Author's response to reviews

Title: Optimization of the diagnostic work-up in patients with suspected obstructive lung disease.

Authors:

Frank J Visser (f.visser@cwz.nl)
Milena JMM van der Vegt (milena.roorda@hetnet.nl)
Gert Jan van der Wilt (G.vanderWilt@mta.umcn.nl)
Julius P Janssen (j.janssen@cwz.nl)

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Author's response to reviews:

Dear Editor-in-Chief,

The enclosed manuscript entitled “Optimization of the diagnostic work-up in patients with suspected obstructive lung disease. A randomised controlled trial comparing protocol-driven test-ordering with usual care.” has been resubmitted for publication in your journal.

In our previous submission (MS: 1699181679332114) you stated: If at some stage you are able to fully address all of the referees' concerns, you may wish to consider submitting a new manuscript to BMC Pulmonary Medicine. If you are able to do this, a full covering letter, explaining the revisions made, should accompany the submission.

In this revised manuscript, we have changed the text according to the suggestions of the 3 reviewers. We hope it is now ready for publication.

The manuscript is not under simultaneous consideration by any other journal.

Thank you in advance for the time and effort that will be expended in processing this work.

We are looking forward to receiving your comments.

Sincerely yours,

Frank Visser, M.D.

department of pulmonology, Canisius Wilhelmina Hospital, Nijmegen the Netherlands

Reviewer's report

Title: Optimization of the diagnostic work-up in patients with suspected obstructive lung disease.
The aim of the study was to assess whether protocol driven test ordering optimized the work-up of patients with suspected asthma and COPD, as compared to physician driven test ordering. It is obvious that a specific diagnostic protocol would lead to reduced costs compared to a non specific workup. The point is not so much to demonstrate this, but to convince clinicians to follow the guidelines in clinical practice.

Major points:

1. Figure 1 presents the flow chart that should be followed in tests. The scheme is one that any physician with good sense would or should follow. Following a different order would denote scarce competence on the part of the physician in that in general tests are requested in a sequential mode, on the basis of the findings of the previous test.

You are right, that most physicians would follow this flow, but now there is no longer a need for a physician to decide what will be the next test. Lung function laboratories are not always located near the outdoor patient department. So it is important that lung function assistants can plan the next step without the need to ask the physician, or another consultation.

2. On page 4, line 10 are stated the criteria on which the final diagnosis of COPD or asthma is established. The patient visit is not included among these criteria. Consider this a serious oversight.

On page 4, line 10 the final diagnosis is made after the mentioned criteria including data collected during the first visit.

I am sorry this is not clear enough. We will change the text as follows:

In the first visit the physician takes a medical history, physical examination, makes a differential diagnosis and orders laboratory testing, chest X ray and so on. Only patients are included in the study for whom the most likely diagnosis was “asthma or COPD”. Note 1 Page 4

3. The authors divided patients into two groups: one which followed the experimental procedure, and another group (control) which underwent usual assessment. This is potentially confounding: the differences in findings could be due to the patients not the procedures. It would have been more interesting to
evaluate the two methods in the same patients, also to see if the experimental procedure improved the diagnosis.

The patient groups were aselect. A crossover study is not possible: you would have to repeat almost the same investigation two times in the same patient. Nor patients nor physicians were part of the selecting process so we do not know why this would be potentially confounding. The two groups are comparable in many aspect (table 1. and table 2.) Note 2 P3

Level of interest: An article of limited interest

We think it is interesting to make our work as effective and efficient as possible. There is very little published on this issue, The findings are extensible to other medical practices.

Quality of written English: Needs some language corrections before being Published

We will ask a specialized office to re-edit the text for the English language. If you desire

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests.

Reviewer’s report
Title: Optimization of the diagnostic work-up in patients with suspected obstructive lung disease.

Version: 1 Date: 18 January 2010
Reviewer: John McKay

Reviewer’s report:
General comments:
This is an interesting paper which investigates the potential benefits of a protocol driven ‘work up’ of patients with suspected obstructive lung disease and enquires as to whether this was more efficient in terms of cost, patient visits and time to diagnosis when compared with an unstructured physician led series of investigations.
I thought that the question posed by the author was well defined and that the methods were appropriate in a practical clinical setting. The methods could certainly be repeated by other interested parties.
Major compulsory revisions

Introduction Section
On Page 2 it would be helpful to describe what your estimate of a cost of €450,000 is based on. The way the figure is presented it rather seems as if it has been 'plucked' out of the air.

Comment
we calculated that the annual costs of PFT and outpatient visits related to diagnostic workup of patients with obstructive lung disease exceed €450,000. These costs consist of salary for lung function assistants, outdoor-ward personnel and depreciation of the lung function equipment.
Not included are costs of the building and the salary of the physicians.
After also reading the 3the reviewer we decided to delete this sentence Note 3 P4

At either the introductory section of the manuscript or in the methods section it would be helpful to explain the context of the referrals to the respiratory out-patient clinic. This is particularly important for readers who will not be familiar with the healthcare system in the Netherlands. For example, are patients mainly referred from primary care physicians, from colleagues within secondary care outpatient settings or as in-patients?
Patients were referred mainly by primary physicians. two patients referred themselves to our outdoor department and some were referred by cardiologists. Note 4 P3

Discussion Section (PS Note 5 does not exist)
In the second paragraph of this section, although the point which you are making is relevant it is in fact a result and should you wish to include it then it could be put in the results section and any appropriate discussion in relation to the result included in the discussion section.
Post-Hoc included in the results section Note 5 and we changed the discussion section as follows: Post hoc, we evaluated the added value in making a diagnosis of asthma with the steroid test in our patients. Note 6 P12

The discussion section is relatively brief and I think would benefit from further discussion of the benefits and possible limitations of the study. For example:
• You mention that some doctors already used the protocol prior to the study. Are you aware whether this was any particular group of doctors, e.g. the more senior doctors? If this is so, is there an educational issue in relation to the doctors who
did not apply the protocol initially.

We started about 3 y before this study with the some medical doctors with the protocol driven lungfunction protocol. These were the author of this study and and two other colleagues followed mostly the protocol driven testing. Two other colleagues one more senior and one younger did not implement this protocol driven ordering and stuck to their old behavior. They were not convinced of the time and lung function sparing effect and wanted proof.

We all had a consensus on performing this study and behavior did change after finishing this study. Note 7 P11,12

• If the protocol is, as you state, widely available in the Netherlands, how would you plan to get comparative data. It is important to know whether your results are indeed generalisable and are there any particular issues within your hospital 'unit' which are likely to be unusual and which could have precipitated the use of ‘redundant’ tests.

It is not the workflow which is widely available but we made the workflow out of the guidelines

We all (physicians) have to decide what additional research is needed for of our patients and we cannot be interrupted, depending on the previous step, too often to discuss the next step to do.. So if the pulmonary function assistant can follow a diagnostic protocol without the need to ask the opinion of the physician on how to proceed, the work will be more efficient. The workflow is based on our national guideline which resembled the international guidelines of the ERS. NOTE 8 P12

Although I am not entirely familiar with your healthcare system, I wondered whether the protocol could be applied by primary care physicians prior to referral or indeed through an open access system with perhaps a nurse practitioner (given that nurses have been shown to be more effective than doctors are following protocols).

Our patients we think are not different from most other countries except that most patients were referred to us from a family doctor, in some other countries a family physician will be skipped more often. So a sort of selection bias is possible. However the criteria how to diagnose COPD or asthma does not depend on the physician the patient is going to. Of course the skills and the tools are different between general practitioners and pulmonary physicians but for this study we included only the most basal lung function tests and omitted test as e.g. diffusion capacity or exercise testing. These test are not always needed to confirm a diagnosis of asthma or COPD. We think indeed that this protocol (or workflow) will be suitable for general practitioners too except they need a lungfunction lab or have to order it e.g. in a hospital based lungfunction lab as is possible at our institution. Note 9 11

There was no time saving in terms of the time taken until the final diagnosis —
why might this be?
At the time of this study we had waiting lists for the outpatient-department and for lung function tests. These waiting lists motivated us to search for a more efficient and less time consuming work-up. So we expected that the waiting list in the CG would be longer, but overall only half of the patients followed the protocol, and that was not enough to shorten waiting. The total time to diagnose from the first visit till the final diagnosis, was not different in both groups but without waiting lists we think we will have a difference between the CG and the EG in favour of the EG.

Note 10 P12,13
Are there issues with your patient population which would make them either typical or atypical from the general population? This is important with regard to generalisability.

We think there is nothing special to our population except that most patients were referred by a general practitioner which may be different in other countries. See also NOTE 9
2.
Was the study undertaken at the time of your ‘trainees’ being new to the department and is there a potential that this may have affected the results. In addition, given the conclusions for your study would you plan to use induction training for the doctors in your departments?
Trainees stays for four years in our hospital, we had that time five trainees in all stages of their educational process. Now we asked our trainees if possible to order according to a test-protocol rather than at their own discretion. We learned them that this is more efficient. Note 11 P12

Did the second physician who independently examined the results for each patient referred for PFTs have any form of calibration with any other colleagues since I presume that there is an assumption that this doctor is correct in their decision making.
The second physician calibrated his findings with the findings of the PFT ordering physician only if there were conflicting findings. In all these cases we had a consensus on the final diagnosis Note 12 P8.

Minor Revisions
Abstract
In the objective section I wonder whether this would read more accurately if stated “to assess whether diagnostic test protocol contributed to optimising the work up in these patients.”
We think you are right. Note 13 P10.

In the results section of the abstract you have “……visit to complete diagnosis was significantly higher in the control group – it would be helpful to add in brackets here the statistical value, similarly ‘a mean cost of work up to diagnosis was € 227 in the CG –v- € 181 in the EG. Again it would be helpful to add the statistical value.
We added statistical values Note 14 P1

In the conclusion section I wonder whether it would be appropriate to add “in this group of patients with suspected …….“
We changed it accordingly Note 15 P1

Introduction Section
In the last paragraph of the introduction you mention “at the start of this study……..” I wonder whether this should read “at the outset of this study there was no evidence …..”
That will be better so we changed it Note 16 P2.

In the final sentence of the introduction you state the aim of the study. It may be helpful to detail what you mean by optimising i.e. reducing the number of redundant pulmonary function tests, decreasing outpatient visits and increasing cost effectiveness.
We adopted this description, it is more precisely of what we meant. Note 17 P3

Methods Section
In this section it would be helpful to detail when the study was undertaken and over what timescale.
Note 18 P3

Table 4 should be Table 1 as this is the first to be referenced in the text and the rest of the tables adjusted accordingly.
Results section
We changed the numbering. Note 19 (tables)

In Table 2 it would be helpful to put in the figures as well as percentages.
In the new table 4 (old table 3) we put in percentages.Note 20 (Tables)

On page 6 reversibility testing is described as one of the two most important sources of redundant costs. From my reading of the table this is incorrect – it is TLC
rather than reversibility, along with the histamine provocation tests that resulted in most redundant costs?
You are right about the number, but the costs are number time costs per unit. And so from table 4 the costs for Histamine provocation resulted in the most costs.

Discussion Section
In the first paragraph you need to emphasize that your results of generalise could reduce the cost of diagnosis and obstructive lung disease.

Note 21 P10

Discretionary Revisions

Abstract
In the results section it might be helpful to add “the mean number of PFT tests to diagnosis..”
It is included Note 22 P1

Introduction Section
In the second paragraph when discussing test ordering you use the word “liberally” – I am not convinced that this is the appropriate word. Do you mean PFTs that have been ordered out-with the recommendations of the protocol?
We changed it: The physician who largely orders PFT as a logical next step in the work-up of asthma and COPD Note 23 P2

Methods
When you mention that “A second physician independently examined the results for each patients …” it may be helpful here to add the reference which was used for your choice of classifications.

The second physician looked if the appropriate tests were done according to the diagnostic flow and decided on the pulmonary pulmonary function classification. He also looked to the decision about the final diagnosis of the PFT referring physician … Note 24 P6

Results Section
In your section on ‘time until the final diagnosis’ I presume that the mean time was calculated from the first initial outpatient consultation.
Yes

Discussion
If there is any data available it would be interesting to know if you discussed with those doctors who had ordered the redundant test why they had done so and
whether they thought that this affected their subsequent consultations, particularly as you quite rightly mention the Hawthorne effect. To minimize the Hawthorne effect we discussed after the inclusion period the whole results within our group. Some doctors want to work efficiently, and they ordered more than was the absolute minimum, so there were no other visits to the physician necessary.

Thank you for so many good remarks, it will make this paper better.

Dr John McKay

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

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests

Reviewer's report
Title: Optimization of the diagnostic work-up in patients with suspected obstructive lung disease.

Version: 1 Date: 3 February 2010
Reviewer: Steven Kesten

Reviewer's report:
Major Compulsory Revisions:
1. The assumption that acute reversibility to single occasion administration of short-acting bronchodilators can be used to reliably distinguish asthma from COPD is a fundamental flaw in the manuscript.

I am sorry but this statement is not supported in this manuscript. We are using a lungfunction protocol to give the physician information in a way that he has at the second visit the most change to come to a founded diagnosis so far lungfunction tests can support him for this. See also the comment made by the first reviewer and the answers. Notes 1, 7 and 24

It is correct to state that reversibility to normal can be used to diagnose asthma. However, incomplete reversibility (i.e. not returning FEV1 to normal) whether or not a pre-determined threshold is met (i.e. increase of 12% + 200ml, 15%, or 10% of predicted) does
not adequately distinguish asthma from COPD. There is now a wealth of evidence supporting this as well as recognition in reviews and guidelines. While the objectives of the study are admirable, this clinically important issue renders the study extremely limited in terms of meaningful conclusions.

We do agree that not on a base of lung function alone a diagnosis of asthma or COPD can be made. When this is what you distract from our paper we hope we made it more clear. See also the comment made by the first reviewer and the answers. Notes 1, 7 and 24.

2. While I understand that the study underwent an IRB review, I cannot understand why informed consent was not needed. One could argue that the protocol enforced group would actually receive decreased medical care which might lead to incorrect assumptions about disease (see point 1). Please explain the rationale further.

The protocol was already used by 3 physicians in our group. At the time of the study, IRB regulations were less strict than they are these days, and informed consent was not considered to be necessary at the time the study started; indeed it might be different today.

3. Page 3 – it appears that the reversibility protocol was not standardized (“…After beta-2 agonists and / or anticholinergics.”). This could potentially influence and bias the results.

No the reversibility is tested in the same way by all our patients: first salbutamol after 20 minutes a retest thereafter they got ipratropium and 30 minutes later a second retest. So there is no bias at this respect we think. We added in the text: , patients on reversibility testing were tested for both bronchodilators, Note 26 P5.

4. Page 4 – reversibility was defined as >9% predicted. There are several quoted criteria in the literature. The authors should defend their selection. Also, the standard accepted criteria do not include >9% , although they include a 10% threshold.

The selection was based on the standard protocol used in the Netherlands that time. It is one of the possibilities also stated in the ATS ERS recommendations (reference 6). The references are included in the manuscript. Especially reference number 8, Dales et al gives evidence that in a normal population the random variation after salbutamol was <9% of predicted normal values. But we did not decide on this fact alone to classify the patient as we stated before.

Minor Essential Revision:

1. Page 2, last line – why was 3 years chosen?

That period was arbitrary chosen, because some included patient were seen in our clinic before that period.
2. Page 3, 3rd paragraph – delete the word “lung”
Corrected Note 28 P4.
3. Table 1 – height is misspelled.
Corrected Note 27 (Tables).
4. Table 1 – why are there between 6 and 10% of patients missing knowledge of their smoking behaviour. This seems unusual given that the data is based on the authors clinical practice.
We agree it should not happen that these data are missing. After reviewing the medical records the smoking status was not stated in a small number of patients. After the study we did give the colleagues feedback about this fact.(see also Note 25)
5. It is not clear why a diffusion capacity would be considered a “redundant” test
It is not necessary to have a diffusion test for the diagnose of asthma, For e.g. COPD however it is not redundant we agree. And in these cases we are not counting it as redundant.
Discretionary Revisions:
1. Page 2 – 450,000 Euros are noted as annual costs of PFTs but is only anecdotal and should not be included unless supported by methods and more data.
See comment and answer reviewer one, ok we removed this sentence Note 3 table 2.
Level of interest: An article of limited interest
We think it is interesting to make our work as effective and efficient as possible. There is very little published on this issue, The findings are extensible to other medical practices .
Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:
I do not have competing interests in relation to the paper.