Author's response to reviews

Title: Inadequate glucose control in type 2 diabetes is associated with impaired lung function and systemic inflammation: a cross-sectional study

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Version: 3 Date: 5 June 2010

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Title: Inadequate glucose control in type 2 diabetes is associated with impaired lung function and systemic inflammation: a cross-sectional study

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Date for version No. 3: 05-Jun-2010
Dear Editors:

Please find attached our revised manuscript entitled “Inadequate glucose control in type 2 diabetes is associated with impaired lung function and systemic inflammation: a cross-sectional study” for consideration of publication in *BMC Pulmonary Medicine*.

We would like to thank both reviewers for their additional comments and critique. The revised manuscript attempts to address the remaining comments from reviewers. We think that the revised manuscript is now much improved in clarity due to their observations. We have copyedited the manuscript to improve the style of written English. Below please find our point by point answers to the observations.

This study was made possible by funding from COLCIENCIAS, Colombia, Code 2239-04-16300. No part of this work has been previously published; an e-presentation was presented at the European Respiratory Society 19th annual congress, Vienna, September 2009. No part of this manuscript is under consideration in any other journals. All of the authors have reviewed the manuscript and approve of its content. As described in the manuscript, all authors have contributed significantly to the manuscript. No author discloses any conflict of interest that relates to this work.

We thank you in advance for your consideration of this revised manuscript and for the length of time provided to us to revise it.

Respectfully,

Rodolfo J Dennis, MD MSc
Head, Departments of Research and Medicine, Fundación Cardioinfantil
Professor of Medicine, Universidad Javeriana
Bogota, Colombia
Reviewer Prof. Davis:

- The decimal points should be represented by full stops not commas.
  
  Reply: this has been done now, thanks.

- Discussion, 2\textsuperscript{nd} paragraph: “can´t” should be spelled as “cannot”.
  
  Reply: this has been done now, thanks.

- Acknowledgements: “y” should be replaced by “and”.
  
  Reply: this has been done now, thanks.

Reviewer Prof. Savage:

- Re. Prof. Davis Comment: Can the authors add the inflammation markers to the multiple linear regression models to see if, after adjusting for age, sex, height, smoking history, and HbA1c, any of them add significantly to the models?
  
  Reply: We have done this now. Please see in red changes in mean residual lung function when the five inflammation markers are included in the MLR models.

<table>
<thead>
<tr>
<th>MEAN RESIDUAL PULMONARY FUNCTION</th>
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<table>
<thead>
<tr>
<th></th>
<th>INADEQUATE CONTROL</th>
<th>ADEQUATE CONTROL</th>
<th>DIFFERENCE IN MEAN RESIDUALS</th>
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<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean</td>
<td>N</td>
</tr>
<tr>
<td>rFEV\textsubscript{1}</td>
<td>352</td>
<td>-164.9</td>
<td>143</td>
</tr>
<tr>
<td>rFEV\textsubscript{2}</td>
<td>345</td>
<td>-160.19</td>
<td>142</td>
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<tr>
<td>rFVC</td>
<td>352</td>
<td>-247.3</td>
<td>143</td>
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<tr>
<td>rFVC</td>
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<tr>
<td>rFEV\textsubscript{1}/FVC</td>
<td>352</td>
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<td>143</td>
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<tr>
<td>rFEV\textsubscript{2}/FVC</td>
<td>345</td>
<td>1.021</td>
<td>142</td>
</tr>
</tbody>
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Differences in subjects included in the analyses represent missing values. Our conclusion is that inclusion of all five inflammatory markers to the models did not significantly change results. The only inflammatory marker that was significantly
(but weakly) associated with residual lung function, after adjustment for all other variables in the models, was C-RP (p=0.04). To reflect this, we have decided to modify the following sentences in the manuscript:

1. In the methods section (page 6, second paragraph): “We also used least-squares multiple linear regression models to further adjust mean residual values for smoking history (current, past, none), body mass index, exposure to indoor wood-smoke inhalation, to assess the significance of interaction terms, and the inclusion of inflammation markers.”

2. In the results section (page 7, 2nd paragraph): “The inclusion of all five inflammation markers to the models did not significantly change results. The only marker significantly associated with residual lung function, after adjustment for all other variables in the models, was C-RP (p=0.04).”

- ... it may be worthwhile to also note that some patients may be optimally controlled at slightly higher levels of HbA1c levels. This could be relevant in older patients with significant lung disease.

Reply: We agree with this suggestion. We have now modified the pertinent paragraph in the methods section (page 6, first paragraph) to read as: “We selected this cutoff point a priori because it is usually selected in clinical practice to discriminate between appropriate and inappropriate control (11), although some patients may be optimally controlled at slightly higher HbA1c values.”