Author's response to reviews

Title: Impact of Chronic Obstructive Pulmonary Diseases clinical pathway on clinical outcomes : A Case Study In A Teaching Hospital In Malaysia

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THE EDITOR

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Dear Editor,

Thank you very much for the excellent review comments. We are happy to address each comment with scientific justification. One or two queries related to the study matters may not have been addressed as the study is already over and we promise to incorporate such in our future endeavor.

I am sure you will accept the revised manuscript with good comments.

Once again, I should thank you for the valuable comments.

Waiting for your kind decision.

Thank you,

Warm regards

Aniza
ANSWERS TO REVIEWERS’ COMMENTS

MANUSCRIPT: IMPACT ON OBSTRUCTIVE PULMONARY DISEASE CLINICAL PATHWAY ON CLINICAL PATHWAY OUTCOMES: A CASE STUDY IN A TEACHING HOSPITAL IN MALAYSIA (8310964526079700)

Editorial’s comment

1. On the ethic approval

Answer – Page 3

All patients gave written informed consent and the study was approved by the Research and Ethics Committee of the Faculty of Medicine, Universiti Kebangsaan Malaysia (FF-154-2008).

Reviewer Comments

A. REVIEWER : Kris Vanhaecht

Comment Overall

1. Should definitely be revised by experienced writer

Answer:

Yes the manuscript has been reviewed by experienced writer.

Answer

The abstract has been improved and we have re-write the abstract.

**Background:** Exacerbations, a leading cause of hospitalization in patients with chronic obstructive pulmonary disease (COPD), affect the quality of life and prognosis. Treatment recommendations as provided in the evidence-based guidelines are not consistently followed, partly due to absence of simplified task-oriented approach to care. In this study, we describe the development and implementation of a clinical pathway (CP) and evaluate its effectiveness in the management of COPD exacerbation.

**Methods:** We developed a CP and evaluated its effectiveness in a non-randomized prospective study with historical controls on patients admitted for exacerbation of COPD to Universiti Kebangsaan Malaysia Medical Centre (UKMMC). Consecutive patients who were admitted between June 2009 and December 2010 were prospectively recruited to be in the CP group. Non-CP historical controls were obtained from case records of patients admitted between January 2008 and January 2009. Clinical outcomes were evaluated by comparing the length of stay (LOS), complication rates, readmissions, and mortality rates.

**Results:** Ninety-five patients were recruited in the CP group and 98 patients were included in the non-CP historical group. Both groups were comparable with no significant differences in age, sex and severity of COPD (p=0.641). For clinical outcome measures, patients in the CP group had shorter length of stay than the non-CP group (median (IQR): 5 (4-7) days versus 7 (7-9) days, p<0.001) and 24.1% less complications (14.7% versus 38.8%, p <0.001). We did not find any significant differences in readmission and mortality rates.

**Conclusion:** The usage of CP –reduced the length of stay and complication rates of patients hospitalized for acute exacerbation of COPD.

**Keywords:** chronic obstructive pulmonary disease, clinical pathway, clinical outcomes, length of stay
3. References:

The references have been corrected.


4. Abbreviations

All the abbreviations were written in full words.

Answer: Page 7

Noninvasive positive pressure ventilation (NIPPV)

Invasive positive pressure ventilation (IPPV)

Hospital acquired pneumonia (HAP)

Acute coronary syndrome (ACS)

Congestive cardiac failure (CCF)

Acute renal failure (ARF)

Upper gastrointestinal bleeding (UGIB)

Urinary tract infection (UTI)

5. Tables

The unit in each variables were corrected in Table 3, 4, 5 and 6.

Table 4, 5 and 6 were merged as advised.
METHODS

1. Only matched for severity? Why not for age and gender?

Answer - Page 4

The case and control matched for age, gender and severity.

2. History effect

Answer – page 4

The retrospective group of patients in this study did not differ in terms of medication usage. We collected data only from one year prior to this study. This was to ensure that the drugs available for treatment of COPD were the same in the two groups. We also took into account the pulmonary rehabilitation programme in our centre which was launched 3 years ago.

3. Inclusion criteria of 12 years?

Answer – Page 3

We included adult patients aged 40 years and above

Why this specific exclusion criteria (for instance LTOT >15day, why these specific comobidities)

Answer - Page 3

Patients with LTOT were excluded as co-existing cor pulmonale would be a confounding factor that could prolong the length of hospitalization.

4. Who was involved in development process?

Answer - Page 4

This included the respiratory consultant and specialist, medical officers, the head nurse, staff nurses, pharmacist, dietitian, physiotherapist, and social worker.
5. Develop based on evidence and clinical practice guideline (CPG)

Answer - Page 4

The clinical management of COPD was based on GOLD and NICE guidelines, as well as local best practices, but team members were allowed to deviate from the pathway depending on the clinical progress of the patient. As a baseline, the expected length of stay was set at 5 days.

6. How was CP implemented?

Answer - Page 4 and 5

In the third phase, we implemented the COPD CP in the medical wards concurrent with the start of the prospective study (June 2009). For the implementation, patients admitted to the medical wards with a diagnosis of exacerbation of COPD were screened within 24 hours of admission and managed according to the COPD CP if the patients fulfilled the inclusion/exclusion criteria. The CP worksheets were attached to the patient’s records, and to ensure compliance to the CP, we designated one study investigator (medical officer) to review the clinical pathway records daily and prompt the team to follow the specific goals set for each day. Each step was documented in the COPD CP form.

The single investigator (medical officer) performed daily ward rounds to enforce compliance on the usage of the pathway. The health care providers were given encouragement and reinforcement to implement the clinical pathway. Additional educational activities were also given to address specific issues raised during the implementation.
7. Why was a pathway chosen as improvement method?

Answer – Page 1 and 2

Existing clinical guidelines for COPD provide evidence-based and consensus-derived statements of optimal care for patients with COPD, such guidelines do not provide an organizational framework for managing patients within a hospital setting, resulting in inconsistent application of clinical plans and variable patient outcomes. COPD CP has been successfully implemented in developed countries and previous studies suggest that its usage results in improved clinical outcomes. The adoption of COPD CP in Asia, however, has lagged behind and evidence of its effectiveness in developing countries is less clear.

We have also previously shown that the compliance to our national guideline of COPD management was only 60% for the treatment of moderate to severe stable COPD. Among the reasons for failure to adhere to the treatment recommendations include lack of awareness of the COPD guidelines particularly among the non-respiratory and primary care physicians, and absence of simplified task-oriented approach to care. Thus, there is a critical need to address this increasing gap between the guidelines and clinical practices, particularly in the hospitals of developing countries, by implementing and evaluating clinical care practices tailored to local settings. Clinical pathways can provide a link between establishing clinical guidelines and practicing them.

8. What are the characteristics of the intervention?

Answer – Page 4

The paper-based pathway for COPD was developed by Universiti Kebangsaan Malaysia Medical Centre (UKMMC) in collaboration with United Nations University International Institute For Global Health (UNU-IIGH).
From 612 identified patients with COPD exacerbation to about 200 included patients.

Answer - Page 6

The non-cp group was recruited retrospectively. This was done by reviewing case reports identified with the diagnosis exacerbation of COPD. These records were made available to us by the record office of UKMMC. Due to the retrospective nature of this part of the study, there were some case notes which were incomplete in documentation and we were unable to use them.

The case notes of 281 COPD patients admitted between January 2008 and January 2009 were reviewed; Case notes of 160 patients had the required and completed documentation, and of these, 98 patients fulfilled the criteria and were included in the control group (61%).

10. How were data collected for both groups? Both patient record analyses? Were surveys used?

Answer – page 4 and 5

We designated one study investigator (medical officer) to review the clinical pathway records daily and prompt the team to follow the specific goals set for each day. Each step was documented in the COPD CP form.

In both groups all the data were documented and collected by medical officers who were in charged in the medical wards. Statistical comparisons were performed using Statistical Software Statistical Product and Services (SPSS) software package (version 19) using appropriate statistical tests at a significance level of 95%.

The prospective CP group data was not just a survey, there was intervention done.

11. Outcomes: readmission rate on 30 days, 6 months? What was the follow up interval?

Answer Page 5

Re-admission: 30 days

The interval of follow up was 30 days and this was done via a telephone call.
12. Were consecutive patients included?

Included.

DISCUSSION

1. First three paragraphs should be in background.

The sentences have been moved to introduction.

2. Next six paragraphs were not about the study.. not so relevant for this study on the impact of a care pathway.

The sentences have been deleted.

3. Discussion on optimal duration; depends on context (organization of home care etc)

Answer: Page 10

There is no optimal duration of hospitalization in patients with COPD exacerbation in view of insufficient data. Study on necessary length of hospital stay for COPD was done by Mushlin et al (1991) in which 6.9 days is considered averaged LOS meanwhile, our COPD populations (non-CP and CP groups) mean LOS was 6.56 days. We developed a 5-day COPD CP based on the recommended average use of antibiotic (3 to 7 days) from GOLD guidelines. Our CP was similar to COPD CP from the Grey Bruce Health Network in this aspect (approximately 5 days target). From this study it showed CP can help in reducing length of stay and indirectly reducing cost of care.

4. Different in readmission and mortality : impact of commodities?

Answer – page 11

There was no significant association between mortality and the non-CP and CP group. Our finding was similar to Santamaria et al study. There were two deaths in the CP group. Both patients were in stage IV COPD. One was a 70-year old male ex-smoker who had hypertension and ischaemic heart disease. The second subject was an 81-year old male who had no co-morbidities. Both deaths were associated with COPD exacerbation.
Reason for readmission.

Answer – page 11

The number of readmissions was similar in both groups. We found no significant difference in the number of unplanned readmissions between the two groups. The main reason for readmission in this study was shortness of breath. The CP group also had longer readmission interval after discharge. Our findings were consistent with the study by Santamaria et al.

5. Was the pathway responsible for the improved results? Can the authors describe the relation between their intervention and the outcomes where they expected or not.

Answer

Yes, the pathway was responsible for the improved results. The outcomes of the study were resulted from the intervention that successfully reduced the length of stay and the shorter LOS in CP group. No significant difference found on readmission rate in both group.

6. Additional information on the continuous follow up would be interesting.

Yes agree.
B. REVIEWER : EUGENE HAYDN WALTERS

Overview

1. I enjoyed reading this paper, although the English language style and grammar (which started well), progressively declined in quality and needs lots of editing.

Major issues:

2. Although I can understand the difficulties in undertaking an formal RCT of this sort of intervention a single institution, an historically controlled study has the inherent problem of potential changes over time in the nature of the study population. This seems to have occurred here with significant differences over time in active smoking, education status and weight profiles, for example. Unfortunately, these factors could well influence the very outcomes of interest.

Answer: Page 9

The CP group had their smoking history taken with the knowledge that they were participating in a clinical trial. There is a possibility that they may have under reported their years of smoking. The historical controls from case notes had smoking history taken and verified over a few entries. This may have been more reflective of an accurate number of pack years and smoking status. However there was no significant association between smoking history and length of stay in the two groups. The study also found no significant association between smoking history and complication.

3. Is not the age spectrum for inclusion rather bizarre for a study of smoking-related COPD, even in Malaysia? I would have thought that age 50 or 55 and above would be necessary to try and limit to non-asthma and non-chronic sepsis etc.

Answer: Page 3

Inclusion criteria, patients with COPD diagnosis aged 40 years and above.
4. Although this paper is about an intervention of a new specific clinical pathway, exactly what this consists of is not detailed nor even the principles outlined. Was the decrease in Type 2 respiratory failure, for example due to better oxygen management?

Answer:

We did not look at the oxygen therapy in detailed in the non-cp group. We also did not compare the differences in oxygen therapy management between the groups. It is possible that the oxygen intervention in the CP group was implemented in a more guided manner. This may explain the decrease in type 2 respiratory failures seen in this group.

5. An important aspect of the discussion relates to cultural resistance to change, but what the local experience was of this needs to be detailed and indeed should be very interesting and important part of the paper for other centers in Asia and beyond to have a reference and learning point.

Answer: Page 11

We encountered minimal initial resistance to the clinical pathway. However, this was not a major issue as we designated one person to follow and ensure the adherence to the COPD CP in the medical wards. This lack of acceptance resulted in some deviation from the clinical pathway.

6. Although it must have been done, I assume, since the details are given on COPD GOLD severity, details of spirometry per se as an inclusion criterion are not given, but should be.

Answer – Page 3 and 4

Besides the clinical diagnosis by the attending physician, we required evidence of spirometry readings consistent with COPD: obstructive lung disease FEV1/FVC <70% with minimal reversibility (<12%), together with a significant smoking history. In our teaching hospital, exacerbation of COPD was managed according to the GOLD [2,8] and Malaysian Clinical Practice Guidelines (CPG) [1].
Conclusion:
I wonder if this paper would not be better as a more descriptive essay on the process of developing clinical pathway guidelines in a developing Asian country, with more emphasis on change strategies, the nature and quantity of resistance to uptake, and patient/junior doctor acceptability etc, rather than this attempt to try and prove a clinical benefit which is always difficult and here not totally convincing. A cost analysis would be worthwhile as part of that, albeit in a fairly general way as the clinical benefit side would not be fully available...but whether this strategy had any inherent cost risks could be included.

Answer - Page 11 and 12

We are currently evaluating the effectiveness of the CP from this current data from a cost analysis point of view (health economics experts). This will be published upon completion of analysis.
C. REVIEWER: CARL LLOR

Reviewer's report:

MAJOR COMPULSORY REVISIONS:

1. First of all, not all the readers are used to the term ‘clinical pathway’ (CP) and this should be explained more in detail. Table 1, explaining the phases of the development of CP, is clearly insufficient.

Answer: Page 4 and 5

Development and implementation of the COPD clinical pathway: The paper-based pathway for COPD was developed by Universiti Kebangsaan Malaysia Medical Centre (UKMMC) in collaboration with United Nations University International Institute For Global Health (UNU-IIGH). The development was conducted in workshops involving the Respiratory Unit of UKMMC, UNU-IIGH, and the Department of Public Health. In the first phase, we determined the roles of the healthcare teams involved in the management of a COPD patient. This included the respiratory consultant and specialist, medical officers, the head nurse, staff nurses, pharmacist, dietitian, physiotherapist, and social worker. The clinical management of COPD was based on GOLD and NICE guidelines, as well as local best practices, but team members were allowed to deviate from the pathway depending on the clinical progress of the patient. As a baseline, the expected length of stay was set at 5 days.

In the second phase, a pilot implementation was carried out to evaluate the feasibility of the COPD clinical pathway, and to modify the pathway accordingly. In the third phase, we implemented the COPD CP in the medical wards concurrent with the start of the prospective study (June 2009). For the implementation, patients admitted to the medical wards with a diagnosis of exacerbation of COPD were screened within 24 hours of admission and managed according to the COPD CP if the patients fulfilled the inclusion/exclusion criteria. The CP worksheets were attached to the patient’s records, and to ensure compliance to the CP, we designated one study investigator (medical officer) to review the clinical pathway.
records daily and prompt the team to follow the specific goals set for each day. Each step was documented in the COPD CP form.

**Evaluation of COPD CP:** The evaluation focused mainly on the care process and outcomes. The variables that were measured for evaluation were length of hospital stay (LOS), complications or morbidity, readmission and mortality. Confounders of LOS would include smoking status of patient, hospital acquired infections, and worsening of co-morbidities.

2. When you explain in the Introduction that CP translates evidence based medicine into a clinical setting, you should also explain how patients assigned to non-CP were treated.

Answer – Page 3 and 4

The non-CP group of COPD patients were taken retrospectively by looking at data. These patients were managed following the GOLD guidelines and the Malaysian CPG. Records were looked as far back as 1 year. This was to ensure that treatment regime and the pulmonary rehabilitation programme was the same in the two groups.

3. In addition, since the authors compared different outcomes between COPD patients assigned to CP implementation and those without, the compliance to this CP implementation should be described more precisely.

Answer: Page 11

The single investigator (medical officer) performed daily ward rounds to enforce compliance on the usage of the pathway. The health care providers were given encouragement and reinforcement to implement the clinical pathway. Additional educational activities were also given to address specific issues raised during the implementation.

We encountered minimal initial resistance to the clinical pathway. However, this was not a major issue. This lack of acceptance resulted in some deviation from the clinical pathway. Several batches of medical officers and house officers were rotated into the medical unit during the duration of this study. Information on the COPD clinical pathway may not be well
disseminated. Our briefing sessions should have been more regular to improve the compliance and adherence to the CP.

4. Secondly, the authors use the terms ‘intervention’ and ‘control’ several times when this study is actually a before and after study (before: non CP, and after: CP). I am particularly concerned about the bias of patient selection and design. The authors use a retrospective analysis for patients assigned to ‘non-CP’ and a prospective analysis for those assigned to ‘CP’. The bias could be important for the non-CP, since out of 281 cases admitted, only 160 were available (please state the reasons for this high drop-out rate) and only 98 patients fulfilled the inclusion and exclusion criteria.

Answer : Page 6

The non-cp group was recruited retrospectively. This was done by reviewing case reports identified with the diagnosis exacerbation of COPD. These records were made available to us by the record office of UKMMC. Due to the retrospective nature of this part of the study, there were some case notes which were incomplete in documentation and we were unable to use them.

5.However, in the second paragraph of the Methods section the authors state that non-CP patients were matched for diagnosis and severity. If only patients with COPD were supposed to be recruited I do not understand why these patients were matched for diagnosis (are you referring to concomitant comorbidities?). And how did you define the severity? Please describe.

Answer: Page 4

They were matched for age, gender and severity with those in the clinical pathway group and the non clinical pathway group serves as a comparison group for evaluation.

We used the GOLD guidelines to classify severity of COPD patients in our study. This is based on the percentage predicted post bronchodilator FEV1.
### Stage of COPD

<table>
<thead>
<tr>
<th>Stage of COPD</th>
<th>Percentage predicted FEV1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1</td>
<td>&gt; Or = 80%</td>
</tr>
<tr>
<td>Stage 2</td>
<td>50-80%</td>
</tr>
<tr>
<td>Stage 3</td>
<td>30-49</td>
</tr>
<tr>
<td>Stage 4</td>
<td>&lt;30%</td>
</tr>
</tbody>
</table>

Reference: GOLD guidelines

6. Thirdly, since it was a before-and-after design, the authors should also describe confounders or variables that could explain the improvement in the two outcome variables (length of stay and complications) other than the clinical pathway. This is an important issue because no randomization was used in this study. The study design used by the authors is perhaps not appropriate to address the objectives of the study and this should be commented in depth in the Discussion section.

Answer: page 5

Confounders of LOS would include smoking status of patient, hospital acquired infections, worsening of comorbidities ie diabetes, hypertension.

Answer: Page 9

It is unfortunate that we failed to match this factor between the groups. The CP group had their smoking history taken with the knowledge that they were participating in a clinical trial. There is a possibility that they may have under reported their years of smoking. The historical controls from case notes had smoking history taken and verified over a few entries. This may have been more reflective of an accurate number of pack years and smoking status. However there was no significant association between smoking history and length of stay in the two groups. The study also found no significant association between smoking history and complication.

**MINOR ESSENTIAL REVISIONS:**
1. How was the diagnosis of COPD defined? When talking about the inclusion criteria you say you included adults over 12 yr. If we are talking about COPD this age seems inappropriate. You should also define acute exacerbations of COPD. Please describe both diseases more clearly.

Answer: Page 3

For this study, an acute exacerbation of COPD (AECOPD) was defined as an acute worsening of dyspnoea, cough or change in quality or quantity of sputum requiring a change of regular medication. These symptoms should have been present for at least 3 days.

We included adult patients aged 40 years and above with a diagnosis of exacerbation of COPD.

In the retrospective (non-CP) and the CP group, the diagnosis of COPD was based on historical data. Our diagnosis of COPD is made using the spirometry data confirming an obstructive lung disease FEV1/FVC <70 with minimal reversibility (<12%) together with a significant smoking history.

2. Different acronyms appear in the text without having first been explained. For instance, UKMMC in the Abstract should be defined, as should several complications such as NIPPV, IPPC, CCF, UGIB, ARF and this is also valid for table 4. In addition, CP should be defined the first time that it appears in the text (Introduction).

Answer: Page 7

The abbreviations were written in full.

Noninvasive positive pressure ventilation (NIPPV)

Invasive positive pressure ventilation (IPPV)

Hospital acquired pneumonia (HAP).

Acute coronary syndrome (ACS)
Congestive cardiac failure (CCF)

Acute renal failure (ARF)

Upper gastrointestinal bleeding (UGIB)

Urinary tract infection (UTI)

3. Page 2, Abstract, in the beginning of the conclusions sentence, there is a spelling mistake. Please correct.

Answer: correction done.

4. Page 5, in the first line of the last paragraph, there is a spelling mistake. Please correct.

Answer: correction done

5. Some tables are not necessary. For instance, table 6 describing the mortality rates in both groups is described in the text. Please delete it and put the p-value in the text.

Answer: Page 7

Correction done