PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Do quality improvement initiatives for diabetes care address social inequities? Secondary analysis of a systematic review.
AUTHORS	Lu, Jacquie Boyang; Danko, Kristin; Elfassy, Michael; Welch, Vivian; Grimshaw, Jeremy; Ivers, Noah

VERSION 1 – REVIEW

REVIEWER	Victor Mogre University for Development Studies Tamale, Ghana
REVIEW RETURNED	02-Sep-2017

GENERAL COMMENTS	In this study authors envisage to review the literature regarding the ways in which QI studies targeted interventions toward disadvantaged populations, looked at risk factors for the disadvantaged patient population, and analysed the impact of interventions on disadvantaged subgroups. The manuscript is nicely written. However, I think there are a number of issues authors will have to address to improve the readability and methodological rigour of the manuscript. Introduction Lines 34-37 should be revised …. ways in which QI studies targeted interventions toward disadvantaged populations, looked at risk factors for the disadvantaged patient population, and analysed the impact of interventions on disadvantaged subgroups. Abstract Authors should include a short background in the abstract and also add more information regarding the objective. The paper looks at QI in disadvantaged groups however the current objective in the abstract does not include that. Methods Although authors have indicated that methods used in the review has been published in a protocol, it is important they provide brief description of the key areas that should be covered in a systematic review. These include the following: a. Information sources i.e. databases that were searched b. How the search for literature was executed as well as a search strategy c. How was screening done? Was it from title to abstract and then to full text? At all of these stages what were considered and who was responsible? Was it done independently done? d. Quality assessment: How did authors evaluate the quality of the reviews to be included? What quality assessment tool was used? e. Were they variations from the published protocol? If there is authors should do well to state it?

REVIEWER	Paolo Giorgi Rossi AUSL Reggio Emilia
REVIEW RETURNED	06-Sep-2017

GENERAL COMMENTS	General comment The paper reports a secondary analysis on a systematic review. The topic is interesting and relevant because many interventions aimed at changing behaviours or at increasing compliance to treatment often are more effective in less disadvantaged groups, thus increasing the existing inequalities. The authors decided that summarising the evidence about which intervention have a positive or a negative impact on inequalities is out of the scope of the review. I can understand this point because this would mean entering in the detail of each intervention. So this review is picture of how researchers take into consideration the issue of inequalities in diabetes QI interventions. In my opinion the review would be much more informative if it would also report, as a whole, how often the general interventions (universal?) have a negative or positive impact on the differences between groups that they took into consideration. This is fundamental information to comment the results: the higher the risk of generating inequalities (sometimes even to have negative absolute effect in the most disadvantaged!) the more important to take into consideration inequalities. The authors declare, among the limits of the study, that they only used the primary publication. I do not think this limit is acceptable, but it could be easily resolved because the secondary publications should be among the excluded studies of the original review. Finally, the authors present two different types of equity oriented trials, targeted and general. For countries with a universalistic National Health Service, targeted interventions often bring the risk of creating dedicated services for disadvantaged people (or at least two ways of access that can then create indirectly segregation). I suggest to show the results distinguishing the setting: countries with universalistic health service and insurance based countries. Furthermore the conclusion should be taken separately for targeted interventions and general interventions because they have different implications. Specific comments Abstract Conclusions: “a substantial gap”. Why do you call this a substantial gap? What was the expected proportion of trials looking at inequalities, 100%? Why? It is really needed for all this kind of interventions? I can surely agree with you that there is substantial gap, but this would be my opinion, based on my values and not on an objective evaluation of what would be expected or needed in this field of research. Furthermore, the sentence is relevant for the “general trials” but not on the “targeted trials”. Your results would be of 100% of equity relevant trials if all the trials were targeted, but I am not sure this would be a good scenario for those countries with a universalistic National Health Service, because it may mean that we are going towards dedicated health services for disadvantaged… I suggest to clearly distinguish the conclusion for targeted and for general interventions. Strengths and limits PROGRESS-plus: The authors say “objective and standardised”, surely standardised, but I do not understand why objective.

	This is not a criticism about the classification that is probably the best in use to date. The classification is based on evidences, but it has elements of subjectivity: for example keeping together ethnicity, culture, language and separate religion is a value-based choice, not an evidence-based choice, that in the case of diabetes is not very effective (there are some issues related to ethnicity in South Asian or Caribbean's due to common genetic or epigenetic background, that are independent from culture and language). Focus on primary papers: see general comment. Last bullet point. In my opinion the most relevant problem for conducting a systematic review on this issue is that often the relevant information is not reported in the abstract. Thus even if the authors of primary literature use standardised methodology is the screening phase failing. In the methods it is not clear if the search for equity relevance among the trials identified for the primary scope of the review was conducted through a screening of abstract and titles or through an analysis of the full text for all trials. Background I suggest to report also those examples in which it has been demonstrated that the interventions had negative effects on the most disadvantaged people (I know many examples for interventions for obesity prevention: Broccoli Pediatrics 2015; Langnase 2004; Plachta-Danielzik et, al 2007 and Plachta-Danielzik et al, 2011; for a review see Olstad 2016). Methods Please clarify how/where you searched the equity terms among the studies identified in the primary systematic review: abstract or full text analysis? If in the full text, how? Electronically, reading… Results Last paragraph: in the comparison between the two calendar periods, are we interested in percentages or in the volume of research conducted? I do not know, but the authors should afford this point in the discussion. I suggest to present data per health system setting: universalistic or insurance. Conclusions Third paragraph, last sentence "given that these populations…": the sentence is correct at least generally, but it is not true for all. In the case of diabetes care, for example educational level and religion and gender and sexual preferences would never identify a group at higher risk than age alone or ethnicity alone (in the case of diabetes). Furthermore the conclusion that we need more interventions targeted to groups with more than one risk facto does not take into consideration feasibility issues or the prevalence of these sub-sub-groups in the population. This sentence is too vague and is not justified simply by the observation that only few papers addressed these groups. If the authors identify a group defined by characteristics that are then easy to use to target the intervention, has an appreciable prevalence in the population and has really higher risk, then they can see if it is actually neglected or not. For conclusions, please see the general comments. I strongly suggest at least to present and discuss how often occurs that the general interventions increase inequalities. Supplemental table 1

	Many of the definitions and justifications of the factors are too vague. For example age you could consider disadvantaged older people, but some others could consider children; there is no direction for the employment status; on the other hand for other factors there is a clear explanation about what is expected (residence, disability, ethnicity).

VERSION 1 – AUTHOR RESPONSE

REVIEWER 1
2. Introduction: Lines 34-37 should be revised …. ways in which QI studies targeted interventions toward disadvantaged populations, looked at risk factors for the disadvantaged patient population, and analysed the impact of interventions on disadvantaged subgroups.

This line has been revised to read – "In this secondary analysis of that review, we examine the extent to which health equity concerns were considered in diabetes QI studies. Specifically, we quantified the proportion of QI studies QI studies targeted interventions toward disadvantaged populations, looked at risk factors for disadvantage in the patient population, and/or analyzed the impact of interventions on disadvantaged subgroups."

3. Abstract: Authors should include a short background in the abstract and also add more information regarding the objective. The paper looks at QI in disadvantaged groups however the current objective in the abstract does not include that.

Background and revised objectives have been added to the abstract -

"Background
Socially disadvantaged populations carry a disproportionate burden of diabetes-related morbidity and mortality. There is an emerging interest in quality improvement (QI) strategies in the care of patients with diabetes, however, the effect of these interventions on disadvantaged groups remains unclear.

Objective
This is a secondary analysis of a systematic review that seeks to examine the extent of equity considerations in diabetes QI studies, specifically quantifying the proportion of studies that target interventions toward disadvantaged populations and/or conduct analyses on the impact of interventions on disadvantaged groups."

4. Methods: Although authors have indicated that methods used in the review has been published in a protocol, it is important they provide brief description of the key areas that should be covered in a systematic review.

The methodology section has been revised to include this information.

REVIEWER 2
5. The paper reports a secondary analysis on a systematic review. The topic is interesting and relevant because many interventions aimed at changing behaviours or at increasing compliance to treatment often are more effective in less disadvantaged groups, thus increasing the existing

inequalities. The authors decided that summarising the evidence about which intervention have a positive or a negative impact on inequalities is out of the scope of the review. I can understand this point because this would mean entering in the detail of each intervention. So this review is picture of how researchers take into consideration the issue of inequalities in diabetes QI interventions. In my opinion the review would be much more informative if it would also report, as a whole, how often the general interventions (universal?) have a negative or positive impact on the differences between groups that they took into consideration. This is fundamental information to comment the results: the higher the risk of generating inequalities (sometimes even to have negative absolute effect in the most disadvantaged!) the more important to take into consideration inequalities.

The following has been added to the results section – "Among the 31 general trials, 12 trials found differential effects among disadvantaged subgroups when intervention outcomes were further analyzed. Notably, 6 trials found differences based on the sex of participants, 5 trials found differences based on age, and 4 trials found differences based on race/ethnicity group."

6. The authors declare, among the limits of the study, that they only used the primary publication. I do not think this limit is acceptable, but it could be easily resolved because the secondary publications should be among the excluded studies of the original review.

The exclusion of secondary publications was thought to appropriate. Primary publications show that equity concerns are being prioritized by the study authors – an important aspect of what we wanted to document in our qualitative analysis.

7. Finally, the authors present two different types of equity oriented trials, targeted and general. For countries with a universalistic National Health Service, targeted interventions often bring the risk of creating dedicated services for disadvantaged people (or at least two ways of access that can then create indirectly segregation). I suggest to show the results distinguishing the setting: countries with universalistic health service and insurance based countries. Furthermore the conclusion should be taken separately for targeted interventions and general interventions because they have different implications.

The breakdown of studies by health system has been attached to Table 1, with the following addition under “Study characteristics” – "Interestingly, 73.7% of equity-relevant trials were based in countries with private health insurance systems, whereas 32.6% of equity-relevant trials were based in countries with universal health insurance. However, this finding may simply reflect the predominance of publications from the United States included within this review, contributing 66 non-equity studies and 63 equity-relevant studies."

Within a universalist model of health care, there are still many patients who face issues with inability to access health due to cost. For example, in Canada, where it would be considered to have universal health care, hospitalizations and physician services are covered but pharmaceutical products are not. Patients without private insurance or additional forms of drug coverage may be unable to afford the cost of medications – particularly relevant in diabetes where cost of oral hyperglycemic agents, insulin, glucometers, etc. can add up. We would argue that including these populations within the benefit analysis of interventions is necessary to achieve equity in health access even within a universal model.

8. Abstract
Conclusions: “a substantial gap”. Why do you call this a substantial gap? What was the expected proportion of trials looking at inequalities, 100%? Why? It is really needed for all this kind of interventions? I can surely agree with you that there is substantial gap, but this would be my opinion, based on my values and not on an objective evaluation of what would be expected or needed in this

field of research. Furthermore, the sentence is relevant for the “general trials” but not on the “targeted trials”. Your results would be of 100% of equity relevant trials if all the trials were targeted, but I am not sure this would be a good scenario for those countries with a universalistic National Health Service, because it may mean that we are going towards dedicated health services for disadvantaged… I suggest to clearly distinguish the conclusion for targeted and for general interventions.

The conclusion section has been revised - "Less than a third of diabetes QI trials included equity-relevant considerations, limiting the relevance and applicability of their data to disadvantaged populations. There is a need for better data collection, reporting, analysis, and interventions on the social determinants of health that may influence the health outcomes of patients with diabetes."

The gap points to the need for researchers to incorporate equity considerations into their research – ie. analyze how the intervention may have differentially impacted different groups of people (white vs. racialized groups, high SES vs. low SES, low vs. high education status). Not necessarily that researchers have to specifically target a subgroup. Researchers often have this stratified data available but do not undertake relevant subgroup analyses. The results of these analyses may inform future practice and policy changes, and may have implications for how interventions can be extrapolated and applied in different locations and health systems.

9. Strengths and limits
PROGRESS-plus: The authors say “objective and standardised”, surely standardised, but I do not understand why objective. This is not a criticism about the classification that is probably the best in use to date. The classification is based on evidences, but it has elements of subjectivity: for example keeping together ethnicity, culture, language and separate religion is a value-based choice, not an evidence-based choice, that in the case of diabetes is not very effective (there are some issues related to ethnicity in South Asian or Caribbean’s due to common genetic or epigenetic background, that are independent from culture and language).

This sentence has been so revised – "The use of the PROGRESS-Plus framework provides a standardized approach for identifying and analyzing equity relevant information within research publications."

10. Last bullet point. In my opinion the most relevant problem for conducting a systematic review on this issue is that often the relevant information is not reported in the abstract. Thus even if the authors of primary literature use standardised methodology is the screening phase failing. In the methods it is not clear if the search for equity relevance among the trials identified for the primary scope of the review was conducted through a screening of abstract and titles or through an analysis of the full text for all trials.

This has been clarified in the methodology section – the screening of equity relevance was performed based on a thorough reading of the full text of all trials.

11. Background: I suggest to report also those examples in which it has been demonstrated that the interventions had negative effects on the most disadvantaged people (I know many examples for interventions for obesity prevention: Broccoli Pediatrics 2015; Langnase 2004; Plachta-Danielzik et, al 2007 and Plachta-Danielzik et al, 2011; for a review see Olstad 2016).
We have added some examples of this from the included studies under “Conclusion” as a follow up to the previous suggestion to report “how often the general interventions have a negative or positive impact on the differences between groups that they took into consideration”.

"Trials designed for the general population which then conducted stratified analyses point to the importance of considering PROGRESS-Plus factors when designing and examining interventions. In fact, QI strategies designed for the general population may not be accessible to disadvantaged groups or may not have the same efficacy in disadvantaged populations and may inadvertently lead to an increase in diabetes related health disparities. For example, a general trial looking at telehome monitoring systems as an affordable and efficient means to monitor patients with diabetes showed greater efficacy in patients who were male, elderly, and/or more educated.[16] Another study examining the efficacy of telephone-based weight loss programs to improve glycemic control found the intervention outcomes differed between Caucasians and non-Caucasians.[19]. Alternatively, adding care guides to the primary care team was more likely to have benefits for patients on Medicaid rather than patients with other forms of health insurance in the United States.[20] These findings emphasize the need for better data collection, reporting, and analysis on the social determinants of health that may influence the health outcomes of patients with diabetes."

12. Methods
Please clarify how/where you searched the equity terms among the studies identified in the primary systematic review: abstract or full text analysis? If in the full text, how? Electronically, reading.

This has been clarified in the methodology section – the screening of equity relevance was performed based on a thorough reading of the full text of all trials.

13. Results
Last paragraph: in the comparison between the two calendar periods, are we interested in percentages or in the volume of research conducted? I do not know, but the authors should afford this point in the discussion.

I think we are interested in the overall volume of research conducted that takes into account equity-relevant data. Of note, the proportion of targeted trials being conducted has increased. The language in this section has been modified to reflect this information.

"Table 3 examines the extent of equity-relevance in diabetes QI trials over time. Prior to 2007, there were 41 equity-relevant trials out of 128 diabetes QI studies. In the period from 2007 to 2014, there were 54 equity-relevant trials out of 150 diabetes QI studies. Targeted trials were responsible for 56.1% of equity-relevant trials prior to 2007. This number increased to 75.9% of equity-relevant trials in the period from 2007 to 2014. The most notable increases in the absolute number of targeted studies occurred with occupation, education, and disability."

14. Conclusions
Third paragraph, last sentence “given that these populations…”: the sentence is correct at least generally, but it is not true for all. In the case of diabetes care, for example educational level and religion and gender and sexual preferences would never identify a group at higher risk than age alone or ethnicity alone (in the case of diabetes). Furthermore the conclusion that we need more interventions targeted to groups with more than one risk facto does not take into consideration feasibility issues or the prevalence of these sub-sub-groups in the population. This sentence is too vague and is not justified simply by the observation that only few papers addressed these groups. If the authors identify a group defined by characteristics that are then easy to use to target the intervention, has an appreciable prevalence in the population and has really higher risk, then they can see if it is actually neglected or not.

I believe this is a fair statement. For example, we know that the racial minorities often concentrate in discrete geographic locations, whether that is due to the availability of social networks, employment opportunities, or socioeconomic status. It is unclear whether one or all of these factors may impact this group’s response to health interventions. An intervention targeting low SES alone may not be able to capture the entire racial minority group, whereas an intervention targeting culturally-relevant practices for the minority group may not capture all low SES patients in that geographic location. There is diversity within each PROGRESS-Plus category. Simply targeting one category with no consideration for the others may oversimplify the causes of inequity in a population.

15. Supplemental table 1
Many of the definitions and justifications of the factors are too vague. For example age you could consider disadvantaged older people, but some others could consider children; there is no direction for the employment status; on the other hand for other factors there is a clear explanation about what is expected (residence, disability, ethnicity).

The definitions and examples have been clarified to have more directionality.

VERSION 2 – REVIEW

REVIEWER	Victor Mogre University for Development Studies, School of Medicine and Health Sciences, Ghana
REVIEW RETURNED	30-Nov-2017

GENERAL COMMENTS	Authors have done a great job revising the manuscripts in light of the comments. However, the aspect regarding quality assessment of the studies still lacking. Authors should indicate whether quality assessment was done or not? If it was done, which type of tool was used? If no they should explain why quality assessment was not done?

REVIEWER	Paolo Giorgi Rossi AUSL Reggio Emilia, IRCCS. Reggio Emilia, Italy
REVIEW RETURNED	16-Nov-2017

GENERAL COMMENTS	The paper has been improved and the authors aswered to all comments. There are some concepts that are clearer in the rebuttal than in the modiified text. I suggest to read both and to carefully choice the clearest and most convincing sentences to put in the final text. discussion, last paragraph before conclusion, the sentence " We believe the effectiveness of interventions may vary based on the participant population and the existing health system" is not really correct, actually many authors showed this possible effect in their trial and some systematic reviews found it in many other preventive interventions. This sentence can be re-worded to mke it clear that it is not an authors' belief, this is an evidence observed in many contexts, interventions and disease, this is why it is so important to give stratified results.

VERSION 2 – AUTHOR RESPONSE

REVIEWER 1: Authors have done a great job revising the manuscripts in light of the comments. However, the aspect regarding quality assessment of the studies still lacking. Authors should indicate whether quality assessment was done or not? If it was done, which type of tool was used? If no they should explain why quality assessment was not done?

Response: Quality assessment was done using an adapted version of the Cochrane's EPOC Risk of Bias assessment tool. We can certainly report this within our methods section but it may not be relevant to this paper as we did not use the risk of bias assessments to select studies or modify effect summaries (in this secondary analysis - since no outcomes were reported, just study methods for design and analysis).

REVIEWER 2: The paper has been improved and the authors answered to all comments. There are some concepts that are clearer in the rebuttal than in the modified text. I suggest to read both and to carefully choice the clearest and most convincing sentences to put in the final text. Discussion, last paragraph before conclusion, the sentence " We believe the effectiveness of interventions may vary based on the participant population and the existing health system" is not really correct, actually many authors showed this possible effect in their trial and some systematic reviews found it in many other preventive interventions. This sentence can be re-worded to make it clear that it is not an authors' belief, this is an evidence observed in many contexts, interventions and disease, this is why it is so important to give stratified results.

Response: This paragraph has been revised to read - "As our objective was to assess the extent to which researchers considered equity-relevant factors, we did not analyze the effect of equity-relevant factors on study outcomes. The effectiveness of interventions often varies based on the participant population and the existing health system. Based on the limited primary data that we have from targeted and general trials, it is difficult to make definitive conclusions about which interventions or QI strategies are effective or ineffective in reducing health disparities and/or improving health outcomes for disadvantaged groups without oversimplifying the issue and potentially misleading future enquiry."