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)	Results dissemination of registered clinical trials across Polish academic institutions: cross-sectional analysis
AUTHORS	Strzebonska, Karolina; Wasylewski, Mateusz; Zaborowska, Lucja; Riedel, Nico; Wieschowski, Susanne; Strech, Daniel; Waligora, Marcin

VERSION 1 – REVIEW

REVIEWER	Christopher Jones Cooper Medical School of Rowan University
REVIEW RETURNED	27-Oct-2019

GENERAL COMMENTS	Thank you for the opportunity to review your manuscript, "Results dissemination of registered clinical trials across Polish academic institutions: cross-sectional analysis." This paper addresses an extremely important topic. It is well written, and the methods mirror those of other previously published studies that have investigated this topic. I have several minor suggestions for your consideration. 1. The main body of your manuscript does not include much detail regarding your specific publication search strategy. I would consider making your current supplementary figure 1 a part of the main manuscript, as the search strategy is really the most important part of your methods. 2. Could you provide 95% confidence intervals surrounding the point estimates for the pediatric and adult publication rates you present in your abstract and results? These proportions may in fact not be significantly different. 3. In my opinion it would be worth noting in the Limitations section that a significant portion of trials in the ClinicalTrials.gov database that are listed as actively recruiting have in fact completed enrollment, but the enrollment status has not been updated (Discrepancies between ClinicalTrials.gov recruitment status and actual trial status: a cross-sectional analysis. BMJ Open. 2017 Oct 11;7(10):e017719). 4. It is also worth noting in the Limitations that your search strategy may have missed some relevant publications. 5. In my opinion, the most striking finding is that just 1.3% of the included studies both published and posted results to ClinicalTrials.gov in a timely fashion. While these standards (12 and 24 months for posting and publication) were adopted by the WHO in 2017 (and I think this is worth noting), it is still significant that accomplishing both standards is so rare. I would suggest

	highlighting this in the abstract rather than the pediatrics-specific findings.

REVIEWER	RuiJun Chen Weill Cornell Medical College, USA; Columbia University, USA
REVIEW RETURNED	13-Nov-2019

GENERAL COMMENTS	The authors sought to determine the rates of publication and results reporting for clinical trials across academic medical centers (AMCs) in Poland between 2009-2013 while also providing descriptive characteristics, comparing pediatric and adult trials, and analyzing features associated with timely dissemination of results. The study addresses an important topic and the effort and likely significant manual review which went into producing this work is commendable. However, it is unclear why the authors chose to use US-based ClinicalTrials.gov to identify trials at Polish academic medical centers. Given that Poland is part of the European Union, it seems that it would also be subject to the EU's Clinical Trial Regulations and potentially more likely to have their clinical trials listed on the EU Clinical Trials Register. The authors themselves note the limitation that the trials on CT.gov are only a small subset of those conducted in Poland (they estimated 2200 total over the same period while only 305 are identified in this study). Perhaps I do not fully understand the landscape of Polish clinical trials but if there is a reason to use CT.gov instead of the EU Register, it should be more clearly elucidated in the manuscript. Otherwise I would be concerned that this CT.gov sample may not be representative of Polish AMCs in general, and it may be helpful to also incorporate results from the EU Register to gain a more complete picture. Other more minor points: the study concludes that Polish AMCs fail to timely disseminate the results of interventional clinical trials but it should be noted that Polish AMCs in this study outperformed previously published results in the literature, including at US and EU AMCs. 80% of trials at Polish AMCs disseminated results while prior estimates describe 25-50% unpublished, with a similar study showing only 66% of US AMCs disseminated results. Perhaps this is evidence we may be improving, although still have a ways to go--particularly in timeliness The authors describe a logistic regression analysis to identify variables associated with timely results dissemination in their Methods, but do not mention the results of this analysis at all in their Results or Discussion. It is included in the supplement but the findings should be mentioned somewhere in the manuscript, and can reference the supplement for details Finally, the authors also conclude that fewer pediatric trials disseminate results which poses ethical concerns. Certainly important to address but based on their results, 73.6% vs 81%, results are quite similar and would not be a statistically significant difference.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Christopher Jones
Institution and Country: Cooper Medical School of Rowan University
Please state any competing interests or state ‘None declared’: None declared

Please leave your comments for the authors below
Thank you for the opportunity to review your manuscript, "Results dissemination of registered clinical trials across Polish academic institutions: cross-sectional analysis." This paper addresses an extremely important topic. It is well written, and the methods mirror those of other previously published studies that have investigated this topic. I have several minor suggestions for your consideration.

1. The main body of your manuscript does not include much detail regarding your specific publication search strategy. I would consider making your current supplementary figure 1 a part of the main manuscript, as the search strategy is really the most important part of your methods.

Response: We made supplementary figure 1 a part of the main body of the manuscript, as suggested (it is figure 1 in the new version). Because of the BMJ Open policy of maximum 5 tables/figures included, we had to make the original figure 1 a supplementary figure (supplementary figure 1 in the new version).

2. Could you provide 95% confidence intervals surrounding the point estimates for the pediatric and adult publication rates you present in your abstract and results? These proportions may in fact not be significantly different.

Response: We provided 95% CI in the results section.

3. In my opinion it would be worth noting in the Limitations section that a significant portion of trials in the ClinicalTrials.gov database that are listed as actively recruiting have in fact completed enrollment, but the enrollment status has not been updated (Discrepancies between ClinicalTrials.gov recruitment status and actual trial status: a cross-sectional analysis. BMJ Open. 2017 Oct 11;7(10):e017719).

Response: Thank you for this remark. We added to the limitations of our study: *"we relied on the recruitment status found in the database which might not had been updated, meaning that some active or recruiting trials could in fact be completed"*.

4. It is also worth noting in the Limitations that your search strategy may have missed some relevant publications.

Response: Thank you. We also added this limitation: "*despite extensive publication search by two researchers independently we could have missed some relevant publications*".

5. In my opinion, the most striking finding is that just 1.3% of the included studies both published and posted results to ClinicalTrials.gov in a timely fashion. While these standards (12 and 24 months for posting and publication) were adopted by the WHO in 2017 (and I think this is worth noting), it is still significant that accomplishing both standards is so rare. I would suggest highlighting this in the abstract rather than the pediatrics-specific findings.

Response: We highlighted this finding in the abstract. *"Dissemination by both posting and publishing results in a timely manner was achieved by 4 trials (1.3%)."*
We also added the year of publishing the WHO statement that defined the standards of timely reporting (however we decided to add 2015, the first statement publication date, as provided by https://www.who.int/ictrp/results/en/).

Reviewer: 2
Reviewer Name: RuiJun Chen
Institution and Country: Weill Cornell Medical College, USA; Columbia University, USA
Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below

The authors sought to determine the rates of publication and results reporting for clinical trials across academic medical centers (AMCs) in Poland between 2009-2013 while also providing descriptive characteristics, comparing pediatric and adult trials, and analyzing features associated with timely dissemination of results. The study addresses an important topic and the effort and likely significant manual review which went into producing this work is commendable. However, it is unclear why the authors chose to use US-based ClinicalTrials.gov to identify trials at Polish academic medical centers. Given that Poland is part of the European Union, it seems that it would also be subject to the EU's Clinical Trial Regulations and potentially more likely to have their clinical trials listed on the EU Clinical Trials Register. The authors themselves note the limitation that the trials on CT.gov are only a small subset of those conducted in Poland (they estimated 2200 total over the same period while only 305 are identified in this study). Perhaps I do not fully understand the landscape of Polish clinical trials but if there is a reason to use CT.gov instead of the EU Register, it should be more clearly elucidated in the manuscript. Otherwise I would be concerned that this CT.gov sample may not be representative of Polish AMCs in general, and it may be helpful to also incorporate results from the EU Register to gain a more complete picture.

Response: Thank you for this comment. We decided to choose ClinicalTrials.gov instead of the EU Clinical Trials Register after preliminary search indication that for the same inclusion criteria (e.g., study conducted in Poland and start date between 01.01.2003 to 31.12.2013) there were 3505 records identified in ClinicalTrials.gov and 1312 in the EU Clinical Trials Register. Moreover, EU Clinical Trials Register unfortunately do not allow to perform search including primary completion date and completion date of registered trials. We added this information to the limitations of our study.

According to the PwC Report Clinical Trials in Poland (https://www.pwc.pl/pl/pdf/clinical-trials-in-poland-pwc-report.pdf**) there were 2243 clinical trials launched in Poland in total between 2009-2013. However, there is no information how many trials were completed in these years. Since the aim of our study was to determine results dissemination of registered clinical trials across Polish academic institutions (as defined in inclusion criteria) we didn't include non-academic clinical trials.**

When performed our search we captured 1267 interventional trials registered on ClinicalTrials.gov that were conducted in the cities with Academic Medical Centres. We assume that about 1000 other trials conducted in Poland were performed in non-academic institutions. We included 305 trials (among 1267) since 962 did not meet our inclusion criteria (e.g., 841 records missed the exact name of the research site). Other exclusion reasons are presented in supplementary figure 1. We clarified this in the manuscript. "our results may be underestimated as in 2009-2013 about 450 new clinical trials were conducted in Poland annually for both academic and non-academic sites, giving a total of 2243 new clinical trials over 5 years.[28] We captured 1267 completed trials and excluded almost 76% of them mainly because the name of the research site was not provided (see also supplementary figure 1)."

Other more minor points: the study concludes that Polish AMCs fail to timely disseminate the results of interventional clinical trials but it should be noted that Polish AMCs in this study outperformed previously published results in the literature, including at US and EU AMCs. 80% of trials at Polish AMCs disseminated results while prior estimates describe 25-50% unpublished, with a similar study showing only 66% of US AMCs disseminated results. Perhaps this is evidence we may be improving, although still have a ways to go--particularly in timeliness

Response: We added this information in the conclusion.

The authors describe a logistic regression analysis to identify variables associated with timely results dissemination in their Methods, but do not mention the results of this analysis at all in their Results or Discussion. It is included in the supplement but the findings should be mentioned somewhere in the manuscript, and can reference the supplement for details

Response: We mentioned the results of the logistic regression analysis in the section "Subgroup analyses".

Finally, the authors also conclude that fewer pediatric trials disseminate results which poses ethical

concerns. Certainly important to address but based on their results, 73.6% vs 81%, results are quite similar and would not be a statistically significant difference.

Response: We provided 95% confidence intervals and p-values.

VERSION 2 – REVIEW

REVIEWER	Christopher Jones Cooper Medical School of Rowan University I have been an investigator on studies funded by Roche, Janssen, Hologic, and AstraZeneca for which my department has received funding.
REVIEW RETURNED	16-Dec-2019

GENERAL COMMENTS	The authors have addressed each of the inquiries I had in response to the initial submission. The manuscript reads well, and is complete. I have no further substantial suggestions.

REVIEWER	RuiJun Chen Weill Cornell Medical College, USA; Columbia University, USA
REVIEW RETURNED	09-Dec-2019

GENERAL COMMENTS	The authors have done a good job of addressing the comments and concerns provided by the initial reviewers. The revisions incorporated into the manuscript both clarify and strengthen the paper. With the explanation on why ClinicalTrials.gov was chosen in the response and the revisions, it is much easier to understand the context and motivation on how the methodology was developed. My only suggestion might be to consider including a sentence or two about this in the Methods section instead of just the limitations part of your Discussion, as it seems like comparing and contrasting ClinicalTrials.gov and the EU Clinical Trials Register was the first step in developing your approach. The secondary analysis of logistic regression to identify variables associated with timely dissemination still seems a bit tangential to the purpose of this paper, but it overall neither helps nor detracts from the main points.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 2
Reviewer Name: RuiJun Chen
Institution and Country: Weill Cornell Medical College, USA; Columbia University, USA
Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below
The authors have done a good job of addressing the comments and concerns provided by the initial reviewers. The revisions incorporated into the manuscript both clarify and strengthen the paper.

With the explanation on why ClinicalTrials.gov was chosen in the response and the revisions, it is

much easier to understand the context and motivation on how the methodology was developed. My only suggestion might be to consider including a sentence or two about this in the Methods section instead of just the limitations part of your Discussion, as it seems like comparing and contrasting ClinicalTrials.gov and the EU Clinical Trials Register was the first step in developing your approach. The secondary analysis of logistic regression to identify variables associated with timely dissemination still seems a bit tangential to the purpose of this paper, but it overall neither helps nor detracts from the main points.

Response: Thank you for this suggestion and all other comments allowing us to strengthen our paper. We added the explanation why we chose ClinicalTrials.gov in the Methods section and we slightly modified our first limitation in the Discussion section.

Reviewer: 1
Reviewer Name: Christopher Jones
Institution and Country: Cooper Medical School of Rowan University
Please state any competing interests or state 'None declared': I have been an investigator on studies funded by Roche, Janssen, Hologic, and AstraZeneca for which my department has received funding.

Please leave your comments for the authors below
The authors have addressed each of the inquiries I had in response to the initial submission. The manuscript reads well, and is complete. I have no further substantial suggestions.

Response: Thank you for all former suggestions and for your help with improving our manuscript.