Reviewer's report

Title: Impact of asthma control on health care costs and quality of life in France and Spain

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Reviewer: Pinar Karaca-Mandic

Reviewer's report:

Second Review of “Impact of asthma control on health care costs and quality of life in France and Spain”

I believe the authors have responded to most of my comments, and the paper has improved.

Several of my original comments below may need to be addressed in more detail.

Original comment: Is it possible to control for asthma severity, and/or length of time since asthma diagnosis?

Authors added the “length of time since asthma diagnosis in the descriptive statistics (Table 1). As Table 1 shows, there is large variation across individuals in this variable. I think it is important to control for it in the multivariate models as well (Table 4 and Table 6), which I don’t think the authors did.

Original comment: Is there a way to assess whether the GPs who participated were similar to those who declined? In what ways were the participant GPs different than those who did not participate?

Authors now state in page 5: “In France, investigators were a sample of GPs selected from a representative panel of 1,200 general practitioners. The panel’s representativeness was established by three criteria: age, sex, and region of practice. The study was proposed to 750 GPs of this panel, randomly selected, and 230 agreed to participate”.

My original comment was not about the representativeness of the “panel”, but rather about the comparison of those who agreed to participate (230) relative to those who did not (520 of the 750 who did not). Given that authors designed the study sample, they must have at least the geographic region and gender information (and perhaps age as well) of the 520 who did not participate. It is important to at least illustrate that the participants were not very different than the non-participants to make generalizable and unbiased statements using results from this study.

My follow-up original comment thus remains not-answered as well: “Similar to the above comment, it is important to show in the paper how the GPs included in the study were similar to the general population of GPs in each country. Currently page 7 notes that GPs included in the study were similar to the general set of GPs in each county, but the results are not shown.”
Original comment: “Data analysis: Please explain why the data is weighted by the number of patients enrolled in each wave. In survey data weighting is typically important to produce nationally representative samples, or to adjust for non-response. It is not clear what the goal is here. Also, please provide tables that show whether/results are much different if the data are unweighted”

I am still not convinced why the data needs to be weighted to compensate the disproportionate number of observations in each quarterly wave. I did not see an argument or conceptual framework that claim the number of patients are spread equally across quarters of the year in real life. Especially for a disease like asthma, there is seasonality and weighting the data to impose equal number of observations in each wave digresses from that reality. At the minimum, authors should represent the unweighted versions of their main findings (all Tables preferably, but Tables 2, 3 and 4 at the minimum) to the editors to confirm the results don’t change much, or change in some expected direction, which they should discuss.

Original comment: The multivariate regression analyses currently control for sex, age, episodes of asthma exacerbation, prescription of a controller treatment and follow-up by a lung specialist. It is important that the authors also control for other co-morbid conditions. Table 1 shows co-morbid conditions (such as depression) vary significantly by the asthma control level.

The response letter states that the authors “added results of multivariate regression analysis for comorbidities”. I am not convinced, because they have collapsed multi-dimensional co-morbidities to a 1/0 variable of whether the patient has at least one co-morbidity (I think they mean other than asthma). Why not put separate indicators for all the co-morbidities they have?

Original comment: The Discussion section states that “the higher costs for patients with uncontrolled asthma were mainly due to costs of controller treatments and not to complications of asthma” (page 17). I do not believe that the authors have provided a statistical test or analysis to claim this. Is this based on Table 3 (which does provide components of the average costs, but does not test for differences)? Even then, Table 3 does not provide information on the components of “additional costs for patients with uncontrolled asthma” (relative to patients with controlled asthma).

Authors responded stating that detailed cost per level of control are presented in Table 3 and that these data show that the cost of controller treatments is the main driver of cost regardless of the control level.

This statement and the presentation on page 17 are somewhat misleading. First, it is correct that controller medications are large components of per-patient costs regardless of control level (51.8 euros for controlled, 69.9 for partially controlled, 95.1 for uncontrolled). Second it is correct that uncontrolled patients have higher costs (225.3 euros direct) relative to controlled (81.2 euros) and partially controlled (116.9 euros). However, these do not mean, as stated on page 17 that “In particular, the costs for patients with uncontrolled asthma were mainly due to costs of controller treatments and not to complications of asthma”. 
Please note that while hospitalization costs are very small (actually zero euros) for the controlled and partially controlled, they are 33.6 euros for the uncontrolled. Similarly, ER costs are $4 for the uncontrolled, while zero for controlled, and 1 euro for partially controlled. In other words, hospitalization and ER costs make up 17% of the direct cost per patient for the uncontrolled, and almost 0% for the other two groups. I am surprised authors do not point this out. More importantly, this means that uncontrolled group suffers from much larger hospitalization and ER costs relative to the other groups. In fact, the share of controller meds in direct costs is much lower for the uncontrolled group (42%) relative to uncontrolled (64%) and partially controlled (60%). This interpretation needs to be corrected/clarified in the text.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests