Author's response to reviews

Title: Occupation, smoking and chronic obstructive respiratory disorders in an industrial area of Catalonia, Spain

Authors:

Angeles Jaen (ajm.ceescat.germanstrias@gencat.net)
Jan-Paul Zock (jpzock@imim.es)
Manolis Kogevinas (kogevinas@imim.es)
Antonio Ferrer (AFERRER@CSPT.ES)
Albert Marin (amarin@cspt.es)

Version: 2 Date: 9 January 2006

Author's response to reviews: see over
Many thanks for the opportunity to revise our manuscript. In general, the reviewers’ comments helped us to improve the manuscript. Principally, we have clarified exposure assessment methodology, and have extended the discussion of the validity of exposure estimates, and the comparison with other studies evaluating the interaction between occupational exposures and smoking. The title now includes study type, and all required sections and information have been included.

Please find below our detailed reply to the reviewers’ comments, including how we handled with these comments in the revised manuscript.

Mark D Eisner:

General
The authors report an interesting study that evaluates an important area: the impact of occupational exposures on the risk of COPD. This is an important area because it has not been studied extensively and has major public health importance.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. The Methods do not describe adequate the questions used to assess exposure to dusts, fumes, and gases. This should be expanded and should include the exact text of the questions because exposure assessment is such a critical issue. Have these questions been used before or were they developed for the study?

We have extended and clarified the paragraph “Occupational exposure assessment” (page 9). We used questions on self-reported exposure to dusts, and gases/fumes from the ATS questionnaire, commonly used in several studies (among others, (Xu et all, Am Rev Respir Dis 1992; Korn et all, ARRD 1987; Krzyzanowski and Kauffmann, Int J Epidemiol 1988; Viegi et all, Eur Resp J 1991). We have included the exact (English) text of the questions, which had been translated and validated into Catalan (Castell et all, Ann Med (Barc) 1988) and into Spanish.

2. In terms of defining occupational exposure, the timing and duration of exposure is critical. COPD is a disease with a long latency period that takes many years to develop. Moreover, it presumably takes many years of exposure to develop.

   2A. Table 2 shows the relation between CURRENT occupation and COPD. This could be problematic if the current job does not reflect lifetime exposure. Longest held job would be a better exposure estimate for a disease like COPD that takes many years to develop. This is especially true for the pulmonary function impairment.

We agree with the reviewer that it would have been more adequate to use lifetime exposure (e.g., longest held job) if available. Nevertheless, experience with studies in
this area with the same age distribution suggested that for the vast majority of subjects current job reflects longest held job.

2B. Table 4. Here a more appropriate metric is used, i.e., "lifetime occupational exposure." However, as discussed in point 1, it is not clear how this was assessed. More detail in the Methods is needed. Was this a never vs. ever exposed assessment? If this "lifetime" exposure metric includes both longest and current jobs, it might "dilute" the estimate of association between exposure and COPD risk, as current jobs of shorter duration would not be expected to confer much risk of COPD (whereas longer held jobs with longer exposure duration might). Proposed solutions would be: look at exposure to longest held job or look at 15+ years of exposure (see 2C)

We only had current job title, but the two questions on exposures (dust, and gases/fumes) referred to lifetime exposures (and not related to job history). We have now clarified this. As mentioned above, in this community current job largely reflected longest held job. We agree, nevertheless, that to some extent misclassification occurred, and this could have diluted the estimates (or in other words, biased the association towards the null). This would have lead to underestimation and therefore conservative findings, but we could have missed potentially relevant effects.

2C. Pertaining to this point, Table 5 has the intriguing observation that 15+ years of exposure is associated with lower FEV1 etc when examined as continuous variables. One option to address point 2B would be to add the analysis of 15+years of exposure to Table 4, especially when evaluating the spirometric definition of COPD.

We agree that it would be interesting to stratify the exposed group by duration. This was, however, not done because of lack of statistical power. The spirometric definition of COPD was dichotomous, and therefore we focussed on the more powerful analysis of the continuous lung function value (FEV1 as in table 5).

3. The evidence is stronger for respiratory symptoms than the spirometric definition of COPD. This requires more discussion of why this is. Is it due to bias in the self-report items? Or is there something biological going on?

We have mentioned this in the discussion. Briefly, we speculate that symptoms of chronic bronchitis preceded measurable airflow chronic obstruction. The majority of our study population were younger than 50 years, and exposure duration was probably not long enough for airflow limitation to become apparent. This has also been found in other population-based studies (reference 8).

4. Table 2 excludes persons who are unemployed or retired from analysis. This could underestimate the association between work exposure and COPD if exposed subjects leave the workplace due to their COPD.
We agree that in this cross-sectional design with only current job, the possibility of health-related selection leading to a bias towards the null is possible. Nevertheless, this approach can be considered conservative and effects are not overestimated. In addition, in the complementary evaluation of self-reported exposures this problem did not occur (lifetime exposure). We have now included this issue in the discussion section.

4A. Were all subjects included in Table 4, regardless of work history?

Yes.

4B. Persons without history of labor force participation should be excluded as they have no exposure opportunity.

We were not able to identify subjects who never had worked, only those who were not working at the time of the study. In any case, it is true that those who had never worked, indeed had no “exposure opportunity”, but we judge it is reasonable to group them with “white collar workers” or others without any history of relevant occupational exposures.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

The choice of spirometric definition differs from the GOLD and should be justified. I actually think the authors chose a better definition than the GOLD which requires FEV1/FVC < 0.7 because of false positives among older persons (i.e., the ratio drops with normal ageing). But there needs to be some description in the Methods about why this was chosen.

In our analyses we evaluated lung function parameters continuously, and three different dichotomous definitions of obstruction. We have now included the reasoning for this in the Methods section making reference to the GOLD definitions.

Definition of chronic bronchitis is provided in the Tables only - it should be included in the Methods.

We used several items from the ATS questionnaire to evaluate chronic bronchitis. We have expanded this in Methods (paragraph “Definitions of COPD and chronic bronchitis” on pages 8-9).

Discretionary Revisions (which the author can choose to ignore)

Table 3 could be deleted - it did not add much for me.

We have kept this table, as we think it gives some insight in where these exposures were experienced for men and women. In most papers using self-reported exposure this type of information is not provided (not available) and remains always a sort of “black box”.

Hans Kromhout:
General
The paper addresses the relation between occupation, smoking and chronic obstructive respiratory disorders in the general population in an industrial area of Catalonia. The design of especially the occupational exposure assessment part of the study seems to be rather weak and given the lack of information provided very hard to judge. More detail is needed for this reviewer and the readership to be able to judge the results.

We have extended and clarified the paragraph “Occupational exposure assessment”. See also comment 1, reviewer 1.

It is also remarkable that the authors do not address the issue of self-reported exposure. An issue they recently discussed at length in a paper published earlier this year: "Comparison of self-reported occupational exposure with a job exposure matrix in an international community-based study on asthma. Am J Ind Med. 2005 May;47(5):434-42”.

We agree and have included more discussion on this issue, quoting this and another recent paper addressing the validity of self-reported exposure.

Detailed comments
Introduction, end of first paragraph
The authors should make a reference to a paper that appeared in this very journal a year ago "Meer G, Kerkhof M, Kromhout H, Schouten JP, Heederik D Environmental Health: A Global Access Science Source 2004, 3:6 (2 June 2004) in which the interaction of smoking and occupational exposure in relation to respiratory effects was addressed! In this study smoking doubled the risk of exposure to mineral dusts.

We agree and have included this paper in the discussion.

Methods
In the referenced paper a number of 642 men and women is mentioned. So, where do the additional 80 individuals come from?

In the referenced paper (Arch Bronconeumol 1999;35:122-8) the same number of 576 interviewed subjects was mentioned. The number of eligible subjects was 642 (and thus 66 refused to participate). The other 80 subjects (722-642) were not eligible (could not be localised or had deceased). We have clarified this now in the first paragraph of the methods.

Please add the year of interview. It seems that the interviews were done in the early nineties.

Agreed and included in Methods, under “Population and questionnaire”.
Indeed, the study was done in the early nineties (between June 1993 and December 1994).

No details at all are provided on the questions posed on job history and exposures. Please add details. At the bottom of page two all of a sudden the individuals seem to be classified according to current job! Was a complete job history recorded?
We have extended and clarified the paragraph “Occupational exposure assessment”. See also comment 1, reviewer 1.

Results
Third paragraph, table 2. Why were analyses not done stratified by smoking status?

We agree that it would be interesting to stratify by smoking status. This was, however, not done because of lack of statistical power given the small numbers of workers in specific industries in combination with the dichotomous outcomes. In table 4, where we used the more frequent (self-reported) lifetime occupational exposure, we were able to evaluate exposure-related effects in the different smoking groups.

Fourth paragraph: it sounds like that these individuals were asked to provide information on lifetime exposure to dust, fumes or gases (one or more than one question) and consequently were asked to provide information on the industry in which it occurred. This way of asking has a very large potential for misclassification of jobs. Individuals that claimed not to be exposed would not be considered to have been active in particular industries. The problem with self-reported exposure "symptomatic individuals over-reporting occupational exposure"(see the paper by de Vocht et al.), could have consequently resulted in a spurious result for a particular industry (e.g., textile industry in this case). An analysis by industry without having a complete job history of all individuals is in my opinion wrong and should be taken from the results (unless a complete job history exists for all participants).

We agree with the reviewer that there would have been a high probability of bias if we had classified the subjects according to the reported “exposed” job. Therefore, we focussed the analyses on (1) the reported exposure to dusts/gases/fumes regardless of in which job it had occurred; and (2) current industry. We did not collect complete job histories, but as mentioned above, in this community current job largely reflected longest held job. This is similar as used in other community-based studies (e.g., the European Community Respiratory Health Survey). Nevertheless, we have included more discussion about his. Briefly, to some extent misclassification will have occurred, in the direction that symptomatic workers leave certain industries. This probably has diluted the estimates (biased the association towards the null) and led to an underestimation of the magnitude of the effects. See also comment 2A, reviewer 1.

Discussion
The presented results should be discussed in relation to results published previously by de Meer et al. 2004, who did find an interaction between smoking and occupational exposure for chronic bronchitis.

OK, done

Third paragraph, the impact of the way job history was assessed (via a subjective estimate of occupational exposure) should be addressed.
We did not use job history assessed via the self-reported exposure in the analyses (see earlier comment). Nevertheless, we have included two paragraphs in the discussion section on limitations of the exposure assessment strategy.

Third paragraph, the authors indicate that this study was not aimed specifically on respiratory disease, but fail to reveal where it was aimed at.

*It said: “…was not aimed specifically to establish the occupational role in respiratory diseases…”*. Thus, it was aimed on respiratory disease, but the objectives included the evaluation of several risk factors on the prevalence of obstructive lung disease in this particular area.

Third paragraph, population specific JEM: why wasn't a similar approach chosen as by Post et al. (ref 19) to create a less-biased PSJEM? Probably because no complete job history was taken?

*Basically because of the limited number of (exposed) individuals for each job title.*

*Indeed, we had reported lifetime reported exposures, but only current job title.*

Page 7, the discussion here does not address an interaction between occupational exposure and smoking and omits the results of the study by de Meer et al. Given the large difference in smoking habits between men and women a further stratification is by sex is preferred above an adjustment for sex. This would allow more insight in the unexpected results.

*We agree that this would be preferred, however the number of symptomatics in certain “cells” would remain very small. Thus, in choosing between stratification by smoking status or by sex, we have chosen to present the table stratified by smoking status. We have now included the results after stratification by sex in the text of the results.*

The sentence "not clearly demonstrated interaction between smoking and occupational exposures in the relationship with COPD" should be revised given the results described by de Meer et al.

*The fact that one study showed this interaction does not provide sufficient evidence to speak of a clearly demonstrated effect.*

Why do the authors think that differential misclassification of occupational exposure among non-smokers is unlikely? Do they have proof of this?

*We stated that “…differential misclassification of occupational exposure … among non-smokers compared to smokers is unlikely”. There is, as expected by the reviewer, no direct proof for this (in fact, to our knowledge very few studies have evaluated this). Nevertheless, we have weakened this statement since it is not impossible that smokers tend to report less occupational exposures than non-smokers that have similar jobs.*

Final paragraph: please add "with better and more up-to-date assessment of occupational exposure" to the sentence starting with "Longitudinal...."
OK, done