

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Research waste management: using HTA and guideline development as a tool for research priority setting the NICE way.
AUTHORS	Sharma, Tarang Choudhury, Moni Rejón-Parrilla, Juan Carlos Jonsson, Pall Garner, Sarah

VERSION 1 – REVIEW

REVIEWER	Amanda Blatch-Jones (nee Young) National Institute for Health Research Evaluation, Trials and Studies Coordinating Centre (NETSCC) UK
REVIEW RETURNED	31-Oct-2017

GENERAL COMMENTS	<p>This is a well written paper that raises an important question. The authors have provided a rich account of the NICE process into the prioritization process and the importance for research and the avoidable waste agenda.</p> <p>There are a couple of points I would like to raise.</p> <ol style="list-style-type: none">1. The abstract is not in a standardized format - Although this is not a piece of research rather a review of process, the abstract does not have any structure to it.2. Limitations are mentioned after the abstract but are not mentioned in the Discussion section of the paper. A conclusion of the limitations could easily be included in the discussion section.3. Page 5 of 19, third paragraph - priorities found by NICE are one of many contributions to the NETS programmes mentioned, which feed into the commissioning process. Where and how was the information retrieved from to complete Table 2? In terms of cost, number of projects etc. The commissioning process was actually founded in 1993 (which was then the HTA programme only, namely National Coordinating Centre for Health Technology Assessment: NCCHTA). This was the uniqueness of the programme as it was set up to deal with commissioned calls only, (later 2005/2006 the researcher-led process began). <p>Small point - NETSCC abbreviation isn't provided.</p> <ol style="list-style-type: none">4. Discussion - small point: top of page 10 of 19 - font style different.5. Discussion - page 10 of 19, third paragraph: the JLA is now part of the NIHR, carried out via NETSCC.6. Discussion - No limitations are discussed.7. I was disappointed not to have read a final concluding paragraph which summed up the purpose (so what factor) of the paper and its review of NICE. It would strengthen the paper if there was a
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	<p>conclusion, rather than the current ending.</p> <p>8. References - some of the links access are more than one year old - can these be reviewed and updated?</p> <p>9. References - it would be worth reviewing the following NETSCC, Research on Research publication - Turner S, Bhurke S, Cook A. Impact of NIHR HTA Programme funded research on NICE clinical guidelines: a retrospective cohort. Health Research Policy and Systems (2015) 13:37.</p> <p>10. References - it might be worth considering in terms of prior research and evidence gaps (page 3 of 19, introduction section) Bhurke S, Cook A, Tallant A, Young A, Williams E, Raftery J. Using systematic reviews to inform NIHR HTA trial planning and design: a retrospective cohort. BMC Medical Research Methodology 2015; 15:108</p> <p>Overall, the paper discusses a valid and important area of the work NICE does. It highlights the how and why to the processes used by NICE and explains how these prioritized areas are followed through to evidence (primary research or reviews).</p> <p>As this is not a research paper but a review of NICE, some of the checklist boxes above are not applicable. However, some could be seen as relevant in terms of how data were retrieved.</p>
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REVIEWER	Robert Fraser Terry TDR (the Special Programme for Research and Training in Tropical Diseases), Switzerland
REVIEW RETURNED	22-Nov-2017

GENERAL COMMENTS	<p>The title needs some clarification or edit. The paper describes an overview of the NICE processes but is less clear how these processes explicitly reduce waste e.g. reducing waste is not listed as part of research priority setting process. It is unclear from the process described here how the quality of evidence is assessed when producing guidance and setting priorities for example the use of GRADE tables.</p> <p>I have added minor comments for clarification in the attached Adobe file.</p> <p>-The reviewer also provided a marked copy with additional comments. Please contact the publisher for full details.</p>
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VERSION 1 – AUTHOR RESPONSE

As for the editorial comments, we have done the following:

- Upon checking your Scholar One, I have noted that you completed the relevant checklist but uploaded none. If there's any please upload the file on scholar one under the file designation Research Checklist. More information on research checklists can be found on the Equator Network here: <http://www.equator-network.org/>. Kindly indicate in the research checklist a page number against each criterion.

Please note that we had selected "There is no relevant guideline" under research checklist (as this is a more health policy type article which as far as the authors are aware does not have any relevant checklist for reporting within EQUATOR).

- Please include Figure legends at the end of your main manuscript.
Please note we have now done this.

- Please EMBED TABLES to your main document file and remove the uploaded file to avoid confusion once embedded.
Please note we have now done this.

- Please ensure to have the same DATA SHARING STATEMENT both in your main document and in Scholar One.
Please note we have now done this.

- Please provide a more detailed contributor ship statement. It needs to mention all the names/initials of authors along with their specific contribution/participation for the article both in your main document and Scholar One.

Please note we have now done this.

For your comment: - Kindly re-upload FIGURES with at least 300 dpi resolution in either TIFF or JPG format.

The figures were created in word itself and are not images as such. We have now converted them to images (TIFF) but this process has cost its resolution but hope it is still within permissible standards.

We are happy to work with your publishing team, if accepted to find the best solution for this.

Editorial Comments:

We agree with reviewer 1's comment about the abstract. We appreciate that for irregular research articles such as this one many of the suggested sub-headings in our instructions for authors are not applicable. However, we would be grateful if you could work on providing a more detailed and structured abstract that states the paper's aims/purpose and describes what this overview covers (as well as any conclusions if applicable).

Many thanks for your comments, we have now made both those amendments.

Reviewer: 1 - Amanda Blatch-Jones (nee Young)

This is a well written paper that raises an important question. The authors have provided a rich account of the NICE process into the prioritization process and the importance for research and the avoidable waste agenda.

Many thanks for your kind words.

1. The abstract is not in a standardized format - Although this is not a piece of research rather a review of process, the abstract does not have any structure to it.

The editors had given us permission to move away from the standard format, as this is a more health policy type piece, to not follow the standard research style structured abstract. That said we have now re-worked the abstract such that it reads better and is more structured. Please refer to abstract on page 2.

2. Limitations are mentioned after the abstract but are not mentioned in the Discussion section of the paper. A conclusion of the limitations could easily be included in the discussion section.

Thanks for pointing that out; we have included this in the discussion section as well. Please refer to discussion on page 9.

3. Page 5 of 19, third paragraph - priorities found by NICE are one of many contributions to the NETS programmes mentioned, which feed into the commissioning process. Where and how was the information retrieved from to complete Table 2? In terms of cost, number of projects etc. The commissioning process was actually founded in 1993 (which was then the HTA programme only, namely National Coordinating Centre for Health Technology Assessment: NCCHTA). This was the uniqueness of the programme as it was set up to deal with commissioned calls only, (later 2005/2006 the researcher-led process began).

Thanks for highlighting the differences at NIHR's end. This was compiled based on the information shared between the two organisations through their annual meetings on research priorities. So only the research that was funded by NIHR based on a research recommendation from NICE.

Small point - NETSCC abbreviation isn't provided.

Thanks for pointing that out; we have now included the full form of NETSCC. Please refer to page 5.

4. Discussion - small point: top of page 10 of 19 - font style different.

Thanks for spotting that, it has now been amended to be the same font/ style.

5. Discussion - page 10 of 19, third paragraph: the JLA is now part of the NIHR, carried out via NETSCC.

We have now added that update to the text, please refer to discussion on page 10.

6. Discussion - No limitations are discussed.

Please see response to comment number 2 and refer to discussion on page 9.

7. I was disappointed not to have read a final concluding paragraph which summed up the purpose (so what factor) of the paper and its review of NICE. It would strengthen the paper if there was a conclusion, rather than the current ending.

Sorry for that! We have now added a conclusion, please refer to page 11.

8. References - some of the links access are more than one year old - can these be reviewed and updated?

As this was drafted over a long period of time, in our spare time the access dates are old. We have now just double-checked and gone through all the links and therefore updated the access dates.

9. References - it would be worth reviewing the following NETSCC, Research on Research publication - Turner S, Bhurke S, Cook A. Impact of NIHR HTA Programme funded research on NICE clinical guidelines: a retrospective cohort. Health Research Policy and Systems (2015) 13:37. Though this paper describes very well the relationship of NIHR and NICE as it is limited to the importance of NIHR funded research underpinning NICE clinical guidelines, we cannot find a good fit for our paper focusing on research prioritisation. We are focusing on the research funded by NIHR as a result of a research recommendation.

10. References - it might be worth considering in terms of prior research and evidence gaps (page 3 of 19, introduction section) Bhurke S, Cook A, Tallant A, Young A, Williams E, Raftery J. Using systematic reviews to inform NIHR HTA trial planning and design: a retrospective cohort. BMC Medical Research Methodology 2015; 15:108

Thanks very much for the reference, this fits very well within the narrative of our paper and we have now included it within our discussion (please refer to page 9 in discussion and page 13 in references: number 31).

Overall, the paper discusses a valid and important area of the work NICE does. It highlights the how and why to the processes used by NICE and explains how these prioritized areas are followed through to evidence (primary research or reviews).

Thanks very much again for your kind words about the importance of our paper.

Reviewer: 2 - Robert Fraser Terry

The title needs some clarification or edit.

We have now amended the title to say:

Using HTA and guideline development as a tool for research priority setting the NICE way: reducing research waste by identifying the right research to fund. Please refer to page 1.

The paper describes an overview of the NICE processes but is less clear how these processes explicitly reduce waste e.g. reducing waste is not listed as part of research priority setting process. As per the reducing research waste and reward diligence (REWARD) campaign, systematic research priority setting is the first step suggested: <http://www.thelancet.com/campaigns/efficiency/priorities> Chalmers I, Bracken MB, Djulbegovic B, Garattini S, Grant J, Gülmezoglu AM, Howells DW, Ioannidis JP, Oliver S. How to increase value and reduce waste when research priorities are set. The Lancet. 2014 Jan 17;383(9912):156-65.

This is also the first reference within our manuscript.

We have now added more to the abstract and introduction section now to clarify this. Please refer to the introduction pages 2 and 3.

The paper describes an overview of the NICE processes but is less clear how these processes explicitly reduce waste e.g. reducing waste is not listed as part of research priority setting process. It is unclear from the process described here how the quality of evidence is assessed when producing guidance and setting priorities for example the use of GRADE tables.

We have now clarified the relationship between reducing research waste and systematic research priority setting as per above in the abstract and introduction. Please refer to pages 2 and 3.

NICE had first introduced GRADE in 2009 and that we have previously published.

Thorton J, Alderson P, Tan T, Turner C, Shaw B, Ruiz F, Latchem S, Reken S, Mugglestone M, Hill J, Neilson J, Westby M, Francis K, Whittington, Jacklin P, Siddiqui F, Sharma T, Ayiku L, Chamberlain K, Kelly V. Introducing GRADE across the NICE clinical guideline programme. Journal of Clinical Epidemiology, February 2013, 66(2):124-131.

We have now added a line about it and added the above reference, please refer to page 4.

I have added minor comments for clarification in the attached Adobe file.

Many thanks for your careful review, please find below responses to your comments on the PDF, also placed here for easy reference.

1. Title

As above - We have now amended the title to say:

Using HTA and guideline development as a tool for research priority setting the NICE way: reducing research waste by identifying the right research to fund. Please refer to page 1.

2. Introduction (Need to define waste in this context e.g. duplication of research, poor quality, low statistical power etc.)

Thanks, for this. We have now amended the introduction, please refer to page 3.

3. Clarify why greater than 100% - The 80% and 40%

What the 80% was related to what the end users wanted research to be on (80% was other research areas and 20% on drugs). The 40% was the spending on research on drugs (non-commercial) – they were not part of the same statistic.

As it may have been unclear, we have now removed one of those numbers. Please refer to introduction page 3.

4. Guidance specific research priorities - This title needs clarification

We have now amended the title to say: Research priorities identified through systematic reviews (guideline or HTA production).

5. NICE - For the international non-UK reader it would be useful to have a brief description of NICE, its role and examples of the type of guidelines it produces. Who are NICE guidelines written for and how are they used

Many thanks for pointing that out. We have added a little more to the introduction (please refer to page 4) based on our website and the following publication where more details are available. Both referenced there.

<https://www.nice.org.uk>

Sharma T, Doyle N, Garner S, Naidoo B, Littlejohns P. NICE supporting England and Wales through times of change. *Eurohealth*.;17(2-3):30.

6. This description is written in the passive tense - why? Better to describe more precisely how committees are constituted and when they make the up takes different forms.

We have now amended the tense and added briefly more about the committees and added the reference to the article where we describe this in much more detail.

Sharma T, Choudhury M, Kaur B, et al. Evidence informed decision making: the use of “colloquial evidence” at NICE. *International Journal of Technology Assessment in Health Care* 2015;31(03):138-46.

Please refer to page 4.

7. Is there any use of methods to explicitly rate the quality of the evidence for example the use of GRADE methodology?

As per above in general comments:

We have now clarified the relationship between reducing research waste and systematic research priority setting as per above in the introduction and abstract. NICE had first introduced GRADE in 2009 and that we have previously published.

Thorton J, Alderson P, Tan T, Turner C, Shaw B, Ruiz F, Latchem S, Reken S, Mugglestone M, Hill J, Neilson J, Westby M, Francis K, Whittington, Jacklin P, Siddiqui F, Sharma T, Ayiku L, Chamberlain K, Kelly V. Introducing GRADE across the NICE clinical guideline programme. *Journal of Clinical Epidemiology*, February 2013, 66(2):124-131.

We have now added a line about it and added the above reference, please refer to page 4.

8. The quality of the evidence may also be insufficient to answer the question with any certainty. Thanks for pointing that out we have now amended it to say: “...for example, due to inadequate reporting or poor quality)...” Please refer to page 5.

9. Can this liaison be clarified give some real examples - this whole passage is very passive.

We get into the details in the paragraphs that follow. This was to just describe the overall process – the next two paragraphs get into the details of the interaction with the research funder and there are examples in the tables and figures. We have now highlighted that in the summary and also

shortened it and added the reference that gives details on the other aspects of the NICE process and this specific one as well. Please refer to page 5.

10. I think this should be Table 3

No, that is correct as Table 2 (summary with research funded by NIHR). Table 3 is different – example of methodological research funded by MRC, meant for the next sub-section.

11. what new insights do these analyses bring - why are they useful. (Indirect or network meta analyses)

Thanks for highlighting that we should have elaborated so we have amended that now to give the rationale. Please refer to page 6.

12. This needs a definition or a ref that provides one - again unclear how the quality of the research is assessed.

We have now the quality is assessed using GRADE and again added previously published references for the same. Please refer to page 6.

13. Methodological priorities - This need defining and clarification.

We have now amended to say: the methodological research needed for future development of the work of the Institute (methodological priorities for research)..., please refer to page 6.

14. So how is 'research waste' explicitly avoided. Not defined above and not listed here as a category for setting priorities.

Many thanks for highlighting that. Reducing research waste was not a methodological research priority identified to send to funders – the process of systematically reviewing what research should be funded, is a key aspect to reducing research waste. As it may have been unclear, we have now amended the paragraph to reflect that and once again added the first reference of the reducing research waste series by Chalmers et al. that describes this. Please refer to page 9.

15. Discussion: It would be useful to know what impact NICE priorities are expected to have (e.g. reduced waste)

We have now amended the discussion to emphasise this more, please refer to pages 9 and 10 in the discussion.

16. Only the potential? As this is the title of the paper there needs to be a sharper definition of how the NICE processes explicitly avoid research duplication, promotes research of sufficient power that will answer the evidence gaps identified in the guidelines.

Maybe we were too soft in our wording, as research has shown systematically prioritising future research questions from for example gaps identified through systematic reviews does reduce waste, we have now amended to reflect that. We have also added more detail here about how it helps reduce waste (duplication, directing appropriate research design etc). Please refer to pages 9 and 10 in the discussion.

17. NCBI - Provide a url or ref

As this is a work in progress there are no method reports on the bookshelf yet so there is no reference we can add. We have amended the text to clarify this.

VERSION 2 – REVIEW

REVIEWER	Robert Terry
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	TDR - the Special Programme for Research and Training in Tropical Diseases WHO Geneva
REVIEW RETURNED	08-Jan-2018

GENERAL COMMENTS	The minor revisions raised in the first review have been addressed
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REVIEWER	Amanda Blatch-Jones NIHR Evaluation Trials and Studies Coordinating Centre, University of Southampton, UK
REVIEW RETURNED	11-Jan-2018

GENERAL COMMENTS	<p>This is a much improved revision of the original paper. The authors have addressed all of the recommendations and where not appropriate have given valid justification. The paper reads well and addresses an important question.</p> <p>The authors have given a clearer indication about how NICE contributes to the adding value in research agenda in terms of process, function and management. The authors have clearly demonstrated the value of the paper hence my recommendation for accepting the paper for publication.</p>
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