

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Impact of community-based chronic obstructive pulmonary disease service, a multidisciplinary intervention in an area of high deprivation: A longitudinal matched controlled study
AUTHORS	Saini, Pooja; Rose, Tanith; Downing, Jennifer; Matata, Bashir; Pilsworth, Samantha; Pemberton, Allan; Comerford, Terence; Wilson, Keith; Shaw, Matthew; Harper, Lesley M; Daras, Konstantinos; Barr, Benjamin

VERSION 1 – REVIEW

REVIEWER	Anabel Sciriha Malta
REVIEW RETURNED	29-Jul-2019

GENERAL COMMENTS	This paper reads very well and offers further input to the area of COPD management and its increase in recommendations to guidelines. It is an interesting view of how a multidisciplinary programme can offer more benefit to COPD patients. Maybe a recommendation is to view whether there is infact a difference in deprived or non deprived areas when it comes to COPD care
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REVIEWER	Chaicharn Pothirat Division of Pulmonary, Critical Care and Allergy, Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand 50200.
REVIEW RETURNED	30-Jul-2019

GENERAL COMMENTS	<p>According to your invitation for reviewing the manuscript with a particular emphasis on the statistical methods and analyses used. In general, this statistical used in this study were appropriated, however, there were 3 major determinants needed to be explored before considering for publication</p> <ol style="list-style-type: none">1. Matching variables in pre-intervention phase had inadequate influences for the outcome variables of your study objective. Several major outcome determined variables were missing, for example COPD stage, lung function indices, frequency of exacerbation and hospitalized exacerbation within 1 years, COPD medications, co-morbidity, patient compliance, proportion of active smokers, area-based air pollution data,etc2. During intervention phase, the authors' team should monitor and demonstrate each of 7 service intervention-bundle compliance and evaluate the effectiveness of each intervention bundle periodically.3. You need to demonstrate pre-intervention variables before and after propensity score computation and show the results both before and after matching.
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REVIEWER	sue Jordan Swansea university, Wales
REVIEW RETURNED	13-Oct-2019

GENERAL COMMENTS	<p>Thank you for the opportunity to read this interesting paper. The intervention sounds worthwhile, and I wondered if other assessment criteria had been used, beyond emergency admission? E.g. use of domiciliary oxygen, oral corticosteroids, out of hours calls. How was 'emergency' admission defined? Were there other admissions? The intervention appears to be a single-site case study, so should not be abandoned without being tried elsewhere.</p> <p>There is no mention of industrial exposure. This should be mentioned, even if to say there isn't any. In South Wales, COPD is changing, as people who worked underground pass on. Are there similar effects in Knowsley?</p> <p>Analysis I'm afraid the analysis is too complicated for me. I should like to see the raw data on numbers of admissions, other outcomes and patient characteristics. A service re-organisation is reported, and this may have affected findings, particularly as a single outcome measure is used. In general, the paucity of data around service re-organisations is worrying. I wondered if you might consider looking at a hinge effect on key outcomes? Our statistician did an interesting analysis in the open access paper below.</p> <p>Style Copy editing will be needed. Some results appear in methods, lines 225 et seq. Akuma AO, Jordan S, Watkins A (2018) The Impact of Neonatal Service Re- Organisation on Feeding of Preterm Infants (<34 Weeks): A Prospective Cohort Study in a Regional Neonatal Unit from 1992 to 2010. J Nurs Health Stud. Vol.3 No.2:4. doi: 10.21767/2574-2825.1000033 http://www.imedpub.com/articles/the-impact-of-neonatal-service-reorganisationon-feeding-of-preterm-infants34-weeks-a-prospective-cohort-study-in-a-regional-neonata.php?aid=23103</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer 1 comments:

4. This paper reads very well and offers further input to the area of COPD management and its increase in recommendations to guidelines. It is an interesting view of how a multidisciplinary programme can offer more benefit to COPD patients. Maybe a recommendation is to view whether there is in fact a difference in deprived or non deprived areas when it comes to COPD care

The authors thank the reviewer for his/her comments, we appreciate that the reviewer shares our view that this is an important topic of high interest. We have taken note of the reviewer's recommendation and added to the manuscript (p18):

“Additionally, as there is a higher prevalence of COPD in more deprived areas, more COPD clinics are available which results in more visits with patients. Therefore the same level of provision is provided in deprived areas but the availability of care is higher.¹² However, nationally accessibility to services can be a postcode lottery as all services are commissioned differently.”

Reviewer 2 comments:

5. According to your invitation for reviewing the manuscript with a particular emphasis on the statistical methods and analyses used. In general, this statistical analysis used in this study were appropriated, however, there were 3 major determinants needed to be explored before considering for publication.

The authors thank the reviewer for his/her comments, and have addressed each point listed below.

i. Matching variables in pre-intervention phase had inadequate influences for the outcome variables of your study objective. Several major outcome determined variables were missing, for example COPD stage, lung function indices, frequency of exacerbation and hospitalized exacerbation within 1 years, COPD medications, co-morbidity, patient compliance, proportion of active smokers, area-based air pollution data,etc

In response to the reviewer's question, it would be difficult to get pre-service data for the variables listed above. For example, the grade severity of COPD could not be matched as its definition of exacerbation might not mean the same within each service and the coding of each variable could be different. Additionally, COPD medication is hard to obtain, however in future this may be possible if all services code the same when using EMIS but services would still need to know that patients are following the guidelines of taking their medication as set out within NICE.

We would also like to clarify that the study design is a difference-in-differences (DiD) analysis. an established approach used in econometrics^{1,2} and increasingly in health research^{3,4} for evaluating the impact of interventions in a non-experimental context. In DiD analysis outcomes are observed for two groups before and after an intervention and one of the groups is exposed to a treatment in the second period but not in the first period and the second group is not exposed to the treatment during the full time frame. The average change in outcomes in the second (control) group is then subtracted from the average change in outcomes the first (treatment) group. This removes biases in second period comparisons between the treatment and control group that could be the result from permanent differences between those groups, as well as biases from comparisons over time in the treatment group that could be the result of trends. This therefore provides a more robust estimate of the effect of the intervention than a simple matched case control study which would be biased by unobserved time invariant differences between groups.

The key assumption of difference-in-differences analysis is the parallel trends assumption. If the trend in the outcome in the intervention and control populations would have been parallel in the absence of the intervention then, the difference between the change in the outcomes between the two groups provides an unbiased estimate of the interventions effect.⁵ The reasons for matching were therefore to identify control populations that were likely to follow similar trends in the outcomes over time. We found that during the pre-intervention period there was no significant difference in trends in emergency admission rates between Knowsley and the control population (Supplementary file, Appendix 4), suggesting that the parallel trend assumption was not violated in this analysis.

We have added additional information to the supplementary Appendix 8 outlining the difference-in-differences method. We have also changed the titles of the tables so that they more clearly describe what the table contents show.

ii. During intervention phase, the authors' team should monitor and demonstrate each of 7 service intervention-bundle compliance and evaluate the effectiveness of each intervention bundle periodically.

Thank you for your comments. We recognise the importance of the work you have suggested, however we have included data for hospital admissions and not each individual service. More information on the effectiveness of each of these services will be collected and published within the Trust's publically available reports.

iii. You need to demonstrate pre-intervention variables before and after propensity score computation and show the results both before and after matching.

The characteristics of Knowsley and matched control LSOAs in the pre-intervention period after propensity score matching are shown in Table 1 in the manuscript. The characteristics of Knowsley and unmatched LSOAs in pre-intervention period before propensity score matching are shown in Supplementary file Appendix 4.

Reviewer three comments:

6. The intervention sounds worthwhile, and I wondered if other assessment criteria had been used, beyond emergency admission? E.g. use of domiciliary oxygen, oral corticosteroids, out of hours calls.

We have added the COPD CLAHRC report (referenced as document 12 within the main document text) to the appendix which contains further detail about the intervention. However, we note to inform the reviewers that it can be difficult to obtain accurate data as access is required from many different avenues such as rapid response calls, rapid oxygen clinics, oral medications, etc. This can be hard to get and specifically for this intervention, the oxygen service did not start within the COPD service until more recently.

7. How was 'emergency' admission defined? Were there other admissions? The intervention appears to be a single-site case study, so should not be abandoned without being tried elsewhere.

Thank you. We have included the full details of the variables in Supplementary file Appendix 1. Emergency admissions for COPD were defined using ICD-10 codes: J40–J44. Annual COPD emergency admission rates per 100,000 population were calculated using Hospital Episode Statistics (HES), with population data obtained from the ONS. Continuous inpatient (CIP) spells were used to calculate emergency admissions per calendar year.

This paper is for a single-site case study, however whole respiratory planning is currently being undertaken nationally and across Cheshire and Merseyside where this service are sharing what they are doing in order for it to be replicated.

8. There is no mention of industrial exposure. This should be mentioned, even if to say there isn't any. In South Wales, COPD is changing, as people who worked underground pass on. Are there similar effects in Knowsley?

Thank you to the reviewer for raising this point. We have now added the following information to the text:

"There is a history of industrial exposure, for example, mining, manufacturing, shipping and dock work; however, comparisons between areas in Knowsley have shown no increase for the rate of hospital admissions where there was evidence of this exposure.²²"

NOTE: new reference added and previous reference list updated.

Analysis

9. I'm afraid the analysis is too complicated for me. I should like to see the raw data on numbers of admissions, other outcomes and patient characteristics.

Thank you. We have added a table showing emergency COPD admission rates per year for the study period to Supplementary file Appendix 9, and as noted above we have added the COPD CLAHRC report to the supplementary file.

10. A service re-organisation is reported, and this may have affected findings, particularly as a single outcome measure is used. In general, the paucity of data around service re-organisations is worrying. I wondered if you might consider looking at a hinge effect on key outcomes? Our statistician did an interesting analysis in the open access paper below.

Thank you. As per the comment above, we would like to clarify that the study design is a difference-in-differences (DiD) analysis which is an established approach used in econometrics^{1,2} and increasingly in health research^{3,4} for evaluating the impact of interventions in a non-experimental context. The strength of DiD analyses is that they provide a more robust estimate of the effect of the intervention than a simple matched case control study which would be biased by unobserved time invariant differences between groups. We have added additional information to the supplementary Appendix 8 outlining the difference-in-differences method.

Style

11. Copy editing will be needed.

This has been completed by the authors reading the draft prior to submission

12. Some results appear in methods, lines 225 et seq.

Thank you for noticing this – we have now updated the results section within the manuscript.

References

1. Angrist JD, Pischke J-S. Mostly Harmless Econometrics: An Empiricist's Companion. Princeton: Princeton University Press 2009.
2. Wooldridge JM. Econometric Analysis of Cross Section and Panel Data. 2nd Revised ed. Cambridge: Mass: MIT Press 2010.
3. Craig P, Dieppe P, Macintyre S, et al. Developing and evaluating complex interventions: the new Medical Research Council guidance. *BMJ* 2008;337:a1655. doi: 10.1136/bmj.a1655 [published Online First: 2008/10/01]
4. Craig P, Katikireddi SV, Leyland A, et al. Natural Experiments: An Overview of Methods, Approaches, and Contributions to Public Health Intervention Research. *Annu Rev Public Health* 2017;38:39-56. doi: 10.1146/annurev-publhealth-031816-044327 [published Online First: 2017/01/27]
5. Dimick JB, Ryan AM. Methods for evaluating changes in health care policy: the difference-in-

VERSION 2 – REVIEW

REVIEWER	Chaicharn Pothirat Chiang Mai University
REVIEW RETURNED	01-Feb-2020

GENERAL COMMENTS	Dear Assistant Editor Thank you for your mail. The authors' point-by-point response sounds clear. I am satisfied with the response and have no additional comments. With regards
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REVIEWER	sue Jordan Swansea University, Wales
REVIEW RETURNED	13-Dec-2019

GENERAL COMMENTS	Thank you for the opportunity to re-read this interesting paper. The future plans for the intervention are of interest, and should be included in the discussion. s The authors have placed the data in relation to my previous comments in supplementary material. I think they should be in the paper. Without these, readers cannot make their own interpretations. If some of these parameters are unavailable, this should be included in the 'limitations'. The point on data for all-cause admission has not been addressed. I'm afraid the statistical analysis is still too complex for me, and possibly other readers. I should like to see the raw numbers in the paper (appendix 7). The full models are informative, but they seem to be dominated by the splines. Can these be removed for clarity? My point on industrial exposure has been misinterpreted. Severe COPD incidence may be declining as the generation affected passes on. I hope these comments will assist development of the paper.
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VERSION 2 – AUTHOR RESPONSE

Editorial requests to respond to reviewer 3 comments:

1. The authors have placed the data in relation to my previous comments in supplementary material. I think they should be in the paper. Without these, readers cannot make their own interpretations. If some of these parameters are unavailable, this should be included in the 'limitations'.

We have included the full details of the variables in Supplementary file Appendix 1. Emergency admissions for COPD were defined using ICD-10 codes: J40–J44. Annual COPD emergency admission rates per 100,000 population were calculated using Hospital Episode Statistics (HES), with population data obtained from the ONS. Continuous inpatient (CIP) spells were used to calculate emergency admissions per calendar year.

Appendix 1 has now been moved to the main paper as Table 1 as per the request of the reviewer. All other tables have been renumbered following this change.

2. The point on data for all-cause admission has not been addressed.

Thank you for your comment, which we have now addressed. The following text has been added to the paper to clarify why we chose to investigate COPD specific admission:

“We chose to investigate COPD specific admissions, since all-cause admissions would likely be affected by other interventions occurring concurrently in Knowsley (e.g. a CVD service intervention)²⁸. Emergency admissions were defined as admissions that are unpredictable and occur at short notice because of clinical need, as per the HES data dictionary.²⁹” (lines 162-166)

We have also clarified this point further within the discussion:

“We did not have access to data on other outcomes such as use of domiciliary oxygen, oral corticosteroids or out of hours calls, and were only able to assess the impact of the intervention on emergency COPD hospital admissions, length of stay and emergency COPD readmission rates. Whilst these outcomes may not fully reflect health benefits to the users of these services, they were the planned outcomes of the intervention agreed by the commissioner in their contract with the service provider.” (lines 363-269)

3. I'm afraid the statistical analysis is still too complex for me, and possibly other readers. I should like to see the raw numbers in the paper (appendix 7). The full models are informative, but they seem to be dominated by the splines. Can these be removed for clarity?

We thank you for the comments and have now made the spline term more clear within the text:

“We included a trend term for time to account for the long term trend in admission rates across the intervention and comparison groups and an additional spline term to account for any change in overall trends across both groups after the intervention. In sensitivity analysis we estimated a model removing the spline term – i.e. just including an annual trend term. We also included a random intercept for each LSOA to account for the longitudinal nature of the data (see Supplementary file, Appendix 5 for full details of the statistical model).” (lines 256-262)

These have been removed and instead a table has been added to the supplementary document for further clarity (see appendix 11):

“Estimating a model removing a spline term allowing for a change in trend across both groups after the intervention did not change the results (Supplementary file, Appendix 11).”(lines 328-330)

4. My point on industrial exposure has been misinterpreted. Severe COPD incidence may be declining as the generation affected pass on.

We have added information on industrial exposure to the discussion as requested:

“It is possible that a reduction in admissions could be a cohort effect related to prior industrial exposure, however this would likely lead to a more gradual decline, not the steep change we see at the intervention point. Comparisons between areas in Knowsley have shown no historic increase for the rate of hospital admissions where there was evidence of this exposure,²² suggesting that this is not leading to a decline as the exposed may have already died. Additionally, matched controls were from other deprived areas in the North West industrial affects would be similar.” (lines 412-418)

VERSION 3 – REVIEW

REVIEWER	sue Jordan Swansea University, Wales, UK
REVIEW RETURNED	23-Feb-2020
GENERAL COMMENTS	Thank you for the opportunity to re-read this interesting paper. Readers will be interested to hear of future plans for the intervention.

	<p>The material in appendices 5-9 are central to understanding the analysis, and, I think, should be in the paper. Tables in appendices 8 & 9 have identical headings, and should be distinguished. The table in appendix 6 contains both means and proportions. This confusion could be removed by separation of the variables. I hope the authors will send a pdf when published.</p>
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VERSION 3 – AUTHOR RESPONSE

We thank you for your comments which we have now addressed.

1) Readers will be interested to hear of future plans for the intervention.

We have added a few sentences within the discussion about future plans for the intervention: "Since implementing the KCOPD service, the service has been expanded to include asthma, community acquired pneumonia (that has higher admission rates), is working closely with the Knowsley cardiovascular disease service (KCVD). Additionally, they have introduced respiratory clinics in the local addiction services to target difficult to reach groups and are offering in-house smoking cessation. The service has also expanded the early supported discharge element of the service to base staff within the local emergency departments to review patients as soon as they arrive at hospital. Further research is needed to examine the impact of the expansion of the service on emergency admissions, length of inpatient stay and readmissions."

2) The material in appendices 5-9 are central to understanding the analysis, and, I think, should be in the paper.

These have now been moved to the main paper following approval from the editor.

3) Tables in appendices 8 & 9 have identical headings, and should be distinguished.

These have been checked and do not seem to be identical. One is looking at COPD emergency admissions and the other length of stay. We hope that the reviewer is reassured that these are different.

4) The table in appendix 6 contains both means and proportions. This confusion could be removed by separation of the variables.

The table has been changed, the order of the variables in the table have percentages grouped together, numbers are grouped etc. All of the values in the table are means and standard deviations. We hope that the reviewer is happy with these updates.