

CLINICAL AND ECONOMIC IMPACT OF TREATMENT-RESISTANT DEPRESSION

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INTRODUCTION

- Major depressive disorder (MDD) is one of the most common psychiatric diagnoses, with an estimated year-prevalence in Spain of 4% and a lifetime prevalence of around 10.6%¹.
- Despite antidepressant treatments available, there is a proportion of patients that fail to respond to these treatments, having been estimated at 33% the theoretical cumulative rate of patients not achieving remission after four acute treatment steps².
- Although there is a lack of consensus on the definition of Treatment Resistant Depression (TRD), the most widely accepted is the failure to respond to 2 or more antidepressants during the current episode^{3, 4}.
- TRD is an important public health problem in terms of both prevalence, patients' suffering and cost to society⁵
- To date, there are no updated data on the incidence of treatment-resistant depression in Spain.

OBJECTIVES

The objective of the study was to **determine the incidence of treatment-resistant depression (TRD) in Spain, and its associated economic burden, using real world data/information.**

METHODS

- A retrospective observational study was carried out using data from the administrative BIG-PAC secondary database@ (<http://www.encepp.eu/encepp/viewResource.htm?id=29236>)⁶. (estimated population: 1.8 million patients).
- All patients with a depressive disorder (DD) diagnosis, aged ≥ 18 years who initiated a new antidepressant treatment (AD; index date) during 2015-2017 were included in the study.
- During the first year of treatment, patients were allocated in 2 cohorts: TRD or non-TRD. TRD was defined as failure to respond to ≥ 2 AD (defined as having ≥ 3 AD or ≥ 2 AD and ≥ 1 antipsychotic/Lithium prescribed during at least 28 days each). Period between treatments no longer than 28 days each^{7,8}.
- Patients were followed up 18 months in each cohort (TRD and non-TRD).
- The incidence rate was calculated as the number of TRD patients per 1,000 persons-year, considering the population attended in the health system (2015-2017).
- Variables of analyzed included: demographic data (age, gender), comorbidities, resource use, and healthcare direct and indirect costs (temporary and permanent occupational disability), and other 18-month outcomes (vital status, and suicidality (according to selected diagnostic codes related to it)).
- Direct health costs of DD were estimated based on the resource use rate during the follow-up period. Indirect costs (temporary and permanent disability) were calculated based on the human capital method using data (average annual earnings) from the National Statistical Institute (INE-Spain).
- Two sensitivity analyses were performed varying the index date and the period used to define TRD patients (6 vs 12 months).

RESULTS

- 21,630 DD patients aged ≥ 18 years (mean age: 53.2 years; female: 67.2%) were analyzed, of whom 3,559 (16.5% 95% CI: 16%-17%) met criteria of TRD. (Table 1).
- The annual incidence rates of TRD were: 0.59, 1.02 and 1.18 per 1,000 person-years, corresponding to an average incidence of 0.93 person-years (95%CI: 0.7–1.1).
- Cumulative mortality and variables related to suicidality were higher in TRD than in non-TRD patients (2.4% vs.1.3%; $p<0.001$) and (4.5% vs 3.3%, $p<0.001$) respectively.
- Mean total cost per patient in 18 months was € 4,147.9. Costs were higher for TRD patients than for non-TRD patients (€ 5,878.8 vs. € 3,801.8; $p<0.001$; difference: € 2,077.0). (Table 2, and Fig. 1).
- Similar differences were found when comparing specific cost components: direct healthcare costs (€ 1,327.2 vs. € 625.5; $p<0.001$), costs due to loss of productivity (€ 1,148.5 vs. € 754.8; $p<0.001$) and costs due to permanent disability (€ 3,403.1 vs. € 2,421.5; $p<0.001$). (Table 2, and Fig. 1).
- Both sensitivity analyses showed no differences with the reported results.

Table 1. Characteristics of the patients with a depressive disorder (DD) diagnosis, aged ≥ 18 years who initiated a new antidepressant treatment (2015-2017), according to treatment response.

	Non-TRD N=18,071 (83.5%)	TRD* N=3,559 (16.5%)	Total N=21,630 (100%)	P
Demographic characteristics				
Number of patients, %				
Age, years (SD)	53.2 (17.3)	53.6 (17.2)	53.2 (17.3)	0.209
Gender (women)	12,178 (67.4%)	2,360 (66.3%)	14,538 (67.2%)	0.210
General comorbidity				
Average number of diagnoses (SD)	1.5 (1.3)	1.7 (1.4)	1.6 (1.4)	<0.001
Average Charlson Index (SD)	0.8 (1.3)	0.8 (1.2)	0.8 (1.3)	0.362
Associated comorbidities				
Arterial hypertension	4,959 (27.4%)	963 (27.1%)	5,922 (27.4%)	0.639
Diabetes mellitus	1,679 (9.3%)	332 (9.3%)	2,011 (9.3%)	0.944
Dyslipidemia	5,205 (28.8%)	1,035 (29.1%)	6,240 (28.8%)	0.738
Obesity	2,117 (11.7%)	455 (12.8%)	2,572 (11.9%)	0.072
Active smoking	1,874 (10.5%)	445 (12.5%)	2,339 (10.8%)	<0.001
Alcoholism	167 (0.9%)	73 (2.1%)	240 (1.1%)	<0.001
Ischemic heart disease	568 (3.1%)	106 (3.0%)	674 (3.1%)	0.605
Stroke	577 (3.2%)	100 (2.8%)	677 (3.1%)	0.230
Heart failure	444 (2.5%)	76 (2.1%)	520 (2.4%)	0.252
Renal insufficiency	569 (3.1%)	112 (3.1%)	681 (3.1%)	0.996
Anxiety	6,856 (37.9%)	1,756 (49.3%)	8,612 (39.8%)	<0.001
Neoplasms	2,195 (12.1%)	420 (11.8%)	2,615 (12.1%)	0.563
Outcome variables (follow-up)				
Death (all causes)	235 (1.3%)	85 (2.4%)	320 (1.5%)	<0.001
Suicide ideation/attempts	596 (3.3%)	164 (4.6%)	760 (3.5%)	<0.001

*TRD, index date corresponds to the start date of the first antidepressant treatment administered
Values expressed as a percentage (N, %) or mean (SD; standard deviation), p: statistical significance, DD: depressive disorder, TRD: treatment-resistant depression; non-TRD: non-treatment resistant depression

Fig 1. Difference in costs by category according to treatment response.



CONCLUSIONS

Population-based TRD incidence in Spain was estimated at 0.93/1,000 person-years. This is similar to recent, first-time published data from other European countries⁹.

TRD is associated with more resources use and higher costs vs non-TRD patients.

Table 2. Health and non-health costs among patients with a depressive disorder diagnosis, aged ≥ 18 years who initiated a new antidepressant treatment (2015-2017), according to treatment response.

	Non-TRD N = 18,071 (83.5%)	TRD * N = 3,559 (16.5%)	Total N = 21,630 (100%)	P
Number of patients, %				
Primary care visits	303.0 (275.2)	503.3 (396.7)	335.9 (307.7)	<0.001
Hospital emergency visits	41.8 (116.7)	63.1 (128.7)	45.3 (119.0)	<0.001
Specialist visits	49.0 (174.4)	189.0 (401.7)	72.1 (233.8)	<0.001
Hospital stays	62.5 (801.9)	140.9 (1190.3)	75.4 (878.1)	<0.001
Lab tests	51.1 (74.9)	60.3 (76.7)	52.6 (75.3)	<0.001
Conventional radiology	10.7 (40.7)	11.7 (39)	10.9 (40.5)	0.184
Axial tomography	0.8 (9.8)	1.5 (12.6)	0.9 (10.3)	<0.001
Magnetic nuclear resonance	2.3 (22.7)	3.2 (26.7)	2.5 (23.4)	0.045
Other complementary tests	3.2 (79.1)	5.1 (92.3)	3.5 (82.6)	<0.001
Electroconvulsive therapy	5.4 (92.3)	8.2 (90.9)	5.9 (92.1)	0.132
Antidepressant medication	95.6 (222.3)	340.9 (767.4)	136.0 (382.7)	<0.001
Healthcare costs				
	625.5 (985.3)	1,327.2 (1,791.3)	741.0 (1,186.0)	<0.001
Loss of labor productivity				
	754.8 (2,537.1)	1,148.5 (3,247.5)	819.6 (2,670.2)	<0.001
Permanent disability				
	2,421.5 (3,686.6)	3,403.1 (4,607.4)	2,587.3 (4,119.5)	<0.001
Total costs				
	3,801.8 (2,985.5)	5,878.8 (3,998.3)	4,147.9 (3,199.3)	<0.001

In Eur. * TRD, index date: corresponds to the start date of the first antidepressant treatment administered.
Values expressed as a percentage (N, %) or mean (SD; standard deviation), p: statistical significance; DD: depressive disorder; TRD: treatment-resistant depression; nTRD: non-treatment resistant depression

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