Author’s response to reviews

Title: A comparison between health research output and burden of disease in Arab countries: evidence from Palestine

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The relation between health research output and burden of disease in Arab countries: evidence from Palestine

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Health Research Policy and Systems

Reviewer reports:

Reviewer #1: Title: The relation between health research output and burden of disease in Arab countries: evidence from Palestine

The authors searched Scopus and PubMed for health-related literature in Palestine for the time period (2000-2015) and compared research output with disease burden in the country using death rates and DALYs. This type of reviews is increasingly becoming of interest to researchers, notably in resource-scarce setting for assessing research focus and research quality, and for better direction of research funds.

This is an interesting study and I was intrigued to read the manuscript; yet my excitement was somehow dampened when going into the manuscript itself, which appeared to have been written in haste. My concerns are presented below under general comments and more specific ones.

General comments:

The abstract and introduction are well written, focused and clear.
Comment: Thanks for your comment

Change: None

Methods:

The methods are not explicit enough and need more elaboration. The eligibility criteria are a bit blurred: for example, did the authors exclude a paper that included Palestinian participants but where none of the authors were affiliated with a Palestinian institution? Also, it is not clear whether papers on health systems research were included or not?

Comment: Thanks for your comment.

Change: We have modified the eligibility criteria section to include the following paragraph to the methods (page 4; line 17-19) "We excluded studies that none of the authors were affiliated with a Palestinian institution, even if they included Palestinian participants. We also excluded studies involving non-human animals as well as studies on health systems research".

Most of the reasons posted for exclusion in the full-text reading could have been identified while screening titles and abstracts (e.g. affiliation, qualitative research, basic science research); and this makes the reader wonder, what were the main reasons identified for excluding the 1650 records based on title and abstract screening?

Comment: Thanks for your comment. We agree that most of the exclusion criteria reported in the full-text screening could have been identified in title and abstract screening. However, some of these studies contains no abstracts or the affiliations of all authors were not fully reported. Further, we preferred to be inclusive during the title and abstract screening step and exclude those fits the exclusion criteria to avoid losing relevant articles.

Change: None

Also, it is not clear how did the authors handle the 'description of disease or condition evaluated according to groups of global burden of disease' when the study tackled more than one disease (e.g. in cross-sectional or cohort studies) and how was the 'sample size' coded when it was a review-non META analyses- paper? Or were the latter excluded as well?

Comment: Thanks for your comment. We agree that the paragraph describing data collection needs to be elaborated.

Change: We added the following sentences to the methods section: page 5; line 1-3 "(in studies tackling more than one disease, we considered the disease relevant to the primary objective of the study, if not reported, then the most highlighted disease throughout the article)"; and page 5; line 2-3 "(in case of a systematic review and/or meta-analysis, we considered the number of included studies/articles as the sample size)".
Table 2 (last 2 columns) and Figures 2 and 3 appear to be addressing the same research question and telling us the same message: there is a mismatch between disease burden and research output. Using various analytical modalities, the question was addressed in table 2 on a multiplicative scale (measured as deaths and DALYs per study), in fig 2 as correlation analyses (measured as rho), and in fig 3 addressed as differences between actual and expected research measured on additive scale. It appears to me that these various modalities have resulted in conflicting results for some conditions (e.g. Maternal, Neonatal and congenital were judged to be most understudied in table 2 while these are presented with the group of Research surplus in Fig 3; also Injuries were slightly more likely to be understudied than cardiovascular diseases (77.1 vs 61.9) in Table 2 but appeared on the null line in Fig 3). The authors may wish to examine and comment on these discrepancies in their discussion.

Comment: Thanks for your comment. We examined this and found that we have mistakenly labelled some of the columns in Figure3. Now, we have corrected this and think that the results of all figures and tables are consistent.

Change: We amended Figure3.

Discussion

The discussion of the paper is not necessarily supported by the analyses and was largely dissociated from the results. For example, while the findings point to a relative lack of studies on NCDs such as cancer and cardiovascular disease, the discussion focused solely on the literature that addressed infectious diseases with no reference to NCDs.

Comment: Thanks for your comment. We tried to support the discussion with available literature, including NCDs which we discussed in a separate paragraph on page 8; line 16-21.

Change: We amended the discussion to accommodate these changes: the paragraphs discussing infectious diseases (page 8; line 29-33) has been rearranged to make it clear: "The observed discordance between the focus of the published research from Palestine and disease burden can be explained by several factors including (i) researchers’ interest and expertise; (ii) limited research infrastructure and funding resources which drive researchers to accept the funder agenda which is not commonly align with local community needs[23-25]; and (iii) lack of communication between policy makers and researchers to agree on national research priority[20, 22]."

Also, while the current submission was not about RCTs specifically, a big portion of the discussion (p. 7-8) was devoted to compare the study findings with others in the literature focusing on those that examined gaps in health research using RCTs (refs 9, 15 and 16). Clearly, some conditions are more appealing to be examined using RCTs than others.

Comment: Thanks. We agree with the reviewer, but these were the only relevant citations that we have found relevant to developing countries.
While the authors alluded to one limitation issue (failure to capture unpublished reports and the grey literature), the paper lacked a clear and focused statement on other limitations. It should be sufficiently discussed that findings from this study and other similar reviews are very much dependent on the search strategy and the inclusion/exclusion criteria used. For example, the exclusion in this paper of lab-based studies - which are generally the main focus of cancer-related research in the Arab region- is likely to result in an undercount of cancer-related studies.

Comment: We thank the reviewer.

Change: We revised our limitations to include these limitations: page 9; line 1-4 "A limitation to this review is that we searched two databases only (PubMed and Scopus), so we may have missed few relevant studies not indexed in PubMed or Scopus, as well as unpublished studies. Similar, excluding lab-based studies might influence the results of our study (for instance, cancer studies are frequently lab-based, therefore, more likely missed due to our eligibility criteria)."

Also, the authors point to certain strengths for their study which in my view are only the standard practice in such a research and not unique to this study (e.g. the independent and in duplicate screening, or the use of the GDB internationally developed measures to assess burden).

Comment: We thank the reviewer.

Change: We have deleted this sentence as per requested.

An ample space was devoted in the discussion on the implications of the findings (p. 9-10), yet the suggested recommendations do not necessarily emanate from the results and/or were not related to the focus of the paper. The observed discordance between the focus of the research output and disease burden cannot be explained by "limited research infrastructure and resources or because of lack of communication between policy makers and researchers" as the authors note in their discussion (p. 8, lines 32-33).

Comment: We thank the reviewer. The above mentioned factors explain the nature of current published research in Palestine.

Change: We modified this paragraph (page 8; line 29-33) to be: "The observed discordance between the focus of the published research from Palestine and disease burden can be explained by several factors including (i) researchers' interest and expertise; (ii) limited research infrastructure and funding resources which drive researchers to accept the funder agenda which is not commonly align with local community needs[23-25]; and (iii) lack of communication between policy makers and researchers to agree on national research priority[20, 22]."

This paper was not about the quality of the research output in Palestine to conclude that it is important to 'Enhance the capacity of national researchers to conduct prioritized research' (p. 9), and additionally there was no reference in the paragraph here about how enhancing capacity can lead to the conduct of prioritized research. Also, there were several messages written under the
recommendation 'Foster dialogue between researchers, policy makers, funders and end users/patients' (p. 9) that do not necessarily fit either with the subtitle or with the overall theme of the paper. The implications of the findings need to be revised in a succinct and more focused approach that is in harmony with the main research questions addressed in the manuscript.

Comment: We thank the reviewer. We agree with the reviewer with this points. Though our findings are limited to the mismatch between current published research and disease burden, we realise that addressing this issue is not a one-step fix. We believe, as supported by the literature that change is a process and in the implication we have outlined the main steps for this process.

Change: We revised the implications as requested.

Finally, the paper needs major edits and revision. The language is often ambiguous with several grammatical and typo errors. For example, one can easily spot 4 such instances in p 3, (Lines 2-3: The statement "which consists of West Bank, including East Jerusalem, and Gaza Strip" appeared to refer to the MENA countries and not to Palestine; Lines 13-15, statement is incomplete; Lines 23-24: "Burden of disease is a measure 'that' represents"; Line 31, 'weak' instead of 'week'; and line 33: "however, there are -instead of is- no previous studies" .. etc)

Comment: We thank the reviewer.

Change: We have revised the text in this section for any ambiguity, any grammatical and typo errors.

The reference list is not aligned with the text. I may have missed these, but it appears that the two studies on sub-Saharan Africa referred to in the discussion on p. 8 are lacking in the ref list.

Comment: Thanks.

Change: We have revised the references to ensure that they are aligned with the text. We also added the two references per requested.

Specific comments

Title:

I am not convinced that the paper is about 'relation' (as is stated in the title). It is more a 'comparison' between output and disease burden. And again on P.4, line 4, the paper is not about 'association' in as much about comparison/contrast or differences/fit between research output and disease burden.

Comment: Thanks.

Change: We revised the title and the objectives as per requested. Title: "A comparison between health research output and burden of disease in Arab countries: evidence from Palestine". We also modified the objectives page 4; line 1-3 "In this study, we compared the distribution of
output of published health and medical research from Palestine and the distribution of burden of disease in Palestine, and investigated whether specific conditions/diseases are under- or over-investigated."

Page 4:

Line 26: Did the two reviewers abstract the needed data also in duplicates?

Comment: Thanks. Yes, two reviewers extract the data independently and in duplicate.

Change: We added the following sentence in the methods: page 4; line 26 "and in duplicate";

The authors note that they abstracted data on impact factor (IF) and number of citations. The limitations of the IF are well noted in the literature. Also, the fact that recent articles are not given thorough opportunity to be cited as the older ones and because the quality of research output is not the focus of this submission, I would suggest that these two parameters be removed from the results. Findings in the case of IF and number of citations may raise more questions than answers.

Comment: We agree with the reviewer.

Change: We deleted the results related to impact factor (IF) and number of citations from the manuscript.

A comment as to the rationale behind considering the first author rather than the corresponding author affiliation in assessing collaborations may be warranted.

Comment: Thanks. We considered the first author as they are usually responsible for most of the work.

Change: We clarified this on the methods: page 4; line 28 "(i.e. the author who did most of the work)"

Page 5:

Line 3: "international/or NGO". It is not clear why the investigators tagged NGO to the international source of funding, it can also apply to local source of funding. Suggest deleting the NGO.

Comment: Thanks. We tagged them together because we have just few reported that their source of funding was from NGO. But we will delete them as suggested.

Change: We deleted the NGO as a source of funding.
Lines 6-7: Why did the investigators choose two sources for assessing the disease burden in Palestine (refs 12 and 14); and what was their decision if there were some discrepancies between the published estimate in the Journal (Lancet) and the one online (Visualization data) source?

Comment: Thanks. We agree with the reviewer that this was not clear. We used the online data as our source for this study. But we cited the journal article as a ref for the GBD study in general.

Change: We revised the methods/ Burden of disease section to clarify that ref 14 used for data and ref 12 is just a ref for the GBD study.

Line 22: The description related to the difference between published articles for each disease/condition with the expected/proportionate number of published is blurred and needs elaboration. It is not clear how were the figures on research deficit and research surplus in Figure 3 estimated?

Comment: Thanks.

Change: We added the following sentence to the methods: page 5; line 26-28 "(e.g. the expected number of published articles for CVD = % of burden caused by CVD × total published reports = 39.3% × 511 = 201)"

Page 6:

Lines 15-16: Suggest revising to "increased over time, almost doubling every 5 years (starting with the %s associated with the earlier years and then the latter ones)

Comment: We thank the reviewer.

Change: We revised this sentence per requested: "increased over time, almost doubling every 5 years (13% between 2000-2004, 32% between 2005-2010, and 55 between 2011-2015)."

Line 25: Suggest moving the sentence "Table 1 provides information on the general characteristics of the included articles" to the beginning of the paragraph (line 10).

Comment: We thank the reviewer.

Change: We moved the sentence.

Many sentences in the section entitled 'Characteristics of included studies' start with a number (eg. 152 on line 11; 279 in line 15; 368 in line 20.. etc). Avoid starting sentences with a number.

Comment: We thank the reviewer.

Change: We revised the paragraph to avoid starting the sentences with a number.
Lines 5-6: Suggest moving the sentence "The distribution of Palestinian health research output and disease burden (DALYs and deaths) across the diseases/conditions is presented in Table 2" to P. 6, line 28.

Comment: We thank the reviewer.

Change: We moved the sentence.

Line 8: the authors picked up cancer, cardiovascular, and maternal, neonatal and congenital conditions as the most understudied topics (based on the DALYs per 100,000 population per study and on deaths per 100,000 population per study). Table 2 shows that 'Musculoskeletal and Neurological' conditions and 'Injuries' were also understudied when considering DALYs but less so when considering death rates. Whilst high case fatality rates for some conditions may inflate death rates (e.g. cardiovascular diseases and cancer), disabling conditions with no cure and long duration (e.g. Musculoskeletal and Neurological) inflate DALYs. Such a kind of distinction may be warranted in the discussion.

Comment: We thank the reviewer. We included this point in our discussion.

Change: We revised the discussion to highlight this point: page 8; line 29-34 "Important to note is the slight discrepancies between the findings related to comparing research output to the death rates and DALYs respectively. Whilst high case fatality rates for some conditions may inflate death rates (e.g. cardiovascular diseases and cancer), disabling conditions with no cure and long duration (e.g. Musculoskeletal and Neurological) inflate DALYs. For instance, we found that 'Musculoskeletal and Neurological' and 'Injuries' conditions were understudied when considering DALYs but less so when considering death rates".

Page 8:

Lines 22-23: As mentioned earlier, discrepancies may have been additionally arisen because of differences in inclusion/exclusion criteria, notably the lab-based studies that characterize cancer-related output in the Arab region

Line 26: skew 'towards or away' from infectious diseases?

Comment: Thanks.

Change: We added "toward".

Line 28: suggest to revise to "with the burden of disease, and found that funding was more strongly associated with DALYs (r=0.62, p < 0.001) than the number of deaths (r=0.40, p=0.03)"

Comment: We thank the reviewer.
Change: We revised this sentence per requested.

Page 9:

Line 4-9, from "important to note… controlled trials": this sentence fits better in a section on limitations.

Comment: We thank the reviewer.

Change: We revised this sentence per requested.

Line 28: add here in addition 'university research boards'

Comment: Thanks.

Change: We added "university research boards".

Line 33: McGregor et al study on priority-setting initiatives was about low and middle Income countries; and hence the statement (McGregor et al found that the majority of the identified priority-setting initiatives took place at the global level with a developing countries focus) is not reflective of the findings of McGregor et al paper.

Comment: We thank the reviewer. Although that McGregor et al reported that in their abstract anf article, we agree with the reviewer that the wording of this sentence needs to be revised.

Change: We revised this sentence in the discussion to be: "In a recent comprehensive assessment of health research priority setting initiatives in developing countries, McGregor et al found that the majority of the 91 identified priority-setting initiatives took place at the global level (i.e. those with global health agenda such as eradicating specific diseases) with a developing countries focus[21]."

Table 1:

Consider revising the categories for the publication year as (2000-2004; 2005-2010; 2011-2015)

Comment: Thanks.

Change: We revised this sentence per requested.

Line 43: define non-RCTs, and how is this category different from the other observational studies listed?

Comment: Thanks. We elaborated on this in the methods. By non-randomised controlled trials, we mean interventional studies which is not randomised such as controlled trials.
Change: We modified the methods to highlight this: page 5; line 5 "non-randomised intervention study (e.g. controlled trials)". Also, we revised Table 1 to be "Non-randomised interventional studies" instead of "Non-RCT".

Table 2:

Comment: need to elaborate on the calculations of the % of total DALY and death as well as DALY and deaths per study in the methods. And what do these measures signify, i.e. what does a higher value or a lower value mean?

Consider adding the source of the data on DALYs and death rate as a footnote.

Comment: Thanks.

Change: We revised Table 2 as per requested. We added the calculations of % of total DALY and death as well as DALY and deaths per study as well as the meaning of these values as footnotes. We also added the reference to the sources of data as a footnote.

Reviewer #2:

A very important paper with implications to academics, researchers and health policy makers. I have some comments:

Abstract:

Line 12: "examining" should be "examined"

Comment: Thanks.

Change: We revised the abstract per requested.

Line 19: "chronic respiratory", should be "chronic respiratory diseases"

Comment: Thanks.

Change: We revised the abstract per requested.

Line 26: "Arab countries", it should be "Palestine". Cannot generalize.

Comment: Thanks.
Change: We revised the abstract per requested.

Introduction:

* Line 5: "Bank and Gaza" add respectively "Bank and Gaza, respectively"

Comment: Thanks.

Change: We revised the sentence per requested.

* Line 13-15: The three lines require revision, as they are not clear

Comment: Thanks. We agree with this comment.

Change: We revised the sentence to be: "Substantial gaps are existed between the health research that is needed and that is conducted, which indicates a lack of appropriate prioritisation of health research"

* Line 15: "In their Lancet seminal report", year of report is needed

Comment: Thanks.

Change: We added "2009" to the sentence.

* Line 20: "The Institute of Medicine". It is an old reference, 1998. Better use a recent one, if the only available, indicate that it is from the US.

Comment: Thanks.

Change: We replaced the reference to another one and revised the sentence to be: "There is a need for accountable, transparent, and sustainable approach for research prioritisation on the basis of societal needs (e.g. disease burden)[8]."

* Line 23: "measure represents" should be "measure that represents"

Comment: Thanks.

Change: We revised the sentence per requested.

Methods:

* Page 4, line 27: Did you use the impact factor of the journal at the time of publication or at the time of study?
Comment: Thanks. As per reviewers' comments, we deleted the impact factor and citation from the methods and results. Therefore, this is no longer an issue.

Change: none specific.

* Page 4, line 28: The number of citations for the publications of 2015, particularly at the end of the year would be less due time. How did you address this?

Comment: Thanks. As per reviewers' comments, we deleted the impact factor and citation from the methods and results. Therefore, this is no longer an issue.

Change: none specific.

* Page 5, line 2: No need for caps

Comment: Thanks.

Change: We revised the sentence per requested.

* Page 5, line 3: Source of funding: The "not reported and not clear" should be listed last.

Comment: Thanks.

Change: We revised the sentence per requested.

* Page 5, line 3: "international/or NGOs": Where all the NGOs international?

Comment: Thanks. Only few national NGOs were reported as a source of funding. Therefore, and based on previous comment from the first reviewer we decided to take this out.

Change: We deleted the NGO as a source of funding to minimise the misunderstanding.

* Page 5, lines 8-13: No need for defining deaths, DALYs, YLL, YLDs

Results:

* Page 6, lines 6-8: No need to repeat the numbers since they are in the figure, just provide %.

Comment: Thanks.

Change: We amended the paragraph as per requested.

* Page 6, line 10: "Regional institutions". What was the definition of regional? MENA or EMR?

Comment: Thanks. MENA region.
Change: We defined that in the methods page 4 line 31: "regional (i.e. the Middle East North Africa 'MENA' region)".

* Page 6, line 18: "less than 5 times or not at all", not at all should not be included with less than 5. It should be "none", "1-5"

Comment: Thanks. This sentence has been deleted as described above.

Change: no changes needed now.

* Page 6, lines 23-25: If you do not put the exact % then they will not correspond with the exact figures in the table. Write instead, "sources of funding were not mentioned in about two thirds of the articles. Of those reporting, over two thirds were international". NGOs are not mentioned in text.

Comment: Thanks.

Change: We revised the sentence per requested.

* Page 7, line 10: put coma before "respectively"

Comment: Thanks.

Change: We revised the sentence per requested.

* Page 7, line 11: replace "over-studies" by "over-studied"

Comment: Thanks.

Change: We revised the sentence per requested.

* Page 7: Double check if figures 2 and 3 are mixed up. "Figure 2 shows that research output was poorly correlated with disease burden, irrespective of whether measured in terms of DALYs (rho = -0.116, p = 0.7) or death (rho = 0.217, p = 0.5)." If you go to figures, it is figure 3.

Comment: Thanks. We agree with the reviewer.

Change: We corrected the number of figures.

Discussion:

* Page 10: In the section "Enhance the capacity of national researchers to conduct prioritised research", I suggest urging academic institutions to have health research plans that addresses the diseases that play a major contribution in the burden of disease in Palestine.
Comment: Thanks. We also highlighted this in the research priority setting paragraph.
Change: We revised the paragraph per requested.

* Page 7, line 28: "maternal and neonatal" should be "maternal and neonatal diseases"

Comment: Thanks.
Change: We revised the sentence per requested.

* Page 8, Line 2: RCT has been used earlier. Use RCT throughout the discussion and not in full.

Comment: Thanks.
Change: We revised the manuscript to replace RCT in full as per requested.

* Page 8, Line 27: "infectious diseases [20]" should be "towards infectious diseases [20]."

Comment: Thanks.
Change: We revised the sentence per requested.

* Page 9, Line 31:"developin" should be "developing"

Comment: Thanks.
Change: We revised the sentence per requested.

* Page 10, line 16: "and should be "change to "should be"

Comment: Thanks.
Change: We revised the sentence per requested.

* Page 10, lines 19-23: In my opinion, there is no need these lines are they are detailed.

Conclusions:

* Page 10, line 26: "Non-communicable disease" add s "Non-communicable diseases"

Comment: Thanks.
Change: We revised the sentence per requested.

Tables:
* Table 1, Line 20: Should be 2011-2015

Comment: Thanks.

Change: We revised the sentence per requested.