Description of Treatment Resistant Depression in France, from the French nationwide claims database

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Abstract

Background: Treatment Resistant Depression (TRD) is a serious health hazard worldwide, which results in significant impairment, increased morbidity and high costs for society. To date, the global epidemiological situation and the clinical characteristics of TRD patients are poorly understood, especially in France.
Objectives: To estimate annual incidence and prevalence of TRD in France, and patient characteristics, from the nationwide claims database SNDS (*"Système National des Données de Santé"*).
Methods: We identified all adult patients (≥ 18 years) with a TRD episode between January 1, 2012 and December 31, 2014 in EGB ("*Échantillon généraliste des bénéficiaires*"), the 1/97th permanent random sample of SNDS. After exclusion of any psychotic disorders, Parkinson's disease, dementia or bipolar affective disorders, a TRD episode was defined as the succession of 3 sequences of different antidepressants (AD), or a combination of an AD with a potentiator (lithium, antiepileptic drugs, antipsychotic drugs or thyroid hormones) over a period of 3 months, with at least 3 weeks of treatment between each AD and with a Medication Possession Ratio ≥ 80%. TRD patients should not have had any AD dispensing or hospitalization for depression within the 6 months preceding the first AD dispensing (*i.e.* initiation date). The incidence rate was estimated yearly from 2012 to 2014 then averaged. The prevalence was estimated according to a Gamma parametric function using treatment duration and a 30-year prediction.
Results: Between 2012 and 2014, 700 patients were identified in EGB with a TRD episode. The mean age was 47.4 years; 52.7% were women, 694 had only one episode and 6 had 2 episodes. The median duration of a completed TRD episode was 5.4 months. The annual incidence of TRD was estimated at 5.8 per 10 000 persons, and the annual prevalence at 25.8 per 10 000 persons.
Discussion: From the estimates we found, TRD may be amenable itself to further analyses, including analysis of treatment trajectories and comparative effectiveness in the full national database.

Declaration of Interest Statement

The DIORAMA study was carried out by the Bordeaux PharmacoEpi platform in collaboration with Janssen® company and supervised by a Scientific Committee.

Background

Resistant Depression (TRD)

- Defined by the failure of ≥ 2 successive well-conducted antidepressant treatments.
- Represents a serious health hazard worldwide because it entails:
  - a significant impairment,
  - a increased morbidity,
  - a high economic cost for society.
- Requires further epidemiological studies, especially in France.

Objectives

- To estimate **annual incidence and prevalence of TRD in France,**
- To describe **TRD patient characteristics,** using data from the **French nationwide claims database SNDS** ***("Système National des Données de Santé")***

Methods

Identification of TRDp patients

- In EGB ("*Échantillon généraliste des bénéficiaires*"), the 1/97th permanent random sample of SNDS,
- Adult patients (≥ 18 years):
  - With ≥ 1 **TRD episode identified based on the patterns of dispensing (TRDp)** between January 1, 2012 and December 31, 2014,

  TRDp episode = succession of 3 sequences of different antidepressants (AD), or a combination of an AD with a potentiator (lithium, antiepileptic drugs, antipsychotic drugs or thyroid hormones) over a period of 3 months, with at least 3 weeks of treatment between each AD and with a Medication Possession Ratio ≥ 80% **(Figure 1)**.

  - Without any psychotic disorders, Parkinson's disease, dementia or bipolar affective disorders,
  - With no AD dispensing or hospitalization for depression within the 6 months preceding the first AD dispensing (*i.e.* initiation date).

Incidence and prevalence estimations

- Incidence and prevalence were estimated yearly from 2012 to 2014 then averaged over the 3 years,
- Prevalence estimated according to a Gamma parametric function using treatment duration and a 30-year prediction.

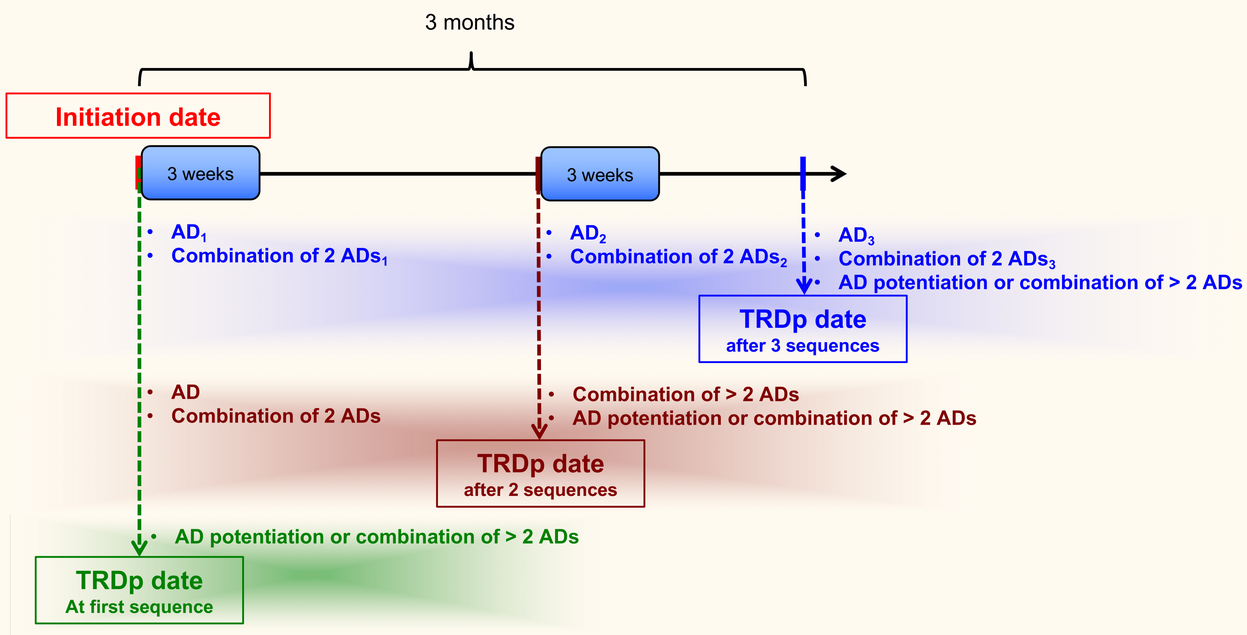

Figure 1. Definition of Treatment Resistant Depression (TRDp) episode according to the different sequences of treatment strategy

Results

Selection of the TRDp population (Figure 2)

- **700 patients** with a TRDp episode identified in EGB between 2012 and 2014:
  - 229 in 2012, 234 in 2013 and 243 in 2014,
  - 694 patients had only 1 TRDp episode,
  - 6 patients had 2 TRDp episodes.

Characteristics of patients with at least one treatment resistant depression episode

- Mean age was **47.4 years** (±15.3 years),
- A little majority of patients were **women (52.7%)**.

Table 2: Description of characteristics of patients with at least one treatment resistant depression episode identified based on pattern of prescription between 2012 and 2014

	2012 n = 229	2013 n = 234	2014 n = 243	Total* N = 700
Female, n (%)	133 (58.1)	112 (47.9)	127 (52.3)	369 (52.7)
Mean (± SD) age at initiation date (in years)	48.0 (16.1)	47.1 (15.0)	47.6 (15.2)	47.4 (15.3)
Psychiatric history within the 2 years prior to initiation date				
LTD registration for psychiatric diagnosis, n (%)	41 (17.9)	61 (26.1)	67 (27.6)	168 (24.0)
LTD registration for depressive disorders	25 (10.9)	35 (15.0)	37 (15.2)	96 (13.7)
Hospitalization with psychiatric diagnosis, n (%)	10 (4.4)	12 (5.1)	17 (7.0)	39 (5.6)
Mean (± SD) number of psychiatric hospitalizations**	2.1 (1,1)	1.6 (1,4)	1.9 (1.5)	1.9 (1,4)
Mean total duration (± SD) of psychiatric hospitalizations (in days)**	16.0 (20.5)	13.0 (21.2)	15.1 (14.5)	14.7 (17.9)
Psychiatric medical visit, n (%)	57 (24.9)	65 (27.8)	56 (23.0)	175 (25.0)
Median number [IQR] of psychiatric medical visit**	6.0 [1.0-18.0]	3.0 [1.0-10.0]	4.0 [1.0-18.5]	4.0 [1.0-17.0]
Psychiatric medications, n (%)				
Antidepressant medications	92 (40.2)	108 (46.2)	101 (41.6)	295 (42.1)
Antidepressant potentiator	67 (29.3)	63 (26.9)	67 (27.6)	192 (27.4)
2nd generation antipsychotic	33 (14.4)	38 (16.2)	37 (15.2)	105 (15.0)
Thyroid hormones	28 (12.2)	17 (7.3)	20 (8.2)	64 (9.1)
Antiepileptic drugs	16 (7.0)	16 (6.8)	14 (5.8)	45 (6.4)
Anxiolytics	153 (66.8)	162 (69.2)	163 (67.1)	472 (67.4)
Hypnotics and sedatives	77 (33.6)	75 (32.1)	86 (35.4)	233 (33.3)
Other antipsychotics	4 (1.7)	3 (1.3)	4 (1.6)	11 (1.6)
Psychostimulants	2 (0.9)	1 (0.4)	0 (0.0)	3 (0.4)
Non-psychiatric history within the 2 years prior to initiation date				
Main LTD registration for non-psychiatric disease, n (%)	65 (28.4)	69 (29.5)	53 (21.8)	184 (26.3)

SD, Standard Deviation; LTD, Long Term Disease, IQR: interquartile range
* Total number of patients over the 3 studied years (2012-2014)
** Among patients concerned

Characteristics of TRDp episodes

- In total, 435 (61.6%) TRDp episodes ended before the end of follow-up:
  - the median duration of a completed TRDp episode was **5.4 months** (IQR: 2.9 – 9.3 months),
  - a TRD episode included a **median of 2 treatment sequences** (IQR: 1 – 3) **(Figure 3).**

- Among the **706 TRDp episodes** (**Figure 3**)
  - 80 (11.3%) were identified by the use of 1 AD alone at the **3rd sequence** of treatment,
  - 6 (0.8%) were identified by a combination of 2 ADs at the **3rd sequence** of treatment,
  - 578 (81.9%) were identified at the first dispensing of an AD(s) with a potentiator:
    - 196 (27.8%) at the **2nd** or **3rd sequence** of treatment,
    - 382 (54.1%) from the **1st sequence** of treatment,
  - 42 (6.0%) were identified by a multiple combination of AD(s) + with a potentiator in **1st**, **2nd** or **3rd** sequence.

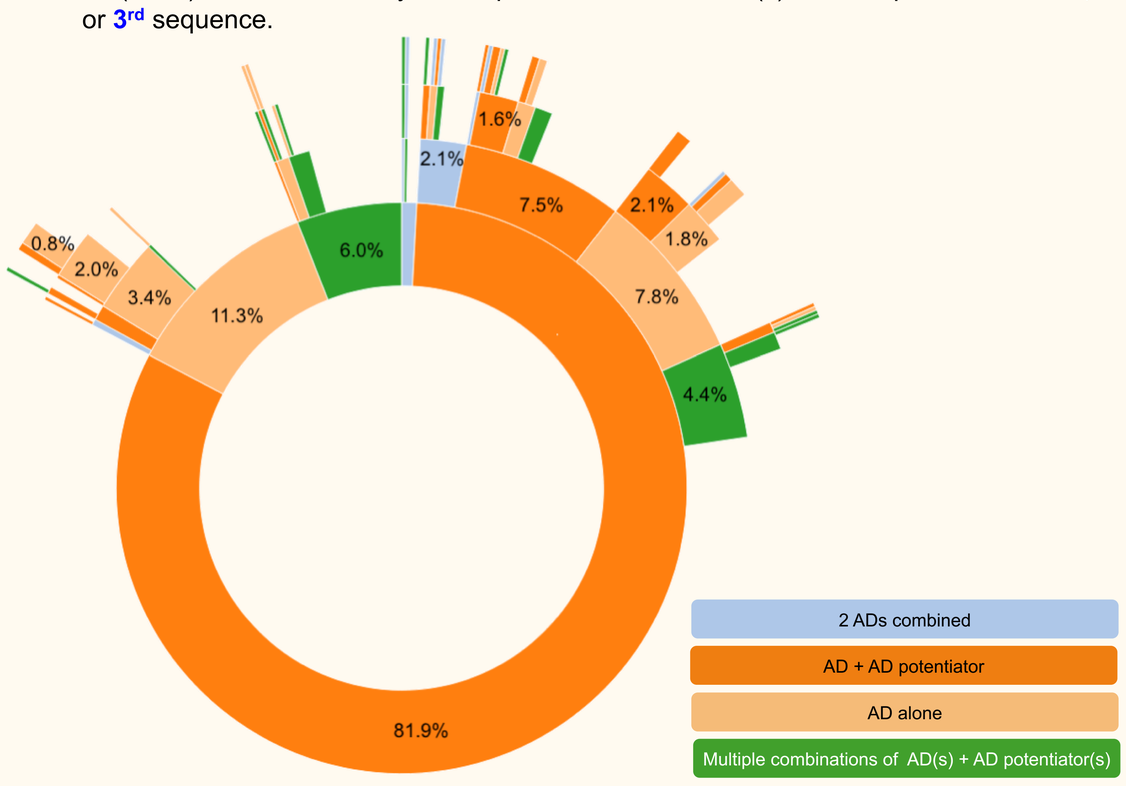

Figure 3. Medications of the TRDp dispensed during the first four lines between 2012 and 2014

Incidence and prevalence of TRD in France between 2012 and 2014

	Annual rate / 10 000 persons	Extrapoled number in French population
Incidence	5.8	29 015
Prevalence	25.8	129 275

Discussion / Conclusion

This study provides **new data on incidence and prevalence of TRD** in France

- These incidence and prevalence estimations of TRD are consistent with those found in the literature but rather in the low range of these estimates
- **Identification algorithm** used to identify TRD has the advantage to **include all treatment strategies** applied in this disease
- TRD may be amenable itself to **further analyses**: analysis of treatment trajectories, comparative effectiveness in the full national database

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