Author's response to reviews

Title: Duration and compliance with antidepressant treatment in immigrant and native-born populations in Spain: a four year follow-up descriptive study.

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Author's response to reviews: see over
Response to the reviewers and associate editor:

We have revised the original text and have incorporated the reviewers’ suggestions. We are most grateful for their comments, which have helped to improve the quality of the manuscript. Below, we outline the changes made in the text.

Comments to the Associate editor:
We agree that the original abstract did not provide an accurate summary of the contents of the discussion, because it simplified excessively the findings of the study and their implications. We have now rewritten the abstract and stress the complexity of the situation (pp 3-4)

Comments to Reviewer 1 (Sara Garfield):
Major 1) Please clarify the pharmacy system in Spain. Are dispensing records of all pharmacies in a region kept centrally so that it is possible to identify all dispensings for a patient that have been carried out in that region?

   Yes, the dispensing records of all the pharmacies in a region are kept centrally. On page 6 we have added information on the public pharmacy system in Spain.

Major 2) It appears that prescribing records were not checked and that it was assumed that the daily dose prescribed would be that defined by the Who Collaborating Centre for Drugs Statistics Methodology. This assumes that prescribing follows the Who recommendations. This should be acknowledged as a limitation and the authors should not refer to '80% of prescribed medication' on the top of page 9.

   We agree that the lack of prescribing records is a limitation of the study. We have now corrected the expression the reviewer mentioned (p. 9, Percentage of medication acquired) and refer to this point specifically in the section on limitations (p. 15)

Major 3) Another limitation is that the study would not identify patients who had never had their first prescription dispensed. This should be acknowledged.

   Linked to the previous point, and for the same reason, primary non-compliers (non-fillers) could not be evaluated. We have added this point in the section on limitations (page 15).
   Some of the studies consulted estimate primary non-compliance at around 4.2% (van Geffen E. et al. Initiation of antidepressant therapy: do patients follow the GP’s prescription? B J Gen Pract 2009; 59:81-87). That same study, performed in the Netherlands, shows that this situation is more common in non-Western immigrants; as a result, it would be very interesting to be able to compare this information in our environment. Unfortunately, at the time the study was performed, data on prescriptions were unavailable.
Major 4) Why was an adherence analysis carried out in which patients who acquired 100% of their medication were excluded (page 8)?

With “patients who acquired 100% of the treatment” we were referring to those who only acquired one package throughout the follow-up period, or single-fillers (1 package in 1 month = 100%). We understand that the wording was confusing, so we have changed it.

In fact we did perform the adherence analysis including those single-fillers, (37.7% of the total). The result was that 76.2% of the total sample was dispensed more than 80% of the required medication.

As the percentage of early drop-outs (within a month) was so high, we repeated the analysis excluding these patients, whose behaviour with regard to diagnosis and adherence may have been different (see the studies by van Geffen, E, van Dijk L and Hansen GH). The result presented corresponds to this subgroup.

To clarify this point, we now include the results of the two analyses (p. 9).

Minor 1) In the sentence 'patients who had not completed treatment by the end of the follow-up were considered as censored', please explain what is meant by 'considered as censored.'

From the statistical point of view a “censored” observation is one in which the information is incomplete. We considered the observations with incomplete information on treatment duration, due to the end of follow-up, as right censored. We have now modified the text for the sake of clarity; it is the treatment duration that is considered censored, not the patients (page 7)

Minor 2) In the second sentence of the discussion, please clarify the time period being referred to for the risk of abandoning treatment.

This is now clarified on page 10. The risk mentioned in the test is an adjusted Hazard Ratio estimated from the Cox model and is equivalent to the mean risk during the entire follow-up period.

Discretionary revision: Table 2 is difficult to follow as it stands.

We have retained table 2 because we think it provides interesting information, since it compares the profile of patients who only acquire one pack with the others as regards sex, age and origin. We have modified the figure legend for the sake of clarity. (page 20)

Comments to Reviewer 2 (Francisco Collazos):
1. Regarding the question posed by the authors, I think the difference between “compliance” and “adherence” is not clear enough. Actually, sometimes they are used “interchangeably”, leading to misunderstanding. It should be better conceptualized.

2. The method used to assess the adherence to antidepressant treatment is inferred from the amount/percentage of packs withdrawn after having been prescribed which is, at least in part, an indirect but imprecise way to evaluate adherence but not compliance.

   We have revised the use of the concepts of adherence and compliance (with the shades of meaning associated with the translation and use in Spanish of the word “compliance”, which is equivalent to “observancia” or “conformidad”). We do not find a clear agreement on their definition. Some authors distinguish between them according to the patient’s involvement in the treatment and prefer the use of the term “adherence”, while others include compliance in the overall concept of adherence when referring to taking the correct doses for the period of time stipulated. They are frequently used interchangeably in the bibliography.

   In this study, as in our previous publication in the general population (Serna MC et al. Duration and adherence of antidepressant treatment (2003-2007) based on prescription database. Eur Psychiatry 2010; 25(4):206-13) we used the term adherence to refer to the percentage of packs dispensed with respect to the total required (the Medication Possession Ratio). Compliance refers to good adherence when maintained for at least four months (in accordance with the treatment guides for depression), combining the concept of dose and adequate duration or persistence. We now clarify the distinction in the new version of the manuscript. (page 7)

4. The discussion should include some kind of critique of how the diagnosis of “depression” was achieved. From a culturally sensitive point of view, some comments about the lack of universalism of the DSM-IV diagnosis criteria should be included.

   This is an important point that we did not address in the original manuscript. In the discussion, in the section on the factors related to immigrant status, we have now added a paragraph linking the lower level of compliance with the possibility of diagnostic bias. Among other factors, this bias may arise from the particular expression of the symptoms in different cultures and from the doubts regarding the validity of the usual diagnostic instruments in some of these immigrant patients. (page 12)

5. Among the limitations of the work, some comments about the excessive generalization of the concept of “immigrants” should be included. I appreciate the efforts to incorporate some comments about the influence of culture on the notion of psychopharmacological treatments and so on, but the authors should have also comment on the difference that can be found not only between subjects from different cultural backgrounds but also between patients belonging to the same group.
We have added this point in the section on limitations. The great heterogeneity inside the immigrant population is well known and we are aware that the classification according to area of origin is not ideal. In fact, in Spain differences have been recorded in the use of certain health services by immigrants from the same background (Regidor E, 2008), indicating differences in the degree of cultural integration, length of residence, etc.

7. I think the title and abstract do not accurately convey what has been found, due to a misuse of the terms “adherence” instead of “compliance”.

We now use the term “compliance” in the title and abstract.