PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Delays in seeking, reaching and access to quality cancer care in sub-Saharan Africa: a systematic review
AUTHORS	Lombe, Dorothy; Mwamba, Monde; Msadabwe, Susan; Bond, Virginia; Simwinga, Musonda; Ssemata, Andrew Sentoogo; Muhumuza, Richard; Seeley, Janet; Mwaka, Amos; Aggarwal, Ajay

VERSION 1 – REVIEW

REVIEWER	Carpenter, Kendall Boston Children's Hospital
REVIEW RETURNED	15-Sep-2022

GENERAL COMMENTS	This paper is very well written with strong research methodology for a systematic review and provides an important review of a necessary but fragmented area of research. Overall, I think the authors did a nice job both explaining the need for this review as well as their methods. The discussion is thorough and, for the most part, supported by their findings. The biggest issue that I found with the paper (which was more likely an oversight in uploading than a problem with the study itself) was that I did not see a full search strategy in the supplemental materials. It will be important to include this in the final manuscript. I think this paper will be a great addition to the literature, please see comments/edits for individual sections below: Introduction: - Page 4 Line 9, add units (per 100,000 people) - For the sentence in Page 4 lines 31 - 34 discussing three distinct groups, please provide citations that back up these groupings in the literature - Page 5 line 10, I would add that robust study design would help compare results between studies - Page 5 lines 36 - 38: strengthen and clarify your research question. Potential edit " to identify common factors influencing diagnostic delays of adult solid tumors and highlight areas that require further study whether that be specific countries, tumor types, or settings, in order to help target resources and inform interventions to that reduce cancer survivorship disparities globally. " Methods: - Ensure full search strategy available in Appendix - Why is the study limited to adult solid tumors? Why not include hematologic malignancies and/or pediatric cancers? I don't think it is a problem that you didn't but I would just justify the choice explicitly.

- Add "reasons for delay" to data items list

Results:
- For table 2 I would indicate the frequency with which each of these delays were discussed in the literature to give some sense of which ones were most common/universal across study settings. You do that a little in the written text but I think it would be helpful to have in the table as well.
- Page 12 Line 33: add citation
- For receiving quality of care (Page 12 lines 36-46), consider adding a sentence about diagnostic limitations if that was a prominent finding in your literature review because I know that comes up a lot as a factor influencing diagnostic delay in the pediatric literature.

Discussion
- I would link your discussion of external funding in Page 13 lines 20 - 24 more directly to your findings about the narrowness of the literature available (limited countries/diagnoses investigated in the literature). Might be worth bringing Page 4 lines 31-34 from the introduction into the discussion to further strengthen this paragraph.
- Page 13 line 51, remove the comma between the words healthcare and appointments
- Page 14 line 33, remove "and managing follow-up" as it seems redundant to the survivorship pathway

Great work!!

REVIEWER	Martins, Tanimola
	University of Exeter, Primary Care
REVIEW RETURNED	09-Oct-2022

GENERAL COMMENTS	In this study, the authors attempted a systematic review of the evidence regarding cancer diagnosis in Sub-Sahara Africa. Overall, this is an important subject area, but I have major concerns about the manuscript in its current form.
	Introduction
	This section appears rather lengthy and could have included relevant findings of recent systematic reviews of evidence in the region. Delays in cancer diagnosis may arise at various stages of patients' journey (and the predictors of the same) may vary considerably depending on the diagnostic route. So, contextualising the barriers to diagnosis in relation to the diagnostic route may help improve clarity and, by extension, delineate the research question. It was not always clear what the authors' main research questions or objectives were.
	The term 'delay' is controversial as it invokes a victim-blaming perception - suggesting that delay in medical help-seeking is mainly behavioural, whereas the disease biology may be attributable. It may also suggest negligence on the part of the providers when this is not always the case. So, using the so-called 'three delay framework' was a surprise when other simple and widely recognised frameworks – such as The Aarhus statement on cancer diagnosis and Andersen Model of Total Patient Delay - could provide more insights into the complexities of cancer diagnosis in the region. Nonetheless, the authors description of how they applied the three delay framework was brief and uninformative.

	Methods
	The methods section lacks clarity and inadequate at times.
	What is the justification for restricting their search to articles published between 1995 and 2021, line 42? Were grey literatures considered?
	Appendix 1 does not include the search strategy.
	"We excluded studies that included paediatric populations, haematologic malignancies…" Any reasons for these exclusions?
	It is unclear what data they extracted from included studies, why, and how. In line 10 (Data items), "Data extracted included the year of article publication, country of study, demographic characteristics... What about data regarding the review main outcomes? Reporting the what, why, and how of data extraction is necessary for a systematic review.
	Selection Process Line 3 "We used the systematic review tool Covidence" for what? Also, were there any conflicts?
	What is the justification for using the Hoy et al. tool, and was this tool applied to the selected study? How did they apply this tool to the 3 or more study designs in this review (cohort, cross-sectional, and Delphi)? What were the main findings from their risk of bias assessment?
	Results
	The numbers in Figure 2 don't add up.
	The description in Table 1 is not very helpful. Traditionally, in addition to the current list, such Tables may include a summary of methods, outcome measures, and main findings.
	Under country and setting profile, the numbers don't add up to 57 studies. The same goes for the description under tumour types - this is not very helpful to say the least.
	The sub-headings (Seeking delay, Reaching care, Receiving quality care) and reported findings under each are, for the most part, broad and not always linked to the selected studies.
	Discussion
	Authors interpretation were not sufficiently linked to the review findings. Also, this review has considerably more limitations than acknowledged here.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Dr. Kendall Carpenter, Boston Children's Hospital
Comments to the Author:
This paper is very well written with strong research methodology for a systematic review and provides an important review of a necessary but fragmented area of research. Overall, I think the authors did a nice job both explaining the need for this review as well as their methods. The discussion is thorough and, for the most part, supported by their findings. The biggest issue that I found with the paper (which was more likely an oversight in uploading than a problem with the study itself) was that I did not see a full search strategy in the supplemental materials.

Thank you. Apologies for this oversight. This has now been added to appendix 1 in the supplementary material.

It will be important to include this in the final manuscript. I think this paper will be a great addition to the literature, please see comments/edits for individual sections below:

Introduction:
- Page 4 Line 9, add units (per 100,000 people)

Thank you this has been added

- For the sentence in Page 4 lines 31 - 34 discussing three distinct groups, please provide citations that back up these groupings in the literature

Thank you we have added references to strengthen this section. Please see Page 4 Paragraph 3.

- Page 5 line 10, I would add that robust study design would help compare results between studies

Thank you this has been added.

- Page 5 lines 36 - 38: strengthen and clarify your research question. Potential edit " to identify common factors influencing diagnostic delays of adult solid tumors and highlight areas that require further study whether that be specific countries, tumor types, or settings, in order to help target resources and inform interventions to that reduce cancer survivorship disparities globally. "

Thank you for this excellent suggestion we have revised this sentence as per your recommendation.

Methods:
- Ensure full search strategy available in Appendix
Apologies for this oversight this has been added in supplementary material as Appendix 1.

- Why is the study limited to adult solid tumors? Why not include hematologic malignancies and/or pediatric cancers? I don't think it is a problem that you didn't but I would just justify the choice explicitly.

Thank you a justification for exclusion has been added. Please see Page 5, paragraph 4.

- Add "reasons for delay" to data items list

Thank you this has been added. Please see Page 6, paragraph 5.

Results:
- For table 2 I would indicate the frequency with which each of these delays were discussed in the literature to give some sense of which ones were most common/universal across study settings. You do that a little in the written text but I think it would be helpful to have in the table as well.

Thank you very much for this feedback. We have included the data extraction sheet as part of the supplementary material to enhance clarity
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Page 12 Line 33: add citation

Thank you this citation has been added. Please see Page 15, paragraph 2.

- For receiving quality of care (Page 12 lines 36-46), consider adding a sentence about diagnostic limitations if that was a prominent finding in your literature review because I know that comes up a lot as a factor influencing diagnostic delay in the pediatric literature.

Thank you. This was a factor and we have added a sentence to this effect as recommended. Please see Page 7-8, paragraph 3.

Discussion
- I would link your discussion of external funding in Page 13 lines 20 - 24 more directly to your findings about the narrowness of the literature available (limited countries/diagnoses investigated in the literature). Might be worth bringing Page 4 lines 31-34 from the introduction into the discussion to further strengthen this paragraph.

This is an excellent suggestion. We have added a sentence to this paragraph to better link the concerns re: external funding and the limited research undertaken both from a country and tumour type perspective.
Please Page 16, paragraph 4.

- Page 13 line 51, remove the comma between the words healthcare and appointments

Thank you. This has been removed.

- Page 14 line 33, remove "and managing follow-up" as it seems redundant to the survivorship pathway

Thank you this has been removed.

Great work!!

Reviewer: 2
Dr. Tanimola Martins, University of Exeter, University of Exeter
Comments to the Author:
In this study, the authors attempted a systematic review of the evidence regarding cancer diagnosis in Sub-Sahara Africa. Overall, this is an important subject area, but I have major concerns about the manuscript in its current form.

Introduction
This section appears rather lengthy and could have included relevant findings of recent systematic reviews of evidence in the region. Delays in cancer diagnosis may arise at various stages of patients' journey (and the predictors of the same) may vary considerably depending on the diagnostic route. So, contextualising the barriers to diagnosis in relation to the diagnostic route may help improve clarity and, by extension, delineate the research question. It was not always clear what the authors' main research questions or objectives were.

Thank you for this feedback. We have added more clarity to our research question and have appropriately referenced contemporary literature in the manuscript on page 5-6 paragraph 4

The term 'delay' is controversial as it invokes a victim-blaming perception - suggesting that delay in medical help-seeking is mainly behavioural, whereas the disease biology may be attributable. It may also suggest negligence on the part of the providers when this is not always the case. So, using the so-called 'three delay framework' was a surprise when other simple and widely recognised frameworks – such as The Aarhus statement on cancer diagnosis and Andersen Model of Total Patient Delay - could provide more insights into the complexities of cancer diagnosis in the region. Nonetheless, the authors description of how they applied the three delay framework was brief and uninformative.

Thank you for this feedback. We have enhanced the text throughout the manuscript. The term delay is used frequently in the literature when considering diagnostic and treatment of cancer, and as you refer to, is used in the "Anderson Model of Total Patient Delay". The frameworks themselves provide a way of conceptualising the issues and aggregating key themes and whilst we are aware of the frameworks you present, we have chosen the three delays framework because it also provided a research design framework, centred on literature assessment, consensus building and detailed qualitative investigation from the patient, health care provider and community perspective which has been used in other disease types. In terms of its application we have provided a description as to the core features of each delay in this framework and has provided a basis for synthesising our results which can be used to inform future policy and practice.

The methods section lacks clarity and inadequate at times.

Thank you for this feedback. We have enhanced the clarity of this section by including subheadings on page 6

What is the justification for restricting their search to articles published between 1995 and 2021, line 42?

Thank you for this query. We restricted the timeframe to allow for relevance and applicability of findings to the evolving health care systems with time
Were grey literatures considered?
Thank you for this question. No grey literature was not considered due to the high propensity of risk of bias given the diverse country settings and type of health research question being investigated.

Appendix 1 does not include the search strategy.
Thank you for this feedback. We have loaded the supplemental material correctly which includes the search strategy as Appendix 1

"We excluded studies that included paediatric populations, haematologic malignancies…" Any reasons for these exclusions?

Thank you for this question. Due to the heterogenous nature of the health system we were investigating, inclusion of paediatric cancers would have required complex considerations beyond the scope pf this article. Paediatric cancer pathway is separate from adult cancers in most health systems.

It is unclear what data they extracted from included studies, why, and how. In line 10 (Data items), "Data extracted included the year of article publication, country of study, demographic characteristics... What about data regarding the review main outcomes? Reporting the what, why, and how of data extraction is necessary for a systematic review.

Thank you for this question and feedback. We have included the Data extraction output as part of the supplemental material as Appendix 2 due to the volume of material

Selection Process Line 3 "We used the systematic review tool Covidence" for what?

Thank you for seeking this clarification. We have clarified the use of Covidence tool and provided a reference on page 6 paragraph 5

Also, were there any conflicts?

Thank you for this question. Conflicts were resolved by AA. This has been stated with more clarity under study selection page 6 paragraph 5

What is the justification for using the Hoy et al. tool, and was this tool applied to the selected study? How did they apply this tool to the 3 or more study designs in this review (cohort, cross-sectional, and Delphi)? What were the main findings from their risk of bias assessment?
Thank you for questions. The clarity of the quality assessment has been enhanced in methods and results sections on page 7 and 8

Results
The numbers in Figure 2 don't add up.
Thank you for this feedback. The numbers have been corrected

The description in Table 1 is not very helpful. Traditionally, in addition to the current list, such Tables may include a summary of methods, outcome measures, and main findings.
Thank you for this valuable feedback. We have the outputs as part of the supplementary material in Appendix 2.

Under country and setting profile, the numbers don't add up to 57 studies. The same goes for the description under tumour types - this is not very helpful to say the least.

Thank you for the feedback. We have forfeited Figure 3

The sub-headings (Seeking delay, Reaching care, Receiving quality care) and reported findings under each are, for the most part, broad and not always linked to the selected studies

Thank you for this valuable feedback. We hope the adding Appendix 2 will enhance the clarity of the findings also linked in Table 2

Discussion
Authors interpretation were not sufficiently linked to the review findings. Also, this review has considerably more limitations than acknowledged here. Use of two databases –although note that a second piece of work looking at qualitative work has been done with further databases.

Thank you for this valuable feedback. We hope the included text and materials in through out the manuscript have enhanced clarity. We have added a paragraph on limitations page 18

VERSION 2 – REVIEW

REVIEWER	Martins, Tanimola
	University of Exeter, Primary Care
REVIEW RETURNED	26-Jan-2023

GENERAL COMMENTS	I am pleased to review an improved version of the paper, with appreciable changes to the methods and results sections. However, I have a few further queries regarding the results section.
	Table 1 is not very informative. If the aim here was to indicate aspects of the Three-Delay-Framework addressed, then a textual description may be sufficient, bearing in mind these elements are also covered in Appendix 2.

	Appendix 2 is unreadable due to small font sizes and excessive information - the bulk of data presented in the Table did not inform their synthesis or interpretation. Authors may consider adding this Table to the main texts but restricting it to fewer columns, for instance: author and date, country of study, methods - to include design and sample size, participants' characteristics (average and gender), education, delay types, and reasons. There is a mismatch between the factors highlighted in Table 2 and the textual description in the results section (from line 35). In other words, the synthesis of results is insufficient. Here, authors may consider categorising these factors further, given the numbers. For instance, they could group them under psychological, economical, and sociocultural factors at individual, interpersonal, and environmental levels. My point here is that, a further re-categorization of the factors may help simplify their synthesis and interpretation. Finally, authors should check for typos throughout the paper. e.g., The common roots of the reasons for delays at each level of seeking, reaching... Also, in the introduction, "Delay 1 seeking care: This is the delay in recognizing illness and deciding to seek appropriate medical help outside the home". Do they mean the delay between the period of recognizing an illness and deciding to seek appropriate medical help? They have addressed my other concerns.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 2

Dr. Tanimola Martins, University of Exeter, University of Exeter Comments to the Author:

I am pleased to review an improved version of the paper, with appreciable changes to the methods and results sections. However, I have a few further queries regarding the results section.

Table 1 is not very informative. If the aim here was to indicate aspects of the Three-Delay-Framework addressed, then a textual description may be sufficient, bearing in mind these elements are also covered in Appendix 2.

Thank you very much. We do appreciate your feedback and perspective on this. We would prefer to avoid removing this table as it follows our narrative approach. Our justification within the author group we do think this is an important table as it highlights the design of the studies and setting which will enable contextualisation for future epidemiological research in this area. For example, we provide information on the tumour type, setting and size of the patient sample as well as the type of research design. This is the more pertinent elements rather than the aspect of the three-delay framework covered. The items listed are considered as the core pieces of information relative to Appendix 2 and in previous work we have seen this as a core element of the presentation of the systematic review results. Appendix 2 is a reference document.

Appendix 2 is unreadable due to small font sizes and excessive information - the bulk of data presented in the Table did not inform their synthesis or interpretation. Authors may consider adding this Table to the main texts but restricting it to fewer columns, for instance: author and date, country of study, methods - to include design and sample size, participants' characteristics (average and gender), education, delay types, and reasons.

Thank you for this feedback. We have amended Appendix 2 to make this easier to review. It remains as our reference document.

There is a mismatch between the factors highlighted in Table 2 and the textual description in the results section (from line 35). In other words, the synthesis of results is insufficient. Here, authors may consider categorising these factors further, given the numbers. For instance, they could group them under psychological, economical, and sociocultural factors at individual, interpersonal, and environmental levels. My point here is that a further re-categorization of the factors may help simplify their synthesis and interpretation.

Thank you very much for this feedback. To follow the advice of our esteemed reviewer, which we value and yet to maintain our narrative approach, we have created five sub-themes namely psychological, sociocultural, economic, geography, health services within Table 2 and aligned the barriers within these. To avoid repetition we have maintained the text, which references where these raw data points can be found for the reader.

Finally, authors should check for typos throughout the paper. e.g., The common roots of the reasons for delays at each level of seeking, reaching... Also, in the introduction, "Delay 1 seeking care: This is the delay in recognizing illness and deciding to seek appropriate medical help outside the home". Do they mean the delay between the period of recognizing an illness and deciding to seek appropriate medical help?

Yes, thank you for the clarification

They have addressed my other concerns.

Reviewer: 2

Competing interests of Reviewer: I declare no competing interest.

VERSION 3 – REVIEW

REVIEWER	Martins, Tanimola University of Exeter, Primary Care
REVIEW RETURNED	15-Mar-2023

GENERAL COMMENTS	Authors have now addressed most of my concern. Could they double check the references are in line with the journal recommendation. e.g., unclear authors for 1,2 and 21. Ref 60 includes authors email addresses