Author's response to reviews

Title: The effect of an active implementation of a disease management programme for chronic obstructive pulmonary disease on healthcare utilization - A cluster-randomised controlled trial

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Author's response to reviews: see over
Dear Editors,

We are very grateful to you for giving us the opportunity to further clarify our manuscript “The effect of an active implementation of a disease management programme for chronic obstructive pulmonary disease on healthcare utilization - A cluster-randomised controlled trial”

Please find below a detailed description of how we have responded to your queries together with the revised manuscript.

We hope that the revised manuscript is acceptable for the reviewing process and publication.

Yours faithfully,

Margrethe Smidth (on behalf of the authors)

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Reviewer 1, Annemarije L Kruis

We would like to emphasise that this paper is part of the randomised trial registered at clinicaltrials.gov. The purpose of this particular paper is to describe the use of health care resources based on data from registries when using the active implementation model. Another paper describing the patients evaluations of their care describe with the tool Patient Assessment of Chronic Illness Care (PACIC) is under review process at BMC Family Practice. We are in the process of publishing a paper on patient health related quality of life using the QE-5D instrument. We have in this present paper added it as a limitation of the paper that a process evaluation is missing.

Major compulsory revisions:

1. To clarify the population we examined in this study the section on Patients has been changed and a section on participants has been added. It reads: “In the CD population, patients were identified from registry data by use of the COPD algorithm. The algorithm was validated in a previous study which suggested that it could be used as a tool to identify patients with obstructive lung disease, primarily COPD [31]. Furthermore, the patients confirmed their diagnosis in the returned questionnaire. The intervention group counted 458 (33.4%) patients, the control group 376 (27.4%) patients and the external control group 538 (39.2%) patients. For the sup-group analysis we wanted to examine the effectiveness of the intervention and therefore allocated the patients from the two practices that declined the invitation to participate and thus received no intervention to the control group. The sub-group, the AT group, had 406 (29.6 %) in the intervention group, 428 (31.2%) in the control group and 538 (39.2%) in the external control group (Figure 1).” We have used the algorithm which was considered a screening tool for the GPs to identify their patients with COPD; the diagnosis should only be made together with the GP’s clinical examination. The patients confirmed their diagnosis in a questionnaire where we in detail had described COPD. We do not expect that patients would confirm this diagnosis unless they were treated for the disease and had talked to their GP or other health professionals about it. We did not report any results of spirometries as we did not perform any specific for this study and the results of test previously done by GPs will be in patients’ confidential files which we did not have access to. We have used the population which has confirmed their diagnosis and they have been identified from their use of the health care system thus we will have the sickest patients in our study population.

2. At the time of the development of the COPD algorithm it was discussed at least in Denmark if the lower age limit should be 35 years to be able to capture the disease in early stages. Therefore, the algorithm was developed and validated from this age limit, and we have used the validated algorithm to identify our population.

3. To explain the COPD algorithm in more detail we have added to the Patients and the COPD algorithm section: “The patient population comprised patients from the two municipalities who were identified by the COPD algorithm. A prerequisite was to be aged 35 years or older as well as resident and registered with a GP practice in the patient’s residing municipality. The patients would have been in contact with the health care system
either because they had been hospitalised during the past five years with a lung related diagnosis, had redeemed prescriptions on lung medication at least twice during the past year or had their lung function tested at their GP on two different occasions during the past year."

4. As in point 3. It is described how we have now reported the inclusion criteria for the COPD algorithm in the Patients and the COPD algorithm section. This are the criteria reported in the clinical trial registry.

5. We have in the section on Patients and the COPD algorithm explained the patients’ inclusion criteria. The Randomisation process and allocation concealment section now starts with a sentence explaining that all GP practices from the two municipalities are included in the study.

6. The research question for this study has now been further defined and states: "The aims were, first, to investigate the impact of the previously developed active implementation model for a disease management programme for COPD as measured by specific indicators to determine to which degree the GPs follow the recommendations; and second to determine healthcare utilization in primary and secondary care for patients with COPD".

7. To support the description of the intervention in this paper an appendix has been added with a PatPlot depicting the elements and the timeline for the interventions.

8. As above in point 7.

9. The intervention is now depicted in the PatPlot in the appendix describing the individual components of the intervention.

10. Outcome in this paper is the distribution of health resources or health care utilisation as the paper is part of the trial registered in clinicaltrials.gov. Therefore, we have also divided the health care utilisation into primary and secondary outcome with adherence to the disease management program as the primary outcome measured at patient level on the use of specific services reported by GPs to the regions to be reimbursed.

11. To reduce the numbers in tables we used 2008 for the year from 1st Nov 2008 to 31st Oct 2009 and 2009 for the year 1st Nov 2009 to 31st 2012. At your suggestion we have now changed it in the tables to 2008-2009 and 2009-2010.

12. We have now added that the outcomes are measured at patient level under Result.

13. In the Methods section we have added an explanation of the poster display. "Furthermore, a poster was displayed in the practice premises informing that this practice was an intervention practice. Only people coming into the premises could see it. In Denmark every citizen belongs to one GP practice and can only use the services from this practice. It rarely happens that a person wants to change practice. It would not be likely that a person change practice because of a poster."
14. 14 and 13 are joined.

15. Indeed the data has a multilevel structure in that violation of the traditional independence- assumption must be expected for observations of patients from the same GP or even regarding the same patient at different times. And of course models exist which address such a setting specifically. However, as the focus in the presented manuscript is the comparison of the two randomisation groups and not of health service-like measures of the variation between GPs or patients, we believe the applied cluster-robust variance estimation to perform well in accounting for the observed dependence between observations for the same GP and consequently also for the correlation between the repeated measures on the same patient. And it immanently takes into account the size of the specified clusters. As concerns a design effect of 1.6 it is admittedly hypothesised on a rather un-academic background, but it should be emphasised that this figure is used for the power-calculation exclusively and has no influence on the reported analyses. Obviously we will be grateful for any suggestions as to how this could be clarified if needed. (Also see answer to point nr. 18.)

16. Joint with point 15

17. We have now kept the two practices that declined the invitation in the intervention group to perform intention to treat analysis. For the as treated analysis they are allocated to the control group.

18. As was the case for design effect commented on under the above point nr. 15, we had no solid scientific argument for expecting a follow-up frequency of 50 %, nor to qualify why an increase of 10 % should mark the limit for clinical relevance. In our notion it is not uncommon, that power calculations must rest on such loose guesstimates or assumptions. However we must concede, that we probably exhibited a little less than the usual precision in the present case, because the dimensioning of the study was basically given by the communities engaging in the study, Thus the aim of a power calculation was not to assess a proper dimensioning of the project, but rather to evaluate whether the project could be used for meaningful research. Please advise if you want us to omit the power calculation from the paper.

19. As in point 10.

20. At your suggestion we have now added a table with some characteristics of the GPs. We did not collect disease characteristics like GOLD stage and lung function for the patients as the patients were identified from administrative data on hospitalisation, redeemed prescriptions and performed spirometries and then on the patients confirmation in the questionnaire. We did not investigate the files in the GPs office.

21. At your suggestion we have reduced the information in the tables.
22. At your suggestion we have reduced the number of tables.

23. At your suggestion we only report on the group we previous called the CD group. Now it is called the study population.

24. To further highlight why we excluded the patients who died we in the Discussion added: “In order to accommodate analysis of time changes, we chose to exclude the patients who died during the trial. In case of large differences in mortality between groups, this could affect the results for comparison of health care use in either direction. However, the nature of the intervention and of the relatively slow-evolving disease convinced us that any influence of the intervention on the endpoint “death” would be negligible in a short-term perspective. This assumption was confirmed by the present data.

25. The intention of this paper is to write about healthcare utilisation. To emphasise that process evaluation would be of interest to study as well we have added the following in the Strength and limitation section: “The understanding of the intervention could have been enhanced by a process evaluation component of the study. For example, we could have interviewed the patients and/or the health professionals.”. In the Unanswered question and limitation section we have added: “The study would benefit from a deeper look into the black box of the intervention which an added process evaluation component could provide. A future study with interviews with patients and/or with health professionals could add this. Another future study could include the component in a mixed methods study.”. We have submitted a paper on the effect of the active implementation model on patients’ assessment of their illness care (PACIC) to BMC Family Practice and a further paper is in the process on the effect on the health related quality of life measure EQ-5D.

26. The abstract has been revised to clearly explain which patient population the results refer to. It now states: “Background More people live longer with chronic conditions placing huge demands on efficient healthcare planning and effective care. Knowledge is scarce about the effect of implementation-processes and the possible effects on patients; only few have examined the effectiveness of disease-management-programmes targeting patients with chronic obstructive pulmonary disease (COPD). The objective of this paper was to determine the effect on healthcare-utilization of an active implementation model for a disease-management-programme for patients with one of the major multimorbidity diseases, COPD. Methods The standard implementation of a new disease-management-programme for COPD was ongoing during the study-period from November 2008 to November 2010 in the Central Denmark Region. We wanted to test a strategy using Breakthrough Series, academic detailing and lists of patients with COPD. It targeted GPs and three hospitals serving approx. 60,000 inhabitants aged 35 or older and included interventions directed at professionals, organisations and patients. The study was a non-blinded block- and cluster-randomised-controlled-trial with GP-practices as the unit of randomisation. In Ringkøbing-Skjern Municipality, Denmark, 16 GP-practices involving 38 GPs were randomised to either the intervention-group or the control-group. A comparable neighbouring municipality acted as an external-control-group including nine GP-practices with 25 GPs. An algorithm based on health-registry-data on lung-related contacts to the
healthcare-system identified 2,736 patients who were alive at the end of the study-period. The population included in this study was 1,372 (69.2%) patients who responded to the baseline questionnaire and confirmed their COPD diagnosis; 458(33.4%) patients were from the intervention-group, 376(27.4%) from the control-group and 538(39.2%) from the external-control-group. The primary outcome was adherence to the disease-management-programme measured at patient-level by use of specific services from general practice. Secondary outcomes were use of out-of-hours-services, outpatient-clinic, and emergency-department and hospital-admissions. **Results** The intervention practices provided more planned-preventive-consultations, additional-preventive-consultations and spirometries. When comparing the development in the intervention-practices with the development in the control-practices, the intervention resulted in more planned-preventive-consultations, fewer conventional consultations and fewer patients admitted without a lung-related-diagnosis. **Conclusion** Use of the active implementation model for the disease-management-programme for COPD changed the healthcare-utilization in accordance with the programme.”

**Minor revisions**

1. We have removed the joint home visits to newly discharged patients even though the change in the algorithm identified population from 2.5% to 6.6% for the intervention group was an increase of 264.0%. The increase in the control group was 110% where there was no change for the external control group.

2. The number of GP practices has been added to the flow chart at your suggestion.

3. The added appendix depicts the different components of the intervention and illustrates that there are more than the two as also Adams et al suggest in their review.

4. The manuscript has again been scrutinised by Professor Morten Pilegaard for language revision.

**Discretionary revision:**

1. More details about the GP practices have been added with added Table 1.
Reviewer 2, Nicholas Zwar

1. The aim of the study was to evaluate the use of an active implementation model for a disease management program thus it is the implementation model and not the disease management programme we evaluate. We knew the programme was developed with all stakeholders; used evidence based practices and was built on the Chronic Care Model wherefore we considered the programme to be a Golden Standard for care for patients with COPD in the Central Denmark Region. The aim has now been rewritten and states: “The aims were, first, to investigate the impact of the previously developed active implementation model for a disease management programme for COPD as measured by specific indicators to determine to which degree the GPs follow the recommendations; and second, to determine healthcare utilization in primary and secondary care for patients with COPD. The programme was developed on the basis of the CCM [28].” In Denmark the GPs are reimbursed for specific services provided to the patients therefore the services provided for planned preventive consultations, the additional preventive consultation, joint homevisits after discharge and for performed spirometries were considered healthcare utilization in primary care. An explanation of this is now inserted in the section on Data: “Adherence was measured in terms of use of the specific services of planned and additional preventive consultations, number of spirometries at patient level. The GP practices report each of these services to the region to be reimbursed.”

2. To address your concerns on the use of the COPD algorithm to identify patients and the patients’ confirmation of their diagnosis the section on Patients and the COPD algorithm has been changed and a section on participants has been added. It reads: “In the study population patients were identified from registry data by the COPD algorithm. The algorithm was validated in a previous study and suggested used as a tool to identify patients with obstructive lung disease primarily COPD. Furthermore the patients confirmed their diagnosis in the returned questionnaire. The intervention group comprised of 458 (33.4%) patients, the control group of 376 (27.4%) and the external control group of 538 (39.2%) patients. For the sub-group we wanted to examine the effectiveness of the intervention and allocated the patients from the two practices that declined the invitation to participate and thus did not receive any of the intervention, to the control group. This sub-group had 406 (29.6 %) in the intervention group, 428 (31.2%) in the control group and 538 (39.2%) in the external control group. (Figure 1).”

3. To support the description of the intervention in this paper an appendix has been added with a PatPlot depicting the elements and the timeline for the interventions.

4. We have now presented the intention to treat analysis as the main analysis and thus kept the two practices which chose not to participate in the intervention group at your suggestion and to not undermine the randomisation. The Result section has been rewritten accordingly.

5. To your concern of not blinding the researchers to the allocation of the groups we can only say that we were a very small group and the researchers were also the ones inventing and
conducting the intervention with the intervention practices. We have mentioned in the Randomising section: "The allocation of both GPs and patients to the intervention and the control group was open and known to the GPs and also the researchers as it was not possible to hide the allocation to the researchers who also delivered the intervention to the GP practices." We have also mentioned this as a weakness in the Strength and limitation section where we state that: "When the GP practices were allocated to the intervention or control group an independent person performed the randomisation. However, we could not conceal the allocation post randomisation to the researchers who performed the analysis as the group of researchers were also the ones who conducted the intervention with the intervention practices. This could be considered a flaw in the study design".

5. As mention above in point 4. the primary analysis is now the intention to treat analysis to draw maximum strength from the randomised design. The as treated analysis is described as a sensitivity analysis. The Result section and the tables have been changed accordingly.

6. At your suggestion of adding process evaluation of the intervention we have now added the following in the Strength and limitation section: "The understanding of the intervention could have been enhanced by a process evaluation component of the study. For example, we could have interviewed the patients and/or the health professionals.". In the Unanswered question and limitation section we have added: "The study would benefit from a deeper look into the black box of the intervention which an added process evaluation component could provide. A future study with interviews with patients and/or with health professionals could add this. Another future study could include the component in a mixed methods study.".

We have revised the manuscript ensuring that it conforms to the journal style.