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# Using filled prescription sequences to rank antidepressants: A nationwide replication study☆

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ABSTRACT

Ranking antidepressants according to their acceptability (i.e., a combination of both efficacy and tolerability) in the general population may help choosing the best first-line medication. This study aimed to replicate the results of a proof-of-concept study ranking anti-depressants according to the proportion of filled prescription sequences consistent with a continuation of the first treatment versus those consistent with a change. We used a nationwide cohort from the French national health data system (SNDS) to support the use of this method as a widely available tool to rank antidepressant treatments in real life settings. About 1.2 million people were identified as new antidepressant users in the SNDS in 2011. The outcome was clinical acceptability as measured by the continuation/failure ratio over the six-month period following the introduction of the first-line treatment. Continuation was defined as at least two refills of the same treatment. Failure was defined as a psychiatric hospitalization, death or at least one filled prescription of another antidepressant, an antipsychotic medication, or a mood-stabilizer. Adjusted Odds Ratios (aOR) and 95% Confidence Interval (CI) were computed through multivariable binary logistic regressions. We ranked antidepressant medications according to clinical acceptability. Escitalopram again was the most acceptable option, and the five following antidepressants were the same as in the replication sample of the proof-of-concept study, in order Fluoxetine, Paroxetine, Sertraline, Citalopram and Venlafaxine with aOR (95% CI) for continuation ranging from 0.79 (0.77–0.81) to 0.66 (0.64–0.67). The present study provides evidence that filled prescription sequences is a widely available, robust and reproductible tool to rank antidepressant treatments in real life settings.

## 1. Introduction

Depressive and anxiety disorders are leading causes of disability worldwide (Cuijpers et al., 2014; GBD 2016 Disease and Injury Incidence and Prevalence Collaborators, 2017; Hoertel et al., 2015; Turecki and Brent, 2016). Antidepressant medications are recommended as the first-line treatment for moderate to severe unipolar major depressive episodes and for most anxiety disorders, with the exception of a specific phobia ("Depression overview - NICE Pathways," 2020; *Traitement par antidépresseurs - ANSM: Agence nationale de sécurité du médicament et des produits de santé*, 2019; Gelenberg et al., 2010). Prior meta-analyses of randomized controlled trials (RCTs) suggest that antidepressants may be ranked according to a combination of their efficacy and tolerability, henceforth referred to as 'acceptability', in the acute treatment of major depressive disorder (Cipriani et al., 2018). Since a treatment must be both efficacious and well tolerated to be clinically useful, acceptability is indeed what patients, physicians and guidelines value when considering first-line treatment. The results of RCTs, however, may be difficult to

*Abbreviations:* RCT, randomized controlled trial; SNDS, système national des données de santé; GP, general practitioner; aOR, adjusted odd ratio; CI, confidence interval; CNAM, caisse nationale d'assurance maladie.

☆ SAS Enterprise version 7.13 (SAS Institute Inc, Cary, NC, USA) was used to create variables and extract data. All analyses were perfomed using R software, version 4.0.3.

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generalize to patients with depression encountered in real-life settings because of their extremely restrictive eligibility criteria (Blanco et al., 2008; Hoertel et al., 2013; Zimmerman et al., 2002). RCT follow-up is usually limited to 6–8 weeks, a very short duration compared to the months or years when treating a depression or anxiety disorder. This is another limitation when generalizing results of RCTs. Results from pragmatic trials may be easier to generalize but are generally underpowered to compare several first-line antidepressant drugs (Trivedi et al., 2006). Administrative claim databases, which store large-scale data from routine clinical settings including filled prescriptions, may be used to address this gap (Commission Expert Group on Safe and Timely Access to Medicines for Patients, 2016). In a proof-of-concept study, we suggested that the sequences of filled prescriptions of antidepressants recorded in administrative claims databases could be used to rank different antidepressant medications according to their relative clinical acceptability on a drug-by-drug basis (Olekhnovitch et al., 2020). Specifically, clinical acceptability was captured for each treatment by the ratio of treatment sequences consistent with a continuation of the first prescribed treatment – suggesting both efficacy and tolerability – on those consistent with a change (either medication switch or combination). We benefited from the linkage of the French large-scale population-based Constances cohort study (which contains detailed individual data) with the SNDS database (Système National des Données de Santé, French national health data system, which contains claims data from the national health insurance system). We demonstrated that patients who followed a "continuation" sequence had a lower level of depressive symptoms than those who followed a "change" sequence. This finding was a first step in supporting the clinical relevance of the continuation/change ratio as a proxy of clinical acceptability. We then used this ratio to rank first-line antidepressant treatments in both the whole Constances cohort and a two-fold larger replication sample representative of the general population. In this later sample of 10,511 individuals, escitalopram had the most favorable continuation/change ratio and the five following antidepressants were in order: fluoxetine, paroxetine, venlafaxine, sertraline and citalopram (Olekhnovitch et al., 2020).

To further support the use of this method as a widely available tool to rank antidepressant treatments in real life settings, a second step was to challenge its robustness by replicating the ranking obtained in the proof-of-concept study in another population. The present study was based on a nationwide cohort using the SNDS and aimed at replicating this ranking with the same methodology.

## 2. Methods

### 2.1. About the SNDS

The SNDS collects the individual characteristics of all the beneficiaries of the various French national health insurance schemes. Individual characteristics include age, sex, commune of residence (i.e., the smallest administrative unit, approximately 36,000 across France), vital status (date of death) and eligibility for complementary health insurance coverage (CMU-C, for individuals aged <60 years), which is attributed to people or households with an annual income below the poverty line in France (Tuppin et al., 2017). A social deprivation index is also available at the scale of the commune, based on data published by the National Institute for Statistics And Economic Studies regarding household income, education level, occupational grade and unemployment rate. The higher the index, the higher the level of social deprivation (Constantinou et al., 2018).

The main national health insurance scheme in France is the general scheme, which covers about 77% of the 66 million inhabitants and this proportion reaches about 86% with the addition of local mutualist sections beneficiaries. The other main schemes are the Mutualité Sociale Agricole (agricultural workers scheme) and the Régime Social des Indépendants (self-employed workers scheme), representing together almost 10% of the population and miscellaneous schemes (4%). This study was limited to general scheme with the addition of local mutualist sections beneficiaries due to lack of completeness of certain data in the other schemes during the study period.

Reimbursed drugs are identified according to the Anatomical Therapeutic Classification (ATC). Drugs dispensed during hospitalization are not reimbursed individually and cannot therefore be identified. The Caisse Nationale d'Assurance Maladie (CNAM), the general health scheme fund, has developed algorithms designed to identify 58 non-exclusive groups of health conditions (diseases, episodes of care, chronic treatments) using ICD-10 codes for long-term diseases (offering 100% reimbursement of health care) or hospitalizations, medications or medical procedures (Constantinou et al., 2018).

In France, there is no insurance or cost restriction regarding the antidepressant medications used in this analysis.

### 2.2. Study population

People were included at the date of their first reimbursement of an antidepressant from 1 January 2011 to 31 December 2011. They were defined as first antidepressant users if they had a filled prescription of antidepressant in 2011 and by the absence of any filled prescription of a psychotropic drug in 2009 and 2010, except benzodiazepines and Z-drugs, together with no prior psychiatric diagnosis identified in the past four or five years. Patients were followed for a rolling year starting on the day of the first filled prescription of antidepressant. Next, people aged less than 18 were excluded.

### 2.3. Primary outcome

The primary endpoint was clinical acceptability as measured by the continuation/failure ratio for each treatment. Continuation sequence was defined as at least two refills of the same antidepressant with no delivery of a different antidepressant over the six-month period following the first prescription. Failure was a composite variable including psychiatric hospitalization, death, or a change sequence. Change sequence was defined as at least one delivery of either a different antidepressant, an antipsychotic medication, or a mood-stabilizer over the six-month period following the first prescription (Fig. 1). Sequences without any refill or only one refill of the first prescribed antidepressant over the 6-month period were considered as "early termination" sequences of uncertain meaning (Olekhnovitch et al., 2020). For instance, patients with only one filled prescription may not have been reevaluated or may have been reevaluated as no longer needing an antidepressant medication.

### 2.4. Covariates

The following covariates were considered: age, sex, social deprivation index (quintiles), eligibility for CMU-C, specialty of the physician who prescribed the first antidepressant classified into three categories (GPs and hospital practitioners, psychiatrists private practice and other specialists private practice), benzodiazepines or Z-drugs intake (i.e., participants having ≥3 filled prescriptions during the year of inclusion), and the presence of ≥1 chronic non-psychiatric disease.

### 2.5. Statistical analysis

All 95% confidence intervals (CIs) were calculated using non-parametric bootstrap sampling with percentile intervals. Multivariable binary logistic regression models were used to calculate adjusted odds ratios (aORs). All CIs were calculated using profile likelihood method (using glm() and confint() functions). Due to missing data, social deprivation index and CMU-C were only used for descriptive analyses. We then ranked first-line treatment according to their clinical acceptability.

Under the worst-case scenario in which an "early termination"

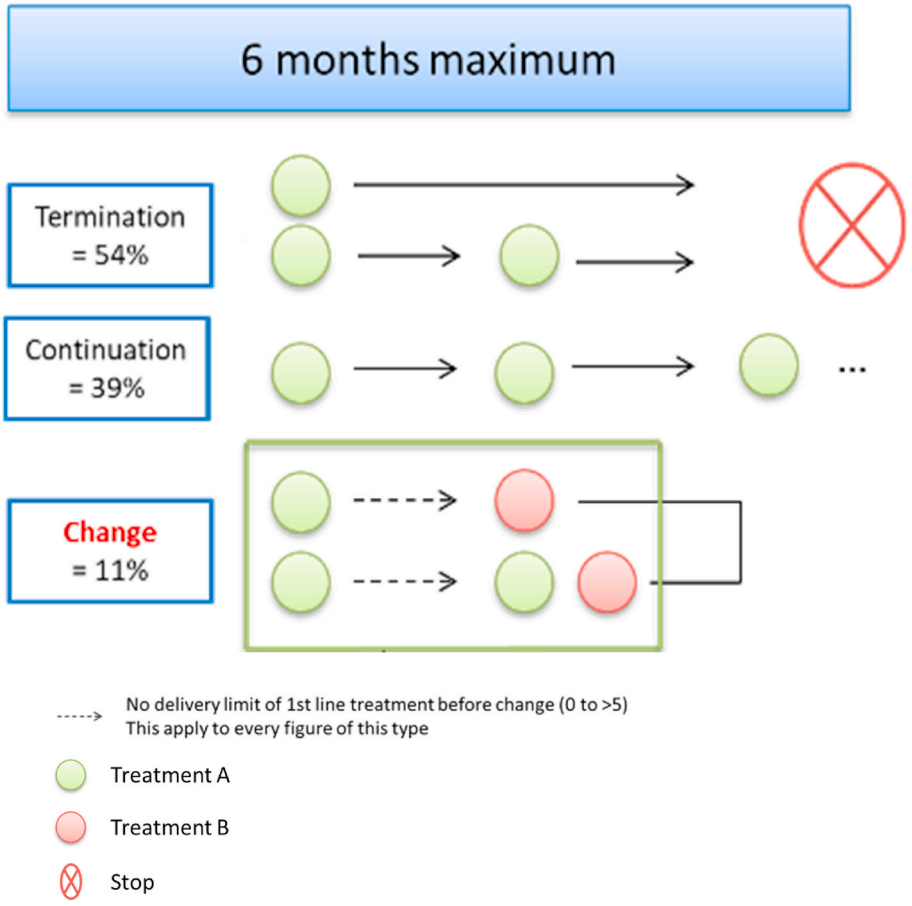


**Fig. 1.** Study design.

sequence would always indicate either poor efficacy or poor tolerability, sensitivity analyses were conducted including this sequence into the composite variable "failure".

The CNAM, as a health research institute, has permanent access to the SNDS database approved by decree and the French data protection authority (Commission Nationale de l'Informatique et des Libertés).

## 3. Results

In 2011, nearly 5.5 million people had at least one antidepressant filled prescription, including 1.2 million new antidepressants. According to inclusion and exclusion criteria, the population included 863,513 participants (Fig. 2, Table 1)."

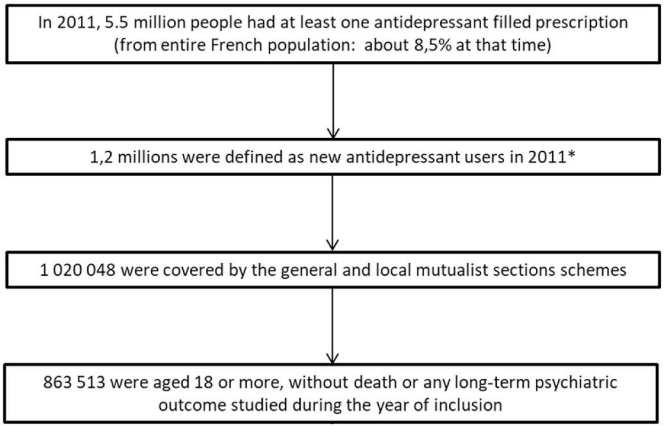


**Fig. 2.** Flowchart.

We ranked antidepressant medications with at least 100 observed sequences according to the continuation/failure ratio after the introduction of the first-line treatment (Table 2). Escitalopram again was the most acceptable option, and the five following antidepressants were the same as in the replication sample of the proof-of-concept study, though in a slightly different order, with venlafaxine ranking 6th instead of 4th (escitalopram, fluoxetine, paroxetine, sertraline, citalopram and venlafaxine).

Including "early termination" sequence in the composite variable failure, led to a significant decrease in the overall continuation rate from 70% to 37%. However, the ranking of antidepressants remained very similar with the same six antidepressants ranking first, though in a slightly different order (escitalopram, sertraline, fluoxetine, venlafaxine, paroxetine, citalopram) (Table S1)

## 4. Discussion

In this nationwide study, we replicated the results of a proof-of-concept study to support the use of filled prescription sequences as a widely available tool to rank antidepressant treatments in real life settings.

Strengths of the study include the large sample size, the duration of the follow-up, the representativeness of the population and the generalizability of the results. We were able to adjust our analyses for various potential confounding factors. Finally, although we aimed to stay as close as possible to the methods of the proof-of-concept study, the exclusion of patients who died or had a psychiatric hospitalization during the year of follow-up might have introduced an immortal time bias. Therefore, our proxy of clinical acceptability was improved to

**Table 1**
Characteristics of the population with incident antidepressant treatment according to the sequences of prescriptions during the first 6 months.

| | All | Sequence | | |
|---|---|---|---|---|
| | | Early termination | Continuation | Change |
| N | 895,513 | 466,901 | 300,175 | 128,437 |
| Row % | 100.0 | 52.1 | 33.6 | 14.3 |
| **Female gender** | 66.4 | 65.0 | 67.5 | 66.6 |
| **Age (years)** | | | | |
| <30 | 13.8 | 16.7 | 9.5 | 13.1 |
| 30–39 | 18.7 | 19.7 | 16.7 | 20.1 |
| 40–49 | 21.2 | 20.8 | 21.1 | 22.8 |
| 50–59 | 17.6 | 16.9 | 18.6 | 18.3 |
| 60–69 | 10.8 | 10.4 | 12.0 | 9.3 |
| ≥70 | 17.9 | 15.5 | 22.0 | 16.4 |
| **Deprivation index (quintiles) n = 799,999** | | | | |
| 1 less deprived | 18.0 | 17.1 | 19.3 | 18.4 |
| 2 | 18.9 | 18.3 | 19.7 | 18.8 |
| 3 | 19.9 | 19.6 | 20.2 | 20.2 |
| 4 | 19.9 | 20.0 | 19.9 | 19.5 |
| 5 more deprived | 21.5 | 22.7 | 19.6 | 21.7 |
| Overseas territories | 1.8 | 2.3 | 1.2 | 1.3 |
| **CMU-C (<60 years) n = 608,393** | 11.3 | 12.8 | 8.6 | 11.5 |
| **First prescriber** | | | | |
| GP or hospital practitioner | 90.0 | 91.7 | 88.4 | 86.5 |
| Psychiatrist, private practice | 5.9 | 4.1 | 7.4 | 9.5 |
| Another specialist, private practice | 4.6 | 4.2 | 4.1 | 4.0 |
| **At least one chronic disease**[a] | 21.7 | 20.0 | 24.6 | 20.2 |
| **Drugs reimbursed**[b] | | | | |
| Z-drugs | 14.7 | 12.9 | 16.3 | 18.1 |
| Benzodiazepines | 31.3 | 27.3 | 34.6 | 39.7 |
| **Mean (SD)** | | | | |
| Age | 50.2 (19.7) | 48.3 (20.5) | 53.2 (18.6) | 49.4 (18.0) |

CMU-C = complementary health insurance coverage.
GP: General Practitioner, SD: Standard Deviation.
[a] In the SNDS, algorithms identify 48 non-exclusive groups of chronic non-psychiatric diseases.
[b] At least three filled prescriptions in the year of inclusion.

**Table 2**
Frequency of continuation and failure by first molecule delivered.

| Molecule | Continuation % (N) | Failure % (N) | aOR (95% CI) |
|---|---|---|---|
| **Total** | 70.0 (300,175) | 30.0 (128,437) | – |
| **ESCITALOPRAM** | 75.3 (119,400) | 24.7 (27,923) | Ref. |
| **FLUOXETINE** | 71.4 (24,145) | 28.6 (8028) | 0.79 (0.77–0.81) |
| **PAROXETINE** | 69.8 (47,308) | 30.2 (15,562) | 0.75 (0.74–0.77) |
| **SERTRALINE** | 68.9 (12,478) | 31.1 (4384) | 0.74 (0.72–0.77) |
| **CITALOPRAM** | 69.2 (19,068) | 30.8 (6674) | 0.70 (0.68–0.72) |
| **VENLAFAXINE** | 66.5 (23,746) | 33.5 (9192) | 0.66 (0.64–0.67) |
| **DULOXETINE** | 66.0 (10,950) | 34.0 (4560) | 0.59 (0.57–0.62) |
| **AMITRIPTYLINE** | 64.0 (3216) | 36.0 (1502) | 0.56 (0.53–0.59) |
| **DOXEPINE** | 63.9 (212) | 36.1 (93) | 0.55 (0.44–0.69) |
| **CLOMIPRAMINE** | 62.8 (2537) | 37.2 (1201) | 0.54 (0.50–0.57) |
| **MIANSERINE** | 64.7 (12,856) | 35.3 (5258) | 0.52 (0.50–0.54) |
| **FLUVOXAMINE** | 60.8 (331) | 39.2 (165) | 0.51 (0.53–0.61) |
| **DOSULEPINE** | 60.3 (679) | 39.7 (374) | 0.48 (0.43–0.55) |
| **MAPROTILINE** | 60.7 (205) | 39.4 (100) | 0.46 (0.37–0.57) |
| **TIANEPTINE** | 61.8 (12,449) | 38.2 (6295) | 0.46 (0.45–0.48) |
| **IMIPRAMINE** | 59.8 (172) | 40.2 (101) | 0.45 (0.36–0.58) |
| **MOCLOBEMIDE** | 62.5 (195) | 37.5 (83) | 0.44 (0.35–0.56) |
| **TRIMIPRAMINE** | 58.0 (236) | 42.0 (156) | 0.44 (0.36–0.53) |
| **MIRTAZAPINE** | 56.6 (5480) | 43.4 (2874) | 0.40 (0.39–0.42) |
| **MILNACIPRAN** | 55.1 (1695) | 44.9 (1131) | 0.40 (0.37–0.42) |
| **AGOMELATINE** | 52.8 (2773) | 47.2 (2003) | 0.39 (0.37–0.41) |
| **AMOXAPINE** | 54.2 (39) | 45.8 (29) | 0.34 (0.32–0.55) |

Failure: psychiatric hospitalization, death, or at least one delivery of another antidepressant, an antipsychotic medication or a mood-stabilizer over the 6-month period.).
Continuation: at least two refills of the same antidepressant with no delivery of a different antidepressant over the 6-month period.
Values indicate row-based percentages and adjusted odds-ratio (aOR) and 95% confidence interval (95% CI) reflecting the extent to which each medication had a lower continuation/failure ratio as compared with escitalopram, adjusting for age, sex, specialty of the prescribing physician, treatments by benzodiazepines or Z-drugs, and presence of at least one chronic non-psychiatric condition.

account for psychiatric hospitalization or death in addition to "change" sequences.

Some limitations should be acknowledged. First, our study is observational, including concerns over confounder control limiting the comparability of treatment groups. For instance, treatments perceived to be most effective might be proposed for the most affected patients and drug-by-drug differences of acceptability in naturalistic studies might be explained by drug channeling. In addition, including patients without any antidepressant dispensing over at least the preceding year allows minimizing the depletion of susceptible bias but does not exclude it. Overall, even if the analyses were adjusted for some potential confounders (i.e. age, sex, education level, occupational status and first prescriber's specialty), residual confounding cannot be excluded since we did not consider other potential confounders (e.g., specific comorbid conditions). Second, although the wealth of data collected in the SNDS allowed taking into account comorbidity, it did not generate information about the disorders that warranted the prescription of antidepressant medications. Third, this analysis does not provide data about actual medication consumption. However, it is unlikely that patients with regular filled prescriptions did not take their medication at all. Fourth, information about prescriptions that were not filled by patients was not available in this database. Fifth, the exclusion of individuals with at least one filled prescription for a mood-stabilizing or antipsychotic medication reduced the risk of including patients with bipolar disorder or schizophrenia, but probably excluded some patients with unipolar depression. Sixth, GPs and hospital practitioners were classified in the same category. Hospital practitioners who prescribe antidepressants are likely to be psychiatrists, with specific characteristics of treatment patterns. However, since the goal of the present study was to use a methodology as close as possible to the proof-of-concept study to validate this novel tool, we used the same variable as in this first study.

Although the frequency with which individual antidepressants were prescribed reflects the prescribing habits of French physicians, our methods were not based on the likelihood of any treatment being prescribed. Instead, the acceptability ratios are based on the likelihood that the treatment was continued once prescribed. A striking example is the case of sertraline, which was prescribed four times less often than paroxetine, twice less often than fluoxetine, venlafaxine or citalopram, but with a similar or even higher acceptability.

While closer from real-life setting that most RCTs, we had to use specific exclusion criteria to reduce the risk of confounding, such as co-prescription of other psychotropic medications, that limits study generalizability (Hoertel et al., 2017, 2021). Future studies using the same framework performed in the fraction of the general population excluded from our analyses (i.e., co-prescription of other psychotropic medications) are needed to examine the applicability of our results to this specific population. Continuation sequences were considered for individuals who received at least two refills of the same antidepressant over the 6-month period after initiation of the treatment. This was demonstrated as clinically relevant in the proof-of-concept study, with patients who followed a "continuation" sequence having a lower level of depressive symptoms than those who followed a "change" sequence. However, it is possible that three filled prescriptions did not really cover

six months of treatment. Finally, although the continuation/failure ratio may be a relevant proxy of clinical acceptability, it may not discriminate between tolerability and effectiveness.

Although the replication sample of the proof-of-concept study was a nationally representative sample, there was no overlap with the population of the current study as inclusion periods differed and only new antidepressant users were included. Furthermore, the present study was based on the same methods as the first one but relied on a complete reprogramming of the algorithms by two of us (COV, TS) who did not take part in the first study. Despite these differences, the results were strikingly similar, suggesting that the use of the continuation/failure or change ratio as a proxy of clinical acceptability may generate robust and reproducible ranking. In a sensitivity analysis considering early termination as indicating a failure, the ranking remained very similar with the same six antidepressants ranking first. It is noteworthy that sertraline, which ranked second in the sensitivity analysis (versus fourth in the main analysis), is only the seventh most prescribed drug, far behind escitalopram and paroxetine. This result further exemplifies that our proxy of clinical acceptability may not be correlated to the frequency of prescription. For instance, sertraline is as prescribed as mianserine, but its clinical acceptability was 1.4–1.7 times higher. The inclusion of early termination as indicating a failure may have increased the weight of poor tolerance in our proxy of clinical acceptability.

## 5. Conclusion

The present study provides evidence that filled prescription sequences is a widely available, robust and reproductible tool to rank antidepressant treatments in real life settings. We believe this study further paves the way to new analyses based on filled prescriptions of antidepressants recorded in administrative claims databases and widely available for research nowadays. Although randomized clinical trials remain the gold standard method to assess the efficacy and tolerability of antidepressant medications, they generally suffer from reduced external validity making their findings difficult to generalize to real-life settings (Hoertel et al., 2021). In addition, the present tool may be used in very large populations and thus offers an opportunity to look at issues that would be hardly addressed by randomized clinical trials. For instance, filled prescription sequences could be used to rank antidepressants according to their clinical acceptability after a failure of a first treatment (Ouazana-Vedrines et al., 2022). Although this gap of knowledge is critical, with barely half of patients responding to a first-line antidepressant treatment in naturalistic studies (Trivedi et al., 2006), a randomized control trial addressing this issue would hardly be sufficiently powered in the light of the number of possible medication combinations. Therefore, we hope that the present results could constitute an impetus for re-analyzing available datasets based on this approach and gain new insights for clinical practice.

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## Author statement

COV, TL, PT and CL designed the study. COV, TL and PD analyzed the data. COV and CL wrote the first draft. All authors contributed to the interpretation of the data, revised the first draft critically for important intellectual content, finally approved of the version to be published and agreed to be accountable for all aspects of the work.

## Declaration of competing interest

CL reports personal fees and non-financial support from Otsuka Pharmaceutical, outside the submitted work. CB holds stock in Sanofi, Eli Lilly and General Electric. NH reports personal fees and non-financial support from Lundbeck, outside the submitted work. The other authors have no competing interests to report.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jpsychires.2022.12.030.

## References

Depression Overview - NICE Pathways, 2020.

Blanco, C., Olfson, M., Goodwin, R.D., Ogburn, E., Liebowitz, M.R., Ev, N., 2008. Generalizability of clinical trial results for major depression to community samples: results from the National Epidemiologic Survey on Alcohol and Related Conditions. J. Clin. Psychiatr. 69, 1276–1280.

Cipriani, A., Furukawa, T.A., Salanti, G., Chaimani, A., Atkinson, L.Z., Ogawa, Y., Leucht, S., Ruhe, H.G., Turner, E.H., Higgins, J.P.T., Egger, M., Takeshima, N., Hayasaka, Y., Imai, H., Shinohara, K., Tajika, A., Ioannidis, J.P.A., Geddes, J.R., 2018. Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis. Lancet 391, 1357–1366. https://doi.org/10.1016/S0140-6736(17)32802-7.

Commission Expert Group on Safe and Timely Access to Medicines for Patients, 2016. Paper for STAMP Meeting 10 March 2016: Update on Real World Evidence Data Collection.

Constantinou, P., Tuppin, P., Fagot-Campagna, A., Gastaldi-Ménager, C., Schellevis, F.G., Pelletier-Fleury, N., 2018. Two morbidity indices developed in a nationwide population permitted performant outcome-specific severity adjustment. J. Clin. Epidemiol. 103, 60–70. https://doi.org/10.1016/j.jclinepi.2018.07.003.

Cuijpers, P., Vogelzangs, N., Twisk, J., Kleiboer, A., Li, J., Penninx, B.W., 2014. Comprehensive meta-analysis of excess mortality in depression in the general community versus patients with specific illnesses. Am. J. Psychiatr. 171, 453–462.

GBD 2016 Disease and Injury Incidence and Prevalence Collaborators, 2017. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet 390, 1211–1259. https://doi.org/10.1016/S0140-6736(17)32154-2.

Gelenberg, A.J., Freeman, M.P., Markowitz, J.C., Rosenbaum, J.F., Thase, M.E., Mh, T., 2010. Practice Guideline for the Treatment of Patients with Major Depressive Disorder.

Hoertel, N., Le Strat, Y., Limosin, F., Dubertret, C., Gorwood, P., 2013. Prevalence of subthreshold hypomania and impact on internal validity of RCTs for major depressive disorder: results from a national epidemiological sample. PLoS One 8, 55448.

Hoertel, N., Franco, S., Wall, M.M., Oquendo, M.A., Kerridge, B.T., F, L., 2015. Mental disorders and risk of suicide attempt: a national prospective study. Mol. Psychiatr. 20, 718–726.

Hoertel, N., Chevance, A., Limosin, F., 2017. Inclusion and exclusion criteria and psychological research. In: Wenzel, A. (Ed.), The SAGE Encyclopedia of Abnormal and Clinical Psychology. A Sage Reference Publication. SAGE Reference, Los Angeles.

Hoertel, N., Rotenberg, L., Schuster, J.-P., Blanco, C., Lavaud, P., Hanon, C., Hozer, F., Teruel, E., Manetti, A., Costemale-Lacoste, J.-F., Seigneurie, A.-S., Limosin, F., 2021. Generalizability of pharmacologic and psychotherapy trial results for late-life unipolar depression. Aging Ment. Health 25, 367–377. https://doi.org/10.1080/13607863.2019.1691146.

Olekhnovitch, R., Hoertel, N., Limosin, F., Blanco, C., Olfson, M., Fagot-Campagna, A., Fossati, P., Haffen, E., Goldberg, M., Zins, M., Lemogne, C., 2020. Using filled prescription sequences to rank antidepressants according to their acceptability in the general population: the Constances cohort. J. Psychiatr. Res. 123, 72–80.

Ouazana-Vedrines, C., Lesuffleur, T., Denis, P., Hoertel, N., Olekhnovitch, R., Olfson, M., Blanco, C., Limosin, F., Rachas, A., Tuppin, P., Lemogne, C., 2022. Acceptability of second-line antidepressant medications using filled prescription sequences in a nationwide cohort study. J. Clin. Psychiatr. 83 https://doi.org/10.4088/JCP.21m14248.

Traitement par antidépresseurs - ANSM, 2019. Agence nationale de sécurité du médicament et des produits de santé.

Trivedi, M.H., Rush, A.J., Wisniewski, N., SR, A.A.W., D, R.L., 2006. Evaluation of outcomes with citalopram for depression using measurement-based care in STAR*D: implications for clinical practice. Am. J. Psychiatr. 163, 28–40.

Tuppin, P., Rudant, J., Constantinou, P., Gastaldi-Ménager, C., Rachas, A., de Roquefeuil, L., Maura, G., Caillol, H., Tajahmady, A., Coste, J., Gissot, C., Weill, A., Fagot-Campagna, A., 2017. Value of a national administrative database to guide public decisions: from the système national d'information interrégimes de l'Assurance Maladie (SNIIRAM) to the système national des données de santé (SNDS) in France. Rev. Epidémiol. Santé Publique 65, S149–S167. https://doi.org/10.1016/j.respe.2017.05.004.

Turecki, G., Brent, D.A., 2016. Suicide and suicidal behaviour. Lancet Lond Engl 387, 1227–1239.

Zimmerman, M., Mattia, J.I., Posternak, M.A., 2002. Are subjects in pharmacological treatment trials of depression representative of patients in routine clinical practice? Am. J. Psychiatr. 159, 469–473.