalência e fatores associados à depressão em adultos: estudo de base populacional. Universidade Federal de Pelotas.
53. Bromet E, Andrade LH, Hwang I, Sampson NA, Alonso J, et al. (2011) Cross-national epidemiology of DSM-IV major depressive episode. *BMC Med* 9: 90.
54. Gabilondo A, Rojas-Farreras S, Vilagut G, Haro JM, Fernández A, et al. (2010) Epidemiology of major depressive episode in a southern European country: results from the ESEMeD-Spain project. *J Affect Disord* 120: 76-85.