Poor availability of essential medicines for women and children threatens Africa's progress towards SDG 3

Dear Editor,

Many thanks for all your invaluable comments and suggestions from the reviewer. We have attempted to respond to and make necessary changes to the manuscript in light of your comments and suggestions. Our responses to your specific comments are below. In addition, I am submitting both the clean copy of the manuscript together with the copy with tracked changes.

Comments to Author:

Editorial comments:

1. Please change your title to: "Poor availability of essential medicines for women and children threatens progress towards Sustainable Development Goal 3 in Africa"
The title has now been changed to "Poor availability of essential medicines for women and children threatens progress towards Sustainable Development Goal 3 in Africa"

2. Please provide evidence of MoH approval(s) for your study.
This retrospective study uses data that is openly available with WHO and also openly available and published as grey literature by the countries. Collection of SARA data is often cleared by the Ministry of health and in the countries, data collection is not anonymous. In fact, when done as a census survey where data are collected from all facilities, the Ministry of Health is often interested to know which specific facilities have important gaps, and this knowledge helps them prioritize the facilities for interventions. Similar retrospective studies have also been published without ethics clearance[1,2]

Reviewer: 1

Comments to the Author
I can see some improvements, but I feel there is still some work to do. Please find below specific comments and suggestions:

Thank you very much for this article which had quite some interesting parts in it. This study takes an original research angle on availability of maternal and child essential medicines in health facilities. I do have some comments and remarks though. I have put the more specific comments into the attached PDF file.

Ethics
Authors did not seek for Ethics approval. This could raise some concerns on facilities' data, as it is possible for instance to identify health facility through the SARA data. Please, authors must clarify this.

[1] DA Spiegel, B Droti et al 2017. Availability of Surgical Services in Africa. BMJ Open 2017;7: e014496. doi:10.1136/bmjopen-2016-014496
[2] Moucheroud C 2018. Service readiness for noncommunicable diseases was low in five countries in 2013-2015. Health Affairs Vol 37, No. 8. https://doi.org/10.1377/hlthaff.2018.0151

As already explained above, this retrospective study uses data that is openly available with WHO and also openly available and published as grey literature by the countries. Collection of SARA data is often cleared by the Ministry of health and in the countries, data collection is not anonymous. In fact, when done as a census survey where data are collected from all facilities, the Ministry of Health is often interested to know which specific facilities have important gaps, and this knowledge helps them prioritize the facilities for interventions. Similar retrospective studies have also been published without ethics clearance

p.1 line 32
There are more than 4 figures
We feel that the figures add understanding of the data and would prefer that they remain

p.7 lines 144-145
"Magnesium sulfate is recommended for treating severe pre-eclampsia and eclampsia which are associated, annually, with an estimated 50,000 maternal deaths worldwide".
Put a reference
A reference for the above statement has now been included in the manuscript

p.8 lines 167-168
"Data analysis was carried in STATA version 11.0 using methods that are appropriate for the survey design used in each country".
What does it mean? Please clarify

Methods
The methods section is not clear. I would invest more time in making clear distinction between the primary SARA work and the secondary work of authors from SARA.
Were authors part of SARA surveys that took place in different countries and thus presenting results from their primary data? If yes, please make it clear and describe how this was carried out, your role, ……
If no, have you used secondary data from SARA? If yes, please
1/ Describe how SARAN survey is conducted
2/ Describe what the authors have done from the existing SARA data.

We have now added some text to the manuscript to improve the clarity of the methods uses. The methods section now reads as follows:

WHO , with funding support from partners such as Global Fund and Global Alliance for Vaccine Initiative (GAVI), provides technical support to countries to conduct SARA surveys every 1-2 years to assess if health facilities meet the basic standards to provide essential service. SARA surveys are conducted at the request of, and in conjunction with, Ministries of Health to support health service planning. Service availability refers to the physical presence of delivery of services. Service readiness meanwhile refers to the ability of health facilities to provide a service – measured through the availability of items such as medicines, trained staff, guidelines, equipment, and laboratory services[8].

The number of facilities surveyed during SARA is often the maximum feasible, depending on available funds. The facilities are sampled nationally using multi-stage stratified random sampling. Stratification

is by facility level and public-private ownership. Where sample size permits, further stratification is done by urban-rural location. Data are collected using WHO's standard SARA core questionnaire, with adaptations to country context for facility classifications, subnational administrative units, and staff categories[9]. The SARA core questionnaire is a validated tool that focuses on key health services and the ability or readiness of facilities to offer the services. The questionnaire does not attempt to measure the quality of services or resources, but it can be used in conjunction with additional modules such as management assessment or quality of care. Availability is assessed by direct observation of the in-date medicine in the facility, regardless of quantity present.

Data are collected through key-informant interviews by trained local data collectors working to established methods under the strict supervision of survey coordinators. Data are collected using both paper questionnaire and mobile electronic devices using census and survey processing (CSPro) software, with paper questionnaires serving as a backup. Quality assurance that includes repeat of surveys in 10% of participating facilities is often provided by external agencies (e.g. John Snow, Inc) or a locally sourced academic institution.

The assessment of availability of priority life-saving medicines in this study is based on 24 of the 30 medicines recommended by WHO : 12 for women and 12 for children (Table 2). Oxytocin is the preferred uterotonic for the prevention and management of postpartum haemorrhage.[10] Misoprostol tablets are recommended when oxytocin is not available or cannot safely be used. Magnesium sulfate is recommended for treating severe pre-eclampsia and eclampsia which are associated, annually, with an estimated 50,000 maternal deaths worldwide[11]. Calcium gluconate is used for treatment of magnesium sulfate toxicity. Dexamethasone or betamethasone injections can improve foetal lung maturity in the case of preterm birth. WHO Guidelines recommend oral rehydration salts (ORS) and zinc supplementation for the treatment of childhood diarrhoea.[12] Artemisinin-based combination treatments are first-line oral treatments for malaria with artesunate rectal formulations recommended for the pre-referral treatment of children with severe malaria.[13] Oral amoxicillin is first-line treatment for community-acquired pneumonia in children; ampicillin, gentamicin and ceftriaxone are used to treat severe pneumonia in children as well as neonatal and maternal sepsis. Vitamin A is used for treatment and prevention of Vitamin A deficiency which is a recognized risk factor for severe measles; a common cause of death in low and middle-income countries (LMICs). Paracetamol and morphine meanwhile are the recommended medicines for relieving pain.

Data analysis was carried in STATA version 11.0 using methods that are appropriate for the survey design in each country. This involves application of sampling weights to reflect the probability of selection of facilities at each stage of the sampling design and using STATA commands for survey data for all analyses. Details of the analysis are as follows: Each variable was assigned value **1** if the medicine was available and **0** if unavailable. Sampling weights were then applied. The percentage of facilities that had the medicine was calculated (sum of facilities with item/total number of facilities *100) with 95% confidence interval overall and then by facility level, public-private ownership, and urban-rural location. The mean of the medicines was then calculated together with the 95% confidence interval overall and then by facility level, public-private ownership, and urban-rural location – ensuring that all medicines carry the same weight as each facility is expected to have them.

Analysis was done only among facilities that indicated that they provided maternal and child health services. as some facilities, by policy design, are not meant to provide certain services.

p.8 lines 167-168

"Analysis was done only among facilities that indicated that they provided maternal and child health services".

This could constitute a huge biais. There is usually a big gap between what is planned in country policy and what is recommended. According to national policy, you will find the basic and comprehensive Emoc. However, for multiple reasons, you find many of those health facilities not providing services. So, limiting analysis only on facilities indicating that they provide services missleads the gap. It would be important to also analyse according to all health facilities that are supposed to provide service (all basic EmOC), even if some of them are not providing, if not, this should be discussed.

Many thanks for these comments. Indeed, analysis of readiness is done only among facilities that provide certain services. WHO does this on purpose; largely as a way of assessing whether facilities that offer a service have the basic items to provide them. The aim is to show that facilities offering a service have or do not have the necessary items to do so; and this is one of the key reasons for doing the SARA surveys. It is true that such analysis can also be done among all facilities regardless of whether they offer services for which readiness is assessed. We have done this severally but often also get asked why we have done this. The question we often get asked, and rightly so, is how we can expect facilities to stock items for a service they do not offer, as doing so overestimates the problem?

It is true that facilities that are expected to offer certain services, as defined by policy, do not offer them. SARA has specific questions on these and they get asked to all facilities. The question asks whether or not the facility offers a specific service. When the facility says yes, then subsequent questions on items for offering the service are ~~then~~ asked. If the facility says no, they do not offer the service, questions on items for offering the service are skipped.

Nonetheless, the results in this manuscript show that availability of essential medicines for mothers and children in facilities that offer the services is low. If the availability is low in facilities saying they offer the services, then it is likely closer to zero in facilities that do not specifically offer child and/or maternal services.

p.9 lines 197-200

"Of the 12 essential medicines for women that were enquired about, only 1% of the facilities in Uganda, Mauritania and Sierra Leone, and none in the rest of the countries had all of them (Table 3). For child health services, none of the facilities had all the nominated 12 essential medicines (Table 4)".

There is a need for more in-depth analysis. For example, there are 3 EMs that seem to pose real challenge in all countries Misoprostol, Azithromycin, Cefixime. So these EMs disturb your means. You should consider doing sensibility analysis, by excluding these EMs and see whether there is a real improvment in term of availability. Therefore, a recommendation could be to focus more on these EMs that concentrate the majority of challenges.

Many thanks for this comment and it is a correct observation. Indeed, one outlier value can alter the mean value. However, the aim of SARA surveys is to demonstrate the provision of essential services at minimal standards and all items enquired about during surveys are expected to be available. We think that sensitivity analysis cannot be used meaningfully in this case. We think that, if data allowed, a more meaningful analysis would have been an examination of association of factors with the mean availability using linear regression. This would involve a careful build-up of a conceptual model and identification of

proximate to distal determinants of availability. Even then, doing so would add little value to understanding of the availability as facilities offering a specific service should meet the minimum standards regardless of confounding variables. Excluding an extremely low outlier value from analysis would underestimate the shortage of essential medicines. The lack of in-depth analysis notwithstanding, this study provides some useful and actionable understanding of gaps in essential medicines availability for mothers and children.

p.12 lines 274-275
"the low availability of azithromycin (range 1% to 11% of facilities) and cefixime (1% to 16%) in part reflects their restriction to use in specialist or referral facilities in most of the eight countries". Indicate the number of countries and also give justification of why in those countries Azithromycin and Cefixime were restricted to use in referral facilities.

The decision to restrict access to certain health care facilities or levels of care is a decision taken by the MoH as part of the development of national essential medicines lists and treatment guidelines. In addition, both azithromycin and cefixime are included in the WHO Watch list of antibiotics that should be used judiciously for selected indications only. Restricting access to nominated groups of clinicians or referral facilities allows better monitoring of use of these agents.
See page 3 of this document:
https://www.who.int/medicines/publications/essentialmedicines/EML_2017_ExecutiveSummary.pdf

p.14 lines 311-312
"Inadequate training and support for health workers in the use of some these priority medicines has been reported elsewhere".
Please correct the sentence

We are not sure what the issue is with the sentence. We have consequently deleted it if it will not be clear to the readers

p.15 lines 333-335
"If the burden of maternal and child morbidity and mortality in sub-Saharan Africa is to be addressed, further efforts are needed to strengthen regulatory systems to ensure the quality of products in circulation"
The quality of drugs is not in line with your objectives and findings from your results. The conclusion must directly derive from your findings and align with your objectives.

Thanks for this observation. This section has now been deleted from the manuscript.

p.22 line 506
ACT: correct and put Artemisinin-based combination therapy
Thanks. This has been corrected in the document

p.24 line 514
ACT: correct and put Artemisinin-based combination therapy
Thanks. This has been corrected in the document

Tables 3 and 4:

- **All numbers should be right aligned:**

Thanks for this observation. All the figures have now been aligned to the right.

- **With only 12 medicines, better to use the median, given that you have in some cases many extreme values.**

Thanks for this comment. Indeed, one extreme value can alter the mean and for this reason, the median is often used. We have, however, used the mean because WHO's assessment of readiness to offer a service is based on the mean; not the median. We would prefer to use the mean in most cases to align this with similar publications.

~~Thanks for this observation. Indeed, one extreme value can alter the mean. We have not u~~

Figure 1:

the title indicates mean availability whereas the figure is represented by the median

Thanks for this comment. Indeed, the box and whisker plot summarises the mean availability of the medicines, with the median of the mean values shown on the boxplot. We do not see anything wrong with the figure and have left it as it is.

~~Will leave you to deal with these formatting issues.~~

Reviewer: 2

Comments to the Author

- The authors of the article have addressed the vast majority of our concerns, however, we believe that ethical issues still exist.
- Just because a study is commissioned and/or conducted by and/or with a country's Ministry of Health does not mean that it is ethical.
-In the absence of having obtained authorization from an ethics committee for the authorization of research, we believe that authors must provide authorization for publication from the ministries of health of the countries concerned.

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As mentioned above, this retrospective study uses data that is openly available with WHO and also openly available and published as grey literature by the countries. Collection of SARA data is often cleared by the Ministry of health and in the countries, data collection is not anonymous. In fact, when done as a census survey where data are collected from all facilities, the Ministry of Health is often interested to know which specific facilities have important gaps, and this knowledge helps them prioritize the facilities for interventions. Similar retrospective studies have also been published without ethics clearance[3,4]

Comments to the Author

-The title refers to a possible causality between the poor availability of essential drugs and universal health coverage, while the article does not at any time correlate the poor availability of drugs with

[3] DA Spiegel, B Droti et al 2017. Availability of Surgical Services in Africa. BMJ Open 2017;7: e014496. doi:10.1136/bmjopen-2016-014496

[4] Moucheroud C 2018. Service readiness for noncommunicable diseases was low in five countries in 2013-2015. Health Affairs Vol 37, No. 8. https://doi.org/10.1377/hlthaff.2018.0151

universal health coverage. I think we need to review the title.
-I think the article is too descriptive, it only describes the availability of the 24 priority drugs in health centres. An analytical component is missing.

-Lack of problematization, the availability of essential medicines is already widely documented in Africa.
-Not taking into account each context of implementation of the WHO guidelines on priority medicines for women and children in each country, difficult to assess the availability of medicines without taking into account the context of implementation of this public policy in each country. A quantitative study alone cannot identify all the contours. A joint study was to better analyse the causes and consequences of the poor availability of priority medicines for women and children in the eight countries.
-What is the period of your study? The duration of the survey conducted?
These cross-sectional assessment surveys usually take 5-8 months; from planning to final report.

-Who are the key informants who have been selected?????? And how were they chosen?
The key informants were the in-charges, their deputies, and administrators of the health facilities and of various departments/units of the health facility where the questionnaire was administered. The key-informants were not pre-selected as they are already defined in the health facility management structure. The Ministry of Health always sent a letter to the health facilities about these assessment surveys specifically asking the in-charges to make themselves available for the interviews. The interviewers upon visit to the health facilities asked to meet with the in-charge of the health facilities who then introduced the interviewers to the department/unit in-charges. We however did not think providing all these details within the word limit of the manuscript would add any value other than being academic.

-Has the study been submitted to an ethics committee?
These assessment surveys are sanctioned by the Ministry of Health. Ethics approval is often not required as it is purely about an inventory of services in the health facilities and capacity of health facilities to offer the services. The study is also never anonymous as the Ministry of Health often wants to know where the gaps are in the health system. In fact, when done as a census survey, the Ministry of Health often wants to identify facilities that have critical gaps and prioritise them.

-How were the private health centres selected in your study?
How facilities were selected has now been made clearer. Facilities in SARA surveys are sampled nationally and through multi-stage stratified random sampling method. Stratification is often by facility level and managing authority (public-private ownership). Where the sample size allows, further stratification is done by urban-rural location. Usually, all subnational administrative units are included in the assessments, but we left these out because they are not comparable. We plan to examine, in another issue, the subnational variation through an equity lense.

-The evaluation of the availability of medicines and services was carried out between 2013 and 2015. However, in the data analysed, it is clear that for Togo, for example, 2012 data were used for the analysis.

Many thanks for this observation. We have searched but failed to find in the document where we may have erroneously stated that evaluation of availability was carried between 2013 and 2015. The evaluation used data from 2012-2015; we included all available usable SARA data at the time and this included Togo 2012.

-**Why have the data been for different years depending on the country? What was the duration and frequency of the surveys in each country? On what basis was the number of health centres surveyed per country chosen?**

Many thanks for this observation. The data are available for different years because the SARA surveys are not done in the countries in the same year. The surveys are country-specific and countries decide when they want to do a SARA survey. WHO recommends that countries should do SARA surveys once every 1-2 years and, to ensure use of the results, they should align the surveys with key events such as annual, mid-term review or end-term evaluation of their health sector strategic plans. However, given shortage of resources, adherence to this recommendation is poor; the reason there are few SARA surveys in the African Region.

-Why did you separate the drugs from children and women in the study?

The study does not demonstrate or compare the two categories, so why separate them since the two were conducted on the same sample, it was necessary to make a list of drugs common to both this should lighten the study.

Thanks for this comment. We thought it is essential to report availability of drugs for women and children separately because WHO separately defines the essential medicines list for women and children. Also given that SARA surveys are done to prioritise areas for intervention, separating the drugs helps to show where the critical gaps are for women and children.

-Why did you choose private health centres knowing that it often does not respect the national drug supply scheme for the purchase of drugs in the vast majority of countries in Africa?

Many thanks for this comment. We included private facilities in this assessment, as also often done by WHO, because the private sector is part and parcel of the health system. Excluding them from any study for whatever reason would be a fundamental mistake because they see just as many patients as the public sector. We also respectfully disagree that the private sector does not respect national drug supply scheme. Most of the private sector facilities source their medicines locally i.e. medicines the governments have allowed to be sold in the country though they may use a different supply chain from that used by the public sector.

-The discussion did not take into account the national drug supply system of each country, does not allow for a comparison between countries. Too descriptive and not analytical.

Many thanks for this comment. It is true that this retrospective study did not examine the association of factors with medicines availability for mothers and children. This is largely because WHO does not collect data on determinants of the medicines. We however strongly believe that this paper presents valuable and usable information for decision-making by both partners and governments. WHO's concept of SARA is that, regardless of the country's national supply system, facilities offering a service should have the basic items to offer them. The results of SARA surveys are then used retrospectively to do a systems assessment. Cross-country comparison in the paper is limited due to different data points.