

## Peer Review File

Article information: <https://dx.doi.org/10.21037/jtd-22-1857>

### Reviewer A

I have no major concerns. Only some minor suggestions:

Reply: Thank you very much for your constructive and positive comments.

Comment 1: The figures are difficult to read, perhaps need to increase quality/resolution

Reply1: Thank you. The figure is now submitted as a separate TIEF file.

Comment 2: Is there any data on morphine prescription as well as codeine? Perhaps the authors could describe in the discussion why physicians might not want to prescribe morphine compared to codeine (54% is quite high), even though the guidelines suggest morphine but not codeine? Is there stigma? Cost? Fear?

Reply2: Thanks. However, morphine prescription is not allowed for cough treatment in Korea.

Changes in the text: We added a sentence to introduce this issue (see Page 6, line 106-108).

Comment 3: The authors should mention in the discussion that physicians need to use better tools to assess efficacy because almost 40% there is no documentation of improvement.

Reply3: We agree and further highlighted the message in the conclusion. The need for PRO has already been mentioned in Page 16, Line 303-305. However, we have added your comments to the conclusions, on the need for integrating PROs and decision protocols to increase the utility of real-world data.

Changes in the text: We added a sentence to address this issue (see Page 18, line 345-349).

Comment 4: I noticed that 173 patients (14%) had prescription for 8-52 weeks. i.e. they used for longer than 8 weeks. I presume this is because they benefitted from it. However, the pie chart suggests 40% improved - do you think this is an over-estimate because if 40% improved, then you might expect more people (closer to 40%) to be taking the medication beyond 8 weeks.

Reply4: Thank you. We looked into the data and found that 49 of 173 patients (28.3%) were documented as “not improved”, and suppose that the codeine prescription might have been inevitable as there was no alternative drug or that physicians may not have been well aware of usually rapid codeine treatment responses.

□ Changes in the text: We added a sentence to address this issue (see Page 17, line 309-313).

Comment 5: The cumulative yearly dose is 1857mg, which means that patients are not

taking the codeine on a regular basis. If you assume 2 tablets/day (total 30mg), then this equates to 61.9 days, - so about 25% of the year. Please clarify this is correct, i.e. patients are likely taking codeine only intermittently?

Reply5: Thanks. Yes, most patients did not take codeine regularly. The mean number of days with codeine prescription was  $51.4 \pm 66.8$  days.

Changes in the text: We added a sentence to address this issue (see Page 17, line 314-317).

## **Reviewer B**

This is an interesting study regarding chronic cough. Whilst the study has limitations, this study is well carried out and the manuscript is well written.

Reply: Thank you very much for your constructive comments.

My specific comments are as below.

Major question:

1. In Line 223-225, 265-267.

You mentioned that several patient characteristics such as older age, longer cough duration, female sex, less smoking history, or more throat abnormal sensation but less dyspnea were associated with codeine prescription and duration.

2. Of factors associated with codeine therapy, proportions of females were higher in both codeine groups (prescribed for  $\leq 8$  wks and  $> 8$  wks) than in the non-codeine group. However, in the logistic regression, neither the codeine  $\leq 8$  wks group nor the  $> 8$  wks group showed statistical significance compared to the non-prescription group.

3. Based on these findings, you need to mull over before making a conclusion, whether female sex is factors with codeine prescription. Please discuss about this issue.

Reply1: Thank you The discussion and conclusions were modified to correct it.

Changes in the text: We have modified our text as advised (see Page 16, line 282-284, line 289-290, Page 18, line 337-339)

Minor question:

1. I think it's better to clarify T2 on table 2. You need to add a brief definition of T2 in table2 footnote.

Reply1: Thanks. We have added the definition.

Changes in the text: We added a sentence to address this issue (see Page 23, line 440-442).

2. In table 2, older age longer cough duration, non-smoker, and throat abnormal sensation were associated with longer codeine prescription.

3. In a categorical variable, the item in parentheses means the object to be compared. Hence, smoking history should be corrected as follows: smoking history (no vs yes) or non-smoking history (yes vs no). It might be better to make them clearer

Reply3: Thank you. We agree and have made the revisions accordingly.

Changes in the text: We changed to “smoking history (no vs yes)” in table 2 (see Page 24, line 444, Table 2).

4. In table 1 p value  $>$ ; correct p in italics.

Reply4: Thank you. We agree and have made the revisions accordingly.

Changes in the text: We changed to “p value” (see Page 22, line 438, Table 1).

5. You have fully explained changes after codeine prescription in the manuscript. I suggest to delete the figure 4.

Reply5: Thanks. We agree and have deleted it.

Changes in the text: We deleted the figure 4. (see Page 14, line 257).