received 14 December 2022 | accepted 18 February 2023 | published 27 February 2023

Doi: 10.31157/an.v28i4.448

PREVALENCE OF TREATMENT RESISTANT DEPRESSION: TRAL STUDY SUB ANALYSIS IN A MEXICAN SAMPLE

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Abstract

Introduction: Epidemiology and burden of disease for psychiatric disorders in Latin America (LatAm) is often limited, particularly for conditions like treatment-resistant depression (TRD), which is a burdensome condition within a significant proportion of major depressive disorder (MDD) patients. The treatment resistant depression in America Latina (TRAL) study aimed to investigate the epidemiology and burden of TRD in MDD patients. This paper focuses on characterizing TRD in the Mexican subset using TRAL study data. **Methods**: The study included 697 adult patients clinically diagnosed with MDD from 14 sites in Mexico. Patients with relevant psychiatric comorbidities or those enrolled in a clinical trial were excluded. Outcomes primarily relied on patient-reported data and assessment scales. **Results**: TRD prevalence in Mexico was found to be 20.7%. Current suicidality was high in TRD patients (20.8%), as was the incidence of suicide behavior disorder (12.5%). Selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) were the most commonly prescribed medications. EQ-5D, SDS and WPAI results indicated significant limitations for TRD patients in their everyday life. **Discussion**: These findings align with available literature on treatment approaches and the prevalence of suicidality and suicide behavior disorder. The high prevalence of TRD among MDD patients poses a management challenge. **Conclusions**: The burden of TRD in Mexico is significant, although less severe than in other LatAm countries. Public health policies should focus on improving diagnosis and availability to more effective therapies.

Keywords: *Mexico, epidemiology, treatment-resistant depressive disorder, major depressive disorder*

Background

According to the World Health Organization (WHO),[1] major depressive disorder (MDD) is the most disabling disease worldwide, with an estimated global prevalence of 6%, affecting multiple dimensions and limiting patients in their instrumental activities of daily living (IADLs).[2,3] In Latina America (LatAm), MDD prevalence varies between 23.0% to 35% in certain contexts.[4]

Between 20% and 33.3% of MDD patients develop treatment-resistant depression (TRD),[5-7] which is defined as a failure to respond to two or more antidepressants at therapeutic doses over an appropriate period, within the current depressive episode,[8] even when novel therapies are considered.[9,10] TRD represents an additional burden to MDD, impacting social, economic, educational and occupational dimensions. In a context of limited healthcare resources, the significant economic burden[11] and the influence of MDD/TRD on Quality of Life (QoL), disability, and work-productivity[5,12,13] are major concerns.

The Treatment Resistant Depression in America Latina (TRAL) study aims to address the gap in MDD/TRD epidemiological data[14] in LatAm, while doing clinical and burden of the disease characterization of MDD/TRD patients. A descriptive comparison between TRD and non-TRD patients was also included. This paper presents the subset of Mexico, with the inclusion of some global results from LatAm for contextual framing.

Objectives

This study has two main objectives:

- To provide epidemiological data on TRD in MDD patients in Mexico;
- To provide a clinical characterization and burden of disease in TRD patients within a larger MDD sample in Mexico;
- To conduct a descriptive comparison between TRD and non-TRD MDD in Mexican patients.

Methods

Study design and population

TRAL was a multicenter, multinational observational study conducted from October 2017 to December 2018 in Argentina, Brazil, Colombia and Mexico. The study comprised two components: one cross-sectional, and 1-year follow-up of TRD patients. The present results pertain to 14 psychiatric centers in Mexico, where cross-sectional data were collected on socio-demographic factors, clinical and psychiatric variables, medication, QoL, work-impairment, and healthcare resource utilization.

Patient were enrolled during routine medical appointments based on MDD screening with the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-V) criteria, and confirmed by the MINI International Neuropsychiatric Interview (MINI), 7.02 version.[15] For more information, please refer to previous TRAL publications.[14]

Data and assessments

All patients were evaluated for depression severity using the Montgomery-Åsberg Depression Rating Scale (MADRS),[16] which was also used to diagnose TRD. TRD diagnosis was established for patients who were under follow-up and had been treated with ≥2 antidepressants during the current episode, with no complete response to treatment based on MADRS scores.[8]

Sociodemographic information, clinical characterization, current and past psychiatric treatments, and healthcare resource utilization in the previous year were collected by the physicians. Patients self-reported on their QoL (EuroQol-5 Dimension [EQ-5D-5L]), work impairment (Work Productivity and Activity Impairment Questionnaire – WPAI), and disability (Sheehan Disability Scale - SDS).

Written informed consent was obtained from all participants. The study was approved by the local Independent Ethics Committee / Institutional Review Board.

Statistical Analysis

TRAL sample size was calculated to be representative of the entire region, although not specifically for each country. Quantitative variables were summarized as mean, median, standard deviation, minimum, and maximum values. Qualitative variables were presented as absolute frequency and percentage, both for overall sample and subgroups based on TRD/non-TRD categorization.

Epidemiology was reported as absolute frequency, percentages, and 95% confidence interval (95% CI). Inferential analysis was conducted for group comparisons. Statistical significance was set at 5%, and all analyses were performed using SAS® (version 9.4, SAS Institute Inc., Cary).

Results

Sociodemographic and clinical characteristics in Mexico

MDD patients had an average age of 43.9 (±15.4) years and were predominantly female (79.1%), as shown in Table 1. Most patients were married or in a consensual union (48.9%), and had more than 10 years of formal education (68%). TRD patients were significantly older than non-TRD patients (47.6 versus 42.9; p = .0004).

Sample and TRD prevalence

The Mexican subset included 697 (47.3%) out of 1475 MDD patients. Most patients (86.2%, n = 601) were under treatment. TRD was identified in 144 patients from the Mexican sample (20.7%, 95%CI: 17.7%; 23.7%) (Supplemental Table 1).

MDD patients received care in both private (50.2%) and public (49.8%) healthcare settings, with a higher prevalence of TRD in the private setting (22.3%, 95%CI: 17.9%; 26.6%) (Supplemental Table 1). More detailed results can be found in a previous publication.[14]

Clinical characterization of MDD and TRD

Overall, MDD patients had a mean score of 26.72 ± 9.78 for MADRS, with 25.4% of them categorized as severely depressed (MADRS ≥ 35). TRD patients (30.17 ±8.63) had higher MADRS scores compared to non-TRD patients (25.82 ± 9.87), and a higher proportion were rated as severely depressed (TRD – 31.9% vs Non-TRD – 23.7%) (see Table 2). Based on the MINI assessment, 13.6% of the sample met the criteria for suicidality, with 11.3% reporting lifetime attempt. Additionally, 4.2% of the sample met the criteria for current suicide behavior disorder, and 2.9% for current posttraumatic stress disorder (PTSD). TRD patients were more likely to

Table 1. Socio-demographic characteristics, overall, and by TRD (TRD *vs*. non-TRD patients)

	MDD (n=697)	Non-TRD (n=553)	TRD (n=144)	p-value
Age (years), mean±SD	43.9 ± 15.4	42.9 ± 15.8	47.6 ± 12.9	.0004*
Female, n (%)	551 (79.1%)	432 (78.1%)	119 (82.6%)	.2352†
Marital status				
Single	266 (38.3%)	219 (39.6%)	47 (33.1%)	
Married/Consensual union	340 (48.9%)	268 (48.5%)	72 (50.7%)	
Divorced/Separated	59 (8.5%)	43 (7.8%)	16 (11.3%)	.3701†
Widower	30 (4.3%)	23 (4.2%)	7 (4.9%)	
Missing	2	0	2	
Years of formal education				
0	2 (0.3%)	2 (0.4%)	0.0	
1-4 years	14 (2.0%)	14 (2.5%)	0.0	
5-9 years	204 (29.4%)	162 (29.3%)	42 (29.6%)	.2341*
10-12 years	227 (32.7%)	184 (33.3%)	43 (30.3%)	
≥ 13 years	247 (35.6%)	190 (34.4%)	57 (40.1%)	
Missing	3	1	2	

Unless otherwise noted, data are expressed as numbers and percentages. P-values indicate TRD *vs* non-TRD comparisons. MDD: major depressive disorder, TRD: treatment-resistant depression, non-TRD: MDD patient without TRDX

Table 2. Depression and anxiety assessment (MADRS and MINI) among participants with MDD, based on TRD status

	MDD (n=697)	Non-TRD (n=553)	TRD (n=144)
Montgomery-Asberg Depression Scale (MADRS)			
Mean score ± SD	26.7 ± 9.8	25.8 ± 9.9	30.2 ± 8.6
Cut-off scores, n (%)			
Symptom absent (0-6)	27 (3.9%)	27 (4.9%)	0 (0.0%)
Mild depression (7-19)	119 (17.1%)	98 (17.7%)	21 (14.6%)
Moderate (20-34)	374 (53.7%)	297 (53.7%)	77 (53.5%)
Severe depression (35-60)	177 (25.4%)	131 (23.7%)	46 (31.9%)
Mini-International Neuropsychiatric Interview (MINI): Suicidality, n (%)			
Current (past month)	95 (13.6%)	65 (11.8%)	30 (20.8%)
Lifetime attempt	79 (11.3%)	40 (7.2%)	39 (27.1%)
Low	57 (8.2%)	39 (7.1%)	18 (12.5%)
Moderate	30 (4.3%)	20 (3.6%)	10 (6.9%)
High	56 (8.0%)	32 (5.8%)	24 (16.7%)
Primary diagnosis of suicidality, n (%)			
Current (past month)	17 (2.4%)	9 (1.6%)	8 (5.6%)
Lifetime attempt	28 (4.0%)	12 (2.2%)	16 (11.1%)
Suicide behaviour disorder, n (%)			
Current	29 (4.2%)	19 (3.4%)	10 (6.9%)
In early remission	31 (4.4%)	13 (2.4%)	18 (12.5%)
Primary diagnosis of suicide behaviour disorder, n (%)			
Current	15 (2.2%)	9 (1.6%)	6 (4.2%)
In early remission	14 (2.0%)	6 (1.1%)	8 (5.6%)
Post-traumatic stress disorder			
Meets criteria, n (%)			
Current (past month)	20 (2.9%)	12 (2.2%)	8 (5.6%)
Primary diagnosis, n (%)			
Current (past month)	6 (0.9%)	2 (0.4%)	4 (2.8%)

Unless otherwise noted, data are expressed as numbers and percentages. a) Range: 0 to 60, with higher values indicating a higher level of depression. MDD: major depressive disorder, TRD: treatment-resistant depression, non-TRD: MDD patient without TRD.

experience current suicidality (20.8% *vs* 11.8%) or lifetime attempt (27.1% vs 7.2%) than non-TRD. As for suicide behavior disorder, TRD patients had a higher proportion in early remission (12.5% vs 2.4%), with a similar pattern observed for current PTSD, where TRD patients had a rate of 5.6% and non-TRD of 2.2% (Table 2).

MDD treatment schemes – overall TRAL sample

Concerning previous medication, 46.5% of MDD patients received psychiatric medication (TRD – 98.6%, non-TRD – 32.9%), versus 86.2% for current medication (TRD – 97.9%, non-TRD – 83.2%). Other current relevant therapy (non-TRD – 33%, TRD – 48%) is present in 29.3% of the participants. Selective-serotonin reuptake inhibitors (SSRIs) were the most used class, accounting for 67.6% of the sample, followed by serotonin and noradrenaline reuptake inhibitors (SNRIs) (22.9%) and antipsychotics (14.6%).

The use of SSRIs was more frequent in non-TRD patients, while for SNRIs, antipsychotics, antiepileptics, psychotherapy, and previous or current use of lithium, TRD patients showed higher frequency of use (Table 3).

Table 3. Previous and current medication for MDD

	MDD (n=697)	Non-TRD (n=553)	TRD (n=144)
Previous psychiatric medication	324 (46.5%)	182 (32.9%)	142 (98.6%)
Other previous relevant medication	43 (6.2%)	30 (5.4%)	13 (9.0%)
Current relevant psychiatric therapy	601 (86.2%)	460 (83.2%)	141 (97.9%)
Current other relevant therapy	204 (29.3%)	150 (27.1%)	54 (37.5%)
Current medication per treatment class:			
Tricyclic antidepressants	2 (0.3%)	2 (0.4%)	0 (0.0%)
SSRIs	416 (67.6%)	340 (71.7%)	76 (53.9%)
SNRIs	141 (22.9%)	78 (16.5%)	63 (44.7%)
SDRIs	4 (0.7%)	2 (0.4%)	2 (1.4%)
Multimodal	8 (1.3%)	7 (1.5%)	1 (0.7%)
Antipsychotics	90 (14.6%)	43 (9.1%)	47 (33.3%)
Antiepileptics	55 (8.9%)	34 (7.2%)	21 (14.9%)
Brain stimulation techniques	2 (0.3%)	0 (0.0%)	2 (1.4%)
Psychotherapy	5 (0.8%)	1 (0.2%)	4 (2.8%)
Others*	8 (1.3%)	4 (0.8%)	4 (2.8%)
Current use of ketamine/esketamine	0	-	-
Previous use of ketamine/esketamine	5 (1.5%)	0 (0.0%)	5 (3.5%)
Current use of lithium	4 (0.7%)	0 (0.0%)	4 (2.8%)
Previous use of lithium	5 (1.5%)	0 (0.0%)	5 (3.5%)

Unless otherwise noted, data are expressed as numbers and percentages. MDD: major depressive disorder, TRD: treatment-resistant depression, non-TRD: MDD patient without TRD. *Modafinil, armodafinil, riluzole.

Quality of life (EQ-5D-5L) and Work productivity impairment due to depression (WPAI:D) and disability (SDS)

The majority of MDD patients reported having no problems walking (60.4%) or washing/dressing themselves (54.9%) (Supplementary Table 2). Nearly 39% of patients reported having moderate or severe problems doing their usual activities. Severe or extreme pain was reported by 10.3% of patients, while 26.3% reported being severely or extremely depressed or anxious. The median current health score in EQ-5D was 65.0. Also, 65.8% of the sample reported being moderately to extremely affected by anxiety/depression. Non-TRD patients (64.52 ± 17.17) had a better subjective assessment of their overall health status than TRD patients (52.90 ± 19.56). TRD patients yielded significantly lower QoL scores compared to non-TRD patients.

The median percentage of work time missed due to depression was 15.0%, and the median percentage of impairment while working was 50.0% (Supplementary Table 2). The median percentage of overall work impairment due to depression was 58.3%, and the percentage of activity impairment was 60.0%. Activity impairment due to depression suggested higher impairment in TRD (62.92 ± 25.08) compared to non-TRD (51.41 ± 25.54) patients.

According to the SDS, patients reported that their symptoms markedly (31.8%) or extremely (37.0%) disrupted the school/work and their social life/leisure activities. The median overall SDS score was 17.0. On average, patients missed school/work or were unable to carry out daily activities for 1.1 days in the previous week due to their symptoms. TRD patients reported significantly higher disability (SDS) in every dimension analyzed, indicating a significant disruption in IADLs compared to non-TRD patients.

Healthcare resource utilization among MDD patients

The proportion of days in ambulatory care is higher for TRD patients, with 36.4% of TRD patients having at least 60 days of ambulatory care compared to only 15.0% of non-TRD patients. Interestingly, both the number of psychiatrist and psychologist consultations were higher in TRD patients (psychiatrist: 10.04 ± 8.92, psychologist: 2.11 ± 5.42) compared to non-TRD patients (psychiatrist - 3.62 ± 3.69, psychologist - 0.80 ± 2.82). The mean number of emergency visits was 0.8 in the previous year. The same trend is observed for the number of consultations with other specialists, with higher values for TRD patients (1.01 ± 3.44) versus non-TRD patients (0.13 ± 0.61). Accordingly, non-pharmaceutical consultations were reportedly higher in TRD patients (0.30 ± 1.72) versus non-TRD patients (0.02 ± 0.19) (Supplemental Table 3).

Discussion

In the TRAL study, Mexico exhibited the lowest prevalence of TRD, including all patients (20.7%) and among treated patients (23.5%),[14] contrasting the highest prevalence observed in Brazil (all patients: 40.4, treated patients: 43.1%). This is consistent with previous research indicating that Mexico has a lower prevalence of depressive disorders.[4,17] Limited access to mental health services in Mexico and challenges in the diagnosis of MDD/TRD or other mental conditions may partially explain this. Nonetheless, TRAL suggests a high prevalence of TRD among MDD individuals receiving attention in healthcare facilities in LatAm,[14] which affects patients, caregivers and society across various dimensions, highlighting the importance of earlier diagnosis and better therapeutic approaches.

TRD patients exhibited poorer outcomes in terms of QoL (EQ-5D), disability (SDS) and work-productivity (WPAI) when compared to non-TRD patients, reiterating previous research findings.[5,12,13] The severe symptomatology observed in TRD patients (MADRS), may partially account for these worse outcomes, underlined by some symptoms, such as suicidality and PTSD. Additionally, TRD patients' age was higher, which might be linked to the chronic neurological changes associated with MDD.

Comorbidities were more frequent among TRD patients, adding to the significant economic burden of TRD.[18,19] The burden extends beyond the toll on patients and caregivers, affecting physicians as well.[20] A study in Brazil showed that health costs and resource utilization are significantly higher in TRD patients when compared to non-TRD.[12]

TRAL[14] is a landmark real-world evidence study in the region where available evidence on TRD was scarce. These findings are relevant to all stakeholders and healthcare decision makers. The sample size, covering four important countries in the region, constitutes a strength of TRAL's methodology.

The sample size of the Mexican study provides an interesting analysis of TRD prevalence and patients characterization. However, the sample size was not calculated considering country-level comparisons or to be representative of the Mexican population. Additionally, only patients under follow-up at local healthcare facilities were included in the study.

The Mexican sample was almost evenly distributed between private and public settings, providing a depiction of the

impact of TRD regardless of patient income. However, fewer therapeutic options and longer time to treatment initiation were found in the public setting.

In Mexico, measures have been implemented to improve mental health resources, but the treatment gap remains relevant, particularly among the elderly[21] and adolescents.[22] Three areas emerge as priorities: prevention, hospitalization and social reintegration.[23] Mexico has one of the highest prevalence of mental disorders in the Americas (42.6%).[24] Fighting social stigma is essential since untreated mental health conditions lead to severe problems. Population should seek help when the first symptoms are identified. Availability of treatment is still insufficient, and the distribution of care services is inadequate, especially in primary care units,[25] but significant efforts are in place.

Conclusions

The data from TRAL provides further evidence on the medical needs for TRD. The prevalence of TRD in LatAm was 29.1, while in the Mexican MDD population, it was 20.7. The results demonstrate that TRD severely impacts mental health, quality of life, as well as significant healthcare resources utilization. Public policies should focus on improving early diagnosis and the availability of therapies for TRD.

Acknowledgments

The authors extend their gratitude to all TRAL investigators, site coordinators, patients, and their families. The Clinical Trial & Consulting Services (CTI) provided statistical analysis support for the LAMBDA study, funded by Janssen LatAm. Diogo Morais, from CTI, offered medical writing assistance and editorial support for this manuscript, with funding by Janssen LatAm. Janssen LatAm participated in data interpretation, content review, and approval. All authors had access to all relevant data and contributed to the manuscript's writing, review, and approval.

Conflict of interest

JLVH and JIB have no conflicts of interest to disclose. LDAS serves as a researcher for Avalon Salud, where he holds the positions of principal investigator and sub-investigator for several original epidemiological research protocols conducted by the institution. He has received professional fees for conducting subject interviews in the present study by Janssen Research & Development, as approved by the Independent Research Ethics Committee. Dr. Alviso has also served as a speaker, participated in advisory boards, or received scientific fees from the following organizations: Janssen, Pfizer, Sanofi Aventis, Schwabe-Pharma, Novartis, Lundbeck, Roche, Lilly, Asofarma, Psicofarma, Ferrer, Servier, and Shire. CC received support from Janssen Cilag. CBP received support from the National Institute of Psychiatry. GK and PC are currently employed at Janssen Pharmaceutical.

Financial support statement

The TRAL (Treatment-Resistant Depression in America Latina) study received funding from Janssen Latin America. Medical writing and editorial support were provided by CTI, and funded by Janssen Latin America.

Author Contribution

All authors contributed significantly to the study's design and data interpretation. They collectively reviewed the final manuscript and granted their approval for its content.

References

1. Malhi GS, Mann JJ. Depression. Lancet. 2018;392(10161):2299-312. doi: 10.1016/S0140-6736(18)31948-2
2. Storeng SH, Sund ER, Krokstad S. Factors associated with basic and instrumental activities of daily living in elderly participants of a population-based survey: The Nord-Trøndelag Health Study, Norway. BMJ Open. 2018;8(3): e018942. doi: 10.1136/bmjopen-2017-018942
3. Xie H, Chen PW, Zhao L, Sun X, Jia XJ. Relationship between activities of daily living and depression among older adults and the quality of life of family caregivers. Front Nurs. 2018;5(2):97–104. doi: 10.2478/fon-2018-0013
4. Castilla-Puentes R, Secin R, Grau A, Galeno R, Feijo de Mello M, Pena N, et al. A multicenter study of major depressive disorder among emergency department patients in Latin-American countries. Depress Anxiety. 2008; 25(12):E199-204. doi: 10.1002/da.20380
5. Mrazek DA, Hornberger JC, Altar CA, Degtiar I. A review of the clinical, economic, and societal burden of treatment-resistant depression: 1996–2013. Psychiatr Serv. 2014; 65(8):977-87. doi: 10.1176/appi.ps.201300059
6. Hasin DS, Sarvet AL, Meyers JL, Saha TD, Ruan WJ, Stohl M, et al. Epidemiology of adult DSM-5 major depressive disorder and its specifiers in the United States. JAMA Psychiatry. 2018; 75(4):336-46. doi: 10.1001/jamapsychiatry.2017.4602
7. Gaynes BN, Warden D, Trivedi MH, Wisniewski SR, Fava M,

Rush AJ. What did STAR*D teach us? Results from a large-scale, practical, clinical trial for patients with depression. Psychiatr Serv. 2009;60(11):1439-45. doi: 10.1176/ps.2009.60.11.1439

8. Conway CR, George MS, Sackeim HA. Toward an evidence-based, operational definition of treatment-resistant depression: When Enough is enough. JAMA Psychiatry. 2017;74(1):9-10. doi: 10.1001/jamapsychiatry.2016.2586
9. Thase M, Connolly R. Unipolar depression in adults: Choosing treatment for resistant depression - UpToDate; 2019. https://www.uptodate.com/contents/unipolar-depression-in-adults-choosing-treatment-for-resistant-depression#H925759895
10. Kraus C, Kadriu B, Lanzenberger R, Zarate CA, Kasper S. Prognosis and improved outcomes in major depression: a review. Transl Psychiatry. 2019;9(1):127. doi: 10.1038/s41398-019-0460-3
11. Johnston KM, Powell LC, Anderson IM, Szabo S, Cline S. The burden of treatment-resistant depression: A systematic review of the economic and quality of life literature. J Affect Disord. 2019;242:195-210. doi: 10.1016/j.jad.2018.06.045
12. Lepine BA, Moreno RA, Campos RN, Couttolenc BF. Treatment-resistant depression increases health costs and resource utilization. Braz J Psychiatry. 2012;34(4):379-88. doi: 10.1016/j.rbp.2012.05.009
13. Chow W, Doane MJ, Sheehan J, Alphs L, Le H. Economic burden among patients with major depressive disorder: An analysis of healthcare resource use, work productivity, and direct and indirect costs by depression severity. Am J Manag Care. 2019. Available from: https://www.ajmc.com/view/economic-burden-mdd
14. Soares B, Kanevsky G, Teng CT, Pérez-Esparza R, Bonetto GG, Lacerda ALT, et al. Prevalence and impact of treatment-resistant depression in Latin America: a prospective, observational study. Psychiatr Q. 2021;92:1797-1815. doi: 10.1007/s11126-021-09930-x
15. Sheehan DV, Lecrubier Y, Sheehan KH, Janavs J, Weiller E, Keskiner A, et al. The validity of the Mini International Neuropsychiatric Interview (MINI) according to the SCID-P and its reliability. European Psychiatry. 1997;12(5):232-41.
16. Montgomery SA, Asberg M. A new depression scale designed to be sensitive to change. Br J Psychiatry. 1979;134:382-9. doi: 10.1192/bjp.134.4.382
17. Kessler RC, Bromet EJ. The epidemiology of depression across cultures. Annu Rev Public Health. 2013;34:119-38. doi: 10.1146/annurev-publhealth-031912-114409
18. Jaffe DH, Rive B, Denee TR. The humanistic and economic burden of treatment-resistant depression in Europe: a cross-sectional study. BMC Psychiatry. 2019;19(1):247. doi: 10.1186/s12888-019-2222-4
19. Ivanova JI, Birnbaum HG, Kidolezi Y, Subramanian G, Khan SA, Stensland MD. Direct and indirect costs of employees with treatment-resistant and non-treatment-resistant major depressive disorder. Curr Med Res Opin. 2010; 26(10):2475-84. doi: 10.1185/03007995.2010.517716
20. Zhang Q, DiBernardo A, Heerlein K, O'Hara M, Benson C, Gonzalez Martin Moro B, et al. Association of treatment resistant depression with healthcare resource utilization and physician satisfaction with disease management. Value Health. 2018;21(Supp 1):S188. doi: 10.1016/j.jval.2018.04.1270
21. Guerra M, Ferri CP, Sosa AL, Salas A, Gaona C, Gonzales V, et al. Late-life depression in Peru, Mexico and Venezuela: The 10/66 population-based study. Br J Psychiatry. 2009;195(6):510-5. doi: 10.1192/bjp.bp.109.064055
22. Borges G, Benjet C, Medina-Mora ME, Orozco R, Wang PS. Treatment of mental disorders for adolescents in Mexico City. Bull World Health Organ. 2008;86(10):757-64. doi: 10.2471/blt.07.047696
23. Pimentel L. The Importance of Mental Health in the Mexican Public Health System. Mexican Journal of Medical Research ICSA. 2019;7(13):1-6. doi: 10.29057/mjmr.v7i13.3794
24. Kohn R, Ali AA, Puac-Polanco V, Figueroa C, López-Soto V, Morgan K, et al. Mental health in the Americas: an overview of the treatment gap. Rev Panam Salud Publica. 2018;42:e165. doi: 10.26633/RPSP.2018.165
25. Martinez W, Galván J, Saavedra N, Berenzon S. Barriers to integrating mental health services in community-based primary care settings in Mexico city: A qualitative analysis. Psychiatr Serv. 2017;68(5):497-502. doi: 10.1176/appi.ps.201600141