PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Scanning the horizon: A systematic literature review of methodologies
AUTHORS	Hines, Philip; Hiu yu, Li; Guy, Richard; Papaluca, Marisa

VERSION 1 - REVIEW

REVIEWER	Dr. Effie Amanatidou University of Manchester UK
REVIEW RETURNED	30-Oct-2018

GENERAL COMMENTS	Dear authors thank you for the paper. This is indeed a comprehensive review of HS methodologies. However, the stated objective is 'to broaden and update knowledge on the methodologies used, and through mapping and evaluation, provide a useful guide for the establishment and optimisation of future horizon scanning initiatives'. Although the mapping is clearly achieved the evaluation of the different mapping dimension is hardly covered and the information in the supplementary file (full mapping) is not that different from that included in the analysis section of the main text. It would be very useful and appreciated to take a step further and comment which of the different approaches / methodologies would be most useful in which cases/conditions or simply put their pros and cons. If the mapping elements are grouped in say 4-5 different approaches/methodologies illustrating 4-5 different example /cases for instance than the pros and cons of each methodological case could be discussed in a separate chapter before the conclusions. Another major comment is that some selection criteria need justification, i.e. why the use of a collaborative approach is a selection criteria and the signal selection phase? Also some conclusions need to be further elaborated, i.e. it is stated 'Undoubtedly, automation and the development of ‘intelligent’ horizon-scanning'. What is 'intelligent horizon-scanning' how would you explain it based on your analysis? Other than those comments I think it is a potentially valuable paper. The extra work suggested only aims to bring the most out of your work. Thank you and Good luck!

REVIEWER	Leigh-Ann Topfer CADTH, Canada
REVIEW RETURNED	06-Nov-2018

GENERAL COMMENTS	Main comments: This is a very useful review of horizon scanning methods, but perhaps the objectives are a little too broad. Objectives: The stated aim is to systematically identify and evaluate HS methodologies. Only the identification aim is accomplished - which is fine, but perhaps the objectives could be narrowed to state this. Also, the HS methods "employed in healthcare and elsewhere" is too broad as the focus has ultimately been on healthcare. Methods: If the aim is to identify HS in healthcare and in other fields, limiting the literature search to biomedical databases (PubMed and Embase) would not adequately cover HS in business, environmental science, and other disciplines. Per comments above, best to limit the focus to healthcare. Rather than a systematic review, this might be better called a literature review or a state-of-the art review, etc., as elements of the systematic review, such as reproducible search strategy, have not been included. Conclusion: Not sure that the conclusion that HS is a "reliable tool" can be drawn from the literature discussed in this paper. There have been some studies of the accuracy of forecasting, etc., but this is beyond the scope of this paper. Not sure that "leverage opportunities and address challenges at an international level" is relevant here. Focus on what the key/common methods used are instead. More detailed comments/suggestions: - inconsistent use of horizon scanning or HS abbreviation - use one or the other throughout - separate Methods and Results in the Abstract - PubMed (not PUBMED) and Embase (not EMBASE) - what is a literature map? Can you explain it further? If this is the supplementary info. on pages 31-40 it isn't clear (no caption) and the font is illegible - under Strengths and limitations of this study, first paragraph, the reference #3 might be incorrect. I think it might refer to reference #14, also by Sun. This reference (#14) is also duplicated as #34. - consider removing "incorporating practices from beyond the health field" as per above - not sure "outcome bias" is used appropriately here Introduction - might be good to discuss terminology a bit first, e.g., forecasting vs. horizon scanning / early alert and awareness. The following might be helpful: This Conference Board of Canada definition: “Scanning is the foundation of effective foresight, which is the practice of creating a variety of forward-facing views and applying the emerging insights in practical ways. It is a systematic, participatory, future-intelligence gathering process designed to detect adverse conditions, guide policy, and shape strategy by exploring new markets, products, and services. Scanning takes place at the beginning of the Conference Board’s foresight process. Its goal is to identify developments at the edge of current thinking that could fundamentally change or disrupt organizations in unexpected ways. In other words, we are actively seeking out insights that conflict with our current understanding of a given system. This

	process helps individuals and organizations better understand their assumptions about the future while avoiding being blinded to change." - Or this UK report, Technology and Innovation Futures 2017 re forecasting. -the HTA Glossary definition of horizon scanning might be helpful: "The systematic identification of health technologies that are new, emerging or becoming obsolete and that have the potential to effect health, health services and/or society. • Note 1: Related terms include early awareness and alert system" - in the Introduction comment on duplication of efforts, might want to mention the EUnetHTA proposal for a coordinated European approach to horizon scanning: "Horizon Scanning, Topic Identification, Selection and Prioritisation for European cooperation on HTA " - draft recommendations and methods. - could also mention other European HS initiatives, such as Beneluxa, and agencies such as ECRI Institute, in the US, which provides HS as a subscription service. - statement that "There have been no recent reviews of horizon scanning methods used in the health sector, or those looking beyond the health sectors" - consider removing beyond the health sectors as the lit. search as is would not have captured these. Methods - what was the date (or date range) when the searches were conducted, add the coverage dates, i.e., January 2008 to June 15, 2018, and whether any update searches performed throughout the project - if possible, provide a copy of the search strategy from at least Medline or PubMed as an appendix - further MeSH term that might have been helpful are: Forecasting and Biomedical technology/Trends. Not saying you need to revise the search, but none of the terms shown in the Search Strategy section are MeSH terms, so could just say keywords instead of MeSH terms, if this is more accurate. Inclusion and exclusion criteria - in the first round of screening may need to say the title as well as the abstract as some citations don't have abstracts - "the horizon scanning undertaken spanned a period of between 2 and 15 years" - some agencies (such as CADTH) do include a shorter time span (under a year, or less to 5 to 10 years out at most), so it varies Results - there are a couple more HS methods you might consider including: 1. Horizon scanning for pharmaceuticals: proposal for the BeNeLuxA collaboration (published by the KCE, in Belgium) 2. Manual on horizon scanning of health technologies (Malaysian Health Technology Assessment Section (MaHTAS) 3. this 2018 HTAi Global Policy Forum paper on Facing the dynamics of future innovation: the role of HTA, industry and health system in scanning the horizon. It includes examples of various HS systems. Available: https://htai.org/wp-content/uploads/2018/02/HTAi_Global_Policy_Forum_2018_Background_Paper.pdf - add refs to the risk of bias tools for BMJ and Cochrane - not sure the publication bias and outcome bias mentioned here are appropriate - rather than "word of mouth", perhaps clinical experts, industry or decision makers??

	- prioritization - spelling here but prioritisation used elsewhere Information sources and signal detection - patents are often cited as a source, but seldom used in HS in healthcare as they are too labour intensive to scan and the uncertainty is too great - most may not ever make it to market Filtration criteria and methods - bullets for Novelty and Level of innovation could be combined - time-frame - consider expanding to <1 to 15 years (most HTA agencies that do horizon scanning use a much shorter time frame than 15 years) Signal assessment and methods - "a detailed risk assessment" - not sure this is typically performed in horizon scanning work in healthcare Dissemination and evaluation - references needed for the last 3 paragraphs in this section - "In the medium-term, an evaluation would include the responsiveness of the horizon-scanning team to requests..." - not sure, this is more applicable to rapid response services than HS - compare findings with "gold standards" - EuroScan didn't conduct joint assessments, AHRQ no longer contracts ECRI Institute or produces HS work, so neither is really a gold standard - mention of "the database" and "access to the database" - not quite clear, most agencies don't make their database publicly accessible. EuroScan has recently changed Secretariats and is in the process of getting their database up and running again. Discussion - the UK Innovation Observatory is pioneering the use of data mining in horizon scanning using clinical trial registries, etc. - might be worth citing their work in the 2nd paragraph http://www.io.nihr.ac.uk/ Limitations - "methodologies from beyond the health field" - maybe modify to includes some examples of methodologies from beyond the health field? Conclusions - would be good to mention BeNeLuxA and EUnetHTA HS initiatives here References - some references from the end might be missing (I.e., in the supplementary section references #63, 64 and 65 are cited), there are a few typos, ref #14 and 34 are duplicates Supplementary info - add copy of lit. search strategy from at least one of the databases (if possible) - add caption to missing section and make text legible (or remove) - Information sources and signal detection - some of this might be worth adding to the main article - "However, public input was not found to be hugely productive" - can you explain further - was it for topic identification or for adding info. to prioritise/select topics? -Prioritisation criteria and methods... - "cost of a signal" - might be better as "cost implications", for example, a low cost technology that will have a high volume of use. Dissemination and evaluation of the results of horizon scanning - some refs missing from reference list (#63,64,65) - updating of horizon scanning info. might be part of assessing the technology over its lifecycle, so not always updating as part of horizon scanning - it may have moved on to full health technology assessment, for example.

	- EuroScan and Agency for Healthcare Research and Quality are not gold standards. - may want to add ECRI Institute paper that assessed their forecasting/HS: Lerner JC, Robertson DC, Goldstein SM. "Case studies on forecasting for innovative technologies: frequent revisions improve accuracy" Health Affairs 2015;34(2):311-318. https://www.healthaffairs.org/doi/full/10.1377/hlthaff.2014.1066?url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org&rfr_dat=cr_pub%3Dpubmed

REVIEWER	Patrick Saunders University of Staffordshire, UK
REVIEW RETURNED	12-Nov-2018

GENERAL COMMENTS	I'm in a bit of a quandary here. I understand the importance and potential value of horizon scanning but I'm unclear about what this review adds to what we already know. Highlighting that would add value. Some clear examples of things that HS has identified and others that could or, accepting this is a challenge, would have been picked up if the recommended combination of scanning techniques would be useful for example. In terms of presentation there is a lot of repetition of the narrative in the supplementary information, few typos, acronym in the abstract, is collaborative/international on page and/or, Fig and Figure are used,

REVIEWER	Jeremy Huddy Imperial College London, UK
REVIEW RETURNED	18-Nov-2018

GENERAL COMMENTS	Thank you for inviting me to review this manuscript. This review systematically reports methodology for undertaking horizon scanning in respect to medical technology. This is timely as horizon scanning is used by a variety of stakeholders to focus and plan future research activities and priorities. Giving the increasing number of reported methodologies and sources that can be used to undertake this an up to date review of the subject is highly relevant and I believe would be of interest to the wider readership of this journal. In general the article is very well written. The introduction is concise, defines horizon scanning, and justifies the objective of the review. The methods are robust and well described. It would be interesting to know how the search terms were selected. Were the terms used that were synonymous with horizon scanning identified from previous experience or literature. Furthermore, in the second round of article selection one of the criteria was that the paper reported an approach that was collaborative or international. I am unclear why this criteria was included. Are you suggesting that horizon scanning can only be undertaken on a collaborative basis? Overall, the results are extremely well written given the number and breadth of included articles and the authors should be

	congratulated for this. Breaking down the stages into the stages of signal detection, filtration, prioritisation, assessment and dissemination works well. A separate "full mapping section" is provided although this is very similar to the original results section. The tables included in the supplementary information I found difficult to utilise in their current form. Given the size of the tables they appear over many pages with a tiny font size and a large amount of white space. I struggled to follow these tables and I think should be amended - not including the abstract of the references may help. The conclusion summarises the study well, compares the results to the literature and provides an appropriate description of limitations. Overall, I think this is a valuable addition to the literature surrounding horizon scanning particularly highlighting the scope of data sources and approaches to analysis that can be utilised.

VERSION 1 – AUTHOR RESPONSE

Reviewer(s)' Comments to Author:

Reviewer 1 and Responses

Reviewer Name: Dr. Effie Amanatidou

Institution and Country: University of Manchester UK

Please state any competing interests or state ‘None declared’: None declared

Please leave your comments for the authors below

Thank you very much for your kind and helpful comments.

Dear authors thank you for the paper. This is indeed a comprehensive review of HS methodologies. However, the stated objective is 'to broaden and update knowledge on the

methodologies used, and through mapping and evaluation, provide a useful guide for the establishment and optimisation of future horizon scanning initiatives'. Although the mapping is clearly achieved the evaluation of the different mapping dimension is hardly covered and the information in the supplementary file (full mapping) is not that different from that included in the analysis section of the main text.

It would be very useful and appreciated to take a step further and comment which of the different approaches / methodologies would be most useful in which cases/conditions or simply put their pros and cons. If the mapping elements are grouped in say 4-5 different approaches/methodologies illustrating 4-5 different example /cases for instance than the pros and cons of each methodological case could be discussed in a separate chapter before the conclusions.

We agree that a greater emphasis on providing a ‘guide’ would be useful to readers, and we discussed grouping the mapping elements into three different use cases: qualitative, quantitative and mixed qualitative and quantitative, or low/medium/high resource, and then providing their pros and cons in a discussion paragraph as you mentioned. However, as written in the paper, we believe that there has not been enough research performed to assess the most efficacious methods of scanning. Although we could extract all the pros and the cons for each methodological element, we do not think that this would produce a representative guide to each of the elements. We therefore did not want to

list the pros and cons where we feel there is not enough grounding. The discussion on each methodological element (albeit limited) represents the pros and cons that we felt comfortable generalising.

Having said this, we completely agree that this was an objective at the outset and therefore we have added to the ‘limitations’ section of the paper the lack of evaluation possible:

“A detailed evaluation, and a more practical guide to all the methodologies, could not be performed for practical reasons: the inconsistent reporting of the horizon-scanning details and their efficacy, and the continually evolving approaches employed.”

We also contemplated expanding the further research suggestion to highlight your point on the need for a more easily accessible guide. Through surveys/workshops with those carrying out these methods to elucidate what works when etc. and then packaging it in a guide. However, because of space and word-count limits, it has not been possible to greatly expand on this subject.

Another major comment is that some selection criteria need justification, i.e. why the use of a collaborative approach is a selection criteria and the signal selection phase?

We agree and have justified this point as follows:

“The foresight period of 2-15 years reflected the fact that signals suggesting impact in less than two years concern innovations that are already in late-stage development, while those anticipated to ‘mature’ in 15-20 years’ time are too distant and uncertain to be useful. A collaborative/international approach was sought because of the global nature of innovation and change.”

Also some conclusions need to be further elaborated, i.e. it is stated 'Undoubtedly, automation and the development of ‘intelligent’ horizon-scanning'. What is 'intelligent horizon-scanning' how would you explain it based on your analysis?

To clarify, we meant artificially intelligent. For example, a software which can search research databases and learn to flag a more and more relevant list of papers. We have amended the text as follows:

“Undoubtedly, automation and the development of artificially ‘intelligent’ horizon-scanning, which self-assesses and improves its signal management, are short-term milestones that will significantly improve the process, enhancing the evidence base, disseminating the acquired outputs efficiently, and facilitating decision-making.”

Other than those comments I think it is a potentially valuable paper. The extra work suggested only aims to bring the most out of your work. Thank you and Good luck!

Reviewer 2 and Responses

Reviewer Name: Leigh-Ann Topfer

Institution and Country: CADTH, Canada

Please state any competing interests or state ‘None declared’: None declared

Please leave your comments for the authors below

Main comments:

Thank you for your comments and the extensive review which, we believe, have led to a much improved and higher-quality paper.

This is a very useful review of horizon scanning methods, but perhaps the objectives are a little too broad.

Objectives: The stated aim is to systematically identify and evaluate HS methodologies. Only the identification aim is accomplished - which is fine, but perhaps the objectives could be narrowed to state this.

We agree that the objective at the outset to evaluate HS was only partially achievable in the end and therefore we have added to the 'limitations' section of the paper accordingly:

"A detailed evaluation, and a more practical guide to all the methodologies, could not be performed for practical reasons: the inconsistent reporting of the horizon-scanning details and their efficacy, and the continually evolving approaches employed."

We believe that there has not been enough research performed to properly evaluate the most efficacious methods of scanning. The discussion on each methodological element (albeit limited) represents the generalizable elements that we were comfortable with.

Also, the HS methods "employed in healthcare and elsewhere" is too broad as the focus has ultimately been on healthcare.

Methods: If the aim is to identify HS in healthcare and in other fields, limiting the literature search to biomedical databases (PubMed and Embase) would not adequately cover HS in business, environmental science, and other disciplines. Per comments above, best to limit the focus to healthcare.

We have changed the text to be more specific:

"The aim of this paper is to systematically identify and evaluate HS methodologies employed in healthcare and biomedical fields."

Rather than a systematic review, this might be better called a literature review or a state-of-the art review, etc., as elements of the systematic review, such as reproducible search strategy, have not been included.

We believe that the amendments above and below, as well in the supplementary sections which detail the search strategy and PRISMA checklist etc., justify our use of "systematic". However, should the editor feel that we continue to over-state the case, we will replace 'systematic' with "state-of-the-art".

Conclusion: Not sure that the conclusion that HS is a "reliable tool" can be drawn from the literature discussed in this paper. There have been some studies of the accuracy of forecasting, etc., but this is beyond the scope of this paper.

This is affair point. We have changed the wording to illustrate the uncertainty regarding its reliability in general, whilst acknowledging that there does seem to be examples/potential for creating reliable methods:

"Horizon scanning, when performed appropriately, is a flexible and potentially reliable tool."

Not sure that "leverage opportunities and address challenges at an international level" is relevant here. Focus on what the key/common methods used are instead.

We have tried to clarify our meaning here, as well as refer to the methods used, specifically:

“Horizon scanning, when performed appropriately, is a flexible and potentially reliable tool, with a wide variety of methods. Horizon scanning can inform and influence decision-making, through identifying opportunities and challenges, from an organisational to an international level.”

More detailed comments/suggestions:

- inconsistent use of horizon scanning or HS abbreviation - use one or the other throughout

We have removed the abbreviation.

- separate Methods and Results in the Abstract

We have separated them.

- PubMed (not PUBMED) and Embase (not EMBASE)

We have made these corrections.

- what is a literature map? Can you explain it further? If this is the supplementary info. on pages 31-40 it isn't clear (no caption) and the font is illegible

The Excel file is the literature map working document. We have attempted to significantly improve legibility.

- under Strengths and limitations of this study, first paragraph, the reference #3 might be incorrect. I think it might refer to reference #14, also by Sun. This reference (#14) is also duplicated as #34.

We have amended the references accordingly and removed the duplication of Sun et al. Thank you for catching this oversight.

- consider removing "incorporating practices from beyond the health field" as per above

We have changed the wording to reflect that there were papers from several fields, e.g., environmental sciences:

“This systematic review offers an up-to-date perspective on horizon scanning methodologies – incorporating practices from a number of different fields”

- not sure "outcome bias" is used appropriately here

We have changed this to “omission bias”.

Introduction

- might be good to discuss terminology a bit first, e.g., forecasting vs. horizon scanning / early alert and awareness. The following might be helpful:

This Conference Board of Canada definition: “Scanning is the foundation of effective foresight, which is the practice of creating a variety of forward-facing views and applying the emerging insights in practical ways. It is a systematic, participatory, future-intelligence gathering process designed to detect adverse conditions, guide policy, and shape strategy by exploring new markets, products, and services. Scanning takes place at the beginning of the Conference Board’s foresight process. Its goal is to identify developments at the edge of current thinking that could fundamentally change or disrupt organizations in unexpected ways. In other words, we are actively seeking out insights that conflict with our current understanding of a given system. This process helps individuals and organizations better understand their assumptions about the future while avoiding being blinded to change.”

- Or this UK report, Technology and Innovation Futures 2017 re forecasting.

-the HTA Glossary definition of horizon scanning might be helpful: "The systematic identification of health technologies that are new, emerging or becoming obsolete and that have the potential to effect health, health services and/or society.

We appreciate the useful definitions. We have used the Conference Board of Canada as a reference and slightly amended the definition used in the introduction below to clarify our general definition. We are up against the word limit so don't have the space to define horizon scanning further, for example to define it as a subset of foresight, but hopefully the citations provide a means for the reader to do so.

"There are many definitions of horizon scanning (12), but most can be captured by its generic characterisation as a systematic examination of information to detect early signs of important developments."

Note 1: Related terms include early awareness and alert system"

- in the Introduction comment on duplication of efforts, might want to mention the EUnetHTA proposal for a coordinated European approach to horizon scanning: "Horizon Scanning, Topic Identification, Selection and Prioritisation for

European cooperation on HTA " - draft recommendations and methods.

- could also mention other European HS initiatives, such as Beneluxa, and agencies such as ECRI Institute, in the US, which provides HS as a subscription service.

We agree and have added a EUnetHTA reference in the introduction (see below):

"This includes the activities of the EMA's recently established Regulatory Science Observatory, as well other international efforts to reduce duplication: the EU Innovation offices Network, European Network for Health Technology Assessment, and the International Coalition of Medicines Regulatory Authorities (ICMRA).(9, 15)."

- statement that "There have been no recent reviews of horizon scanning methods used in the health sector, or those looking beyond the health sectors" - consider removing beyond the health sectors as the lit. search as is would not have captured these.

Methods

We have amended the text accordingly as follows:

"There have been no recent reviews of horizon scanning methods used in the health or broader biomedical sectors (5, 12)."

- what was the date (or date range) when the searches were conducted, add the coverage dates, i.e., January 2008 to June 15, 2018, and whether any update searches performed throughout the project

We have amended the text to reference the supplementary material which provides the further information requested:

"Medline and Embase bibliographic databases were searched to identify research papers on the use of horizon scanning, and the methods used for this purpose. The date range was between 2018-01-01 and 2018-07-04. The final search took place on 2018-07-04. Grey literature and bibliographies of the most relevant research papers supplemented this search."

- if possible, provide a copy of the search strategy from at least Medline or PubMed as an appendix

This has now been added to the supplementary material.

- further MeSH term that might have been helpful are: Forecasting and Biomedical technology/Trends. Not saying you need to revise the search, but none of the terms shown in the Search Strategy section are MeSH terms, so could just say keywords instead of MeSH terms, if this is more accurate.

We have deleted reference to MeSH terms in both the article and the supplementary material.

Inclusion and exclusion criteria

- in the first round of screening may need to say the title as well as the abstract as some citations don't have abstracts

This change has been made as below:

“In the first round of quality appraisal and screening (see Supplementary Information), the publication abstracts or title had to indicate: (a)…”

- "the horizon scanning undertaken spanned a period of between 2 and 15 years" - some agencies (such as CADTH) do include a shorter time span (under a year, or less to 5 to 10 years out at most), so it varies

We appreciate this point being highlighted. We recognise a shorter timeframe is particularly relevant for HTA bodies for example. We choose this timeframe to best capture horizon scanning methodologies that also detect signals at an early stage:

“The foresight period of 2-15 years reflected the fact that signals suggesting impact in less than two years concern innovations that are already in late-stage development, while those anticipated to ‘mature’ in 15-20 years’ time are too distant and uncertain to be useful.”

Results

- there are a couple more HS methods you might consider including:

1. Horizon scanning for pharmaceuticals: proposal for the BeNeLuxA collaboration (published by the KCE, in Belgium)

2. Manual on horizon scanning of health technologies (Malaysian Health Technology Assessment Section (MaHTAS)

3. this 2018 HTAi Global Policy Forum paper on Facing the dynamics of future innovation: the role of HTA, industry and health system in scanning the horizon. It includes examples of various HS systems. Available: https://htai.org/wp-content/uploads/2018/02/HTAi_Global_Policy_Forum_2018_Background_Paper.pdf

We are grateful that our attention has been drawn to these references – particularly the HTAi 2018 Global Policy Forum which nicely outlines the CADTH process. Unfortunately, space constraints prevent the addition of any detailed discussion of these methods.

- add refs to the risk of bias tools for BMJ and Cochrane

We have added a reference.

- not sure the publication bias and outcome bias mentioned here are appropriate

We have changed ‘outcome bias’ to “omission bias”.

We have also clarified the publication bias paragraph:

“A form of publication bias was likely in which only horizon scanning undertaken in organisations with a strong background in publishing academic publications and transparency were discovered. It was not possible to correct for this.”

- rather than "word of mouth", perhaps clinical experts, industry or decision makers??

We feel word of mouth captures the way much information is still circulated, e.g., via informal discussions, for example, with clinical experts, industry representatives or decision-makers.

- prioritization - spelling here but prioritisation used elsewhere

Corrected!

Information sources and signal detection

- patents are often cited as a source, but seldom used in HS in healthcare as they are too labour intensive to scan and the uncertainty is too great - most may not ever make it to market

We explored the use of patents with a customisable analytics tool:
https://ec.europa.eu/jrc/en/scientific-tool/tools-innovation-monitoring

While we agree with the level of potential uncertainty, patens can be a first indication of a new trend.

Filtration criteria and methods

- bullets for Novelty and Level of innovation could be combined

We use Level of Innovation here as having a qualitative meaning beyond novelty, i.e., a filtration criterion which denotes the added value of a signal over just its novelty.

- time-frame - consider expanding to <1 to 15 years (most HTA agencies that do horizon scanning use a much shorter time frame than 15 years)

We have addressed this point above.

Signal assessment and methods

- "a detailed risk assessment" - not sure this is typically performed in horizon scanning work in healthcare

We have removed “detailed”, as the lack of clarity for many signals does indeed prevent a detailed assessment:

“The expected utilisation and availability of the innovation across different geographical regions is also important (5,34,46), as is an assessment of risk.“

Dissemination and evaluation

- references needed for the last 3 paragraphs in this section

We have added appropriate references.

- "In the medium-term, an evaluation would include the responsiveness of the horizon-scanning team to requests..." - not sure, this is more applicable to rapid response services than HS

This is intended more from the angle of ‘customer’ satisfaction, i.e., when a HS unit is asked to scan for a specific topic, how quickly do they perform the task? Is the unit viewed as responsive?

- compare findings with "gold standards" - EuroScan didn't conduct joint assessments, AHRQ no longer contracts ECRI Institute or produces HS work, so neither is really a gold standard

We have removed AHRQ, and amended the EuroScan mention to the following:

“to compare findings with other horizon scanning agencies/databases (e.g., EuroScan);”

- mention of "the database" and "access to the database" - not quite clear, most agencies don't make their database publicly accessible. EuroScan has recently changed Secretariats and is in the process of getting their database up and running again.

We amended the EuroScan reference as indicated above. The final mention of “the database” has been amended as follows:

“A focus group of users can be employed to review the information input and dissemination and to develop a user-friendly interface through which to access a database (40,59).”

Discussion

- the UK Innovation Observatory is pioneering the use of data mining in horizon scanning using clinical trial registries, etc. - might be worth citing their work in the 2nd paragraph http://www.io.nihr.ac.uk/

We have added a reference as suggested.

Limitations

- "methodologies from beyond the health field" - maybe modify to includes some examples of methodologies from beyond the health field?

We have amended the text to include an example:

“however, this review offers an up-to-date and wider perspective, and includes methodologies from beyond the health field, e.g., conservation.”

Conclusions

- would be good to mention BeNeLuxA and EUnetHTA HS initiatives here

We agree and we have referenced them here.

References

- some references from the end might be missing (I.e., in the supplementary section references #63, 64 and 65 are cited), there are a few typos, ref #14 and 34 are duplicates

We have deleted the duplication as mentioned above and updated referencing in the supplementary material.

Supplementary info

- add copy of lit. search strategy from at least one of the databases (if possible)

This can now be found in an additional supplementary file.

- add caption to missing section and make text legible (or remove)

We added a caption and improved the legibility.

- Information sources and signal detection - some of this might be worth adding to the main article

Unfortunately, due to space constraints, our ability to add more text is necessarily limited.

- "However, public input was not found to be hugely productive" - can you explain further - was it for topic identification or for adding info. to prioritise/select topics?

The researchers found this to be the case in topic identification:

“Although providing an opportunity for patients and the public to input into an EAA system by enabling them to alert the system to emerging health technologies is relatively easy and requires few resources, we found that this to be the least valuable aspect of PPIE in our system.”

We have amended our text to reflect this:

“However, public input was not found to be hugely productive in topic identification”

-Prioritisation criteria and methods...

- "cost of a signal" - might be better as "cost implications", for example, a low cost technology that will have a high volume of use.

We have amended the text as suggested.

Dissemination and evaluation of the results of horizon scanning

- some refs missing from reference list (#63,64,65)

These are now referenced.

- updating of horizon scanning info. might be part of assessing the technology over its lifecycle, so not always updating as part of horizon scanning - it may have moved on to full health technology assessment, for example.

We agree that one can view it this way. However, as we are following the sequential nature of EuroScan’s HS stages, we felt that updating the signal logically follows dissemination.

- EuroScan and Agency for Healthcare Research and Quality are not gold standards.

We agree and have addressed this above.

- may want to add ECRI Institute paper that assessed their forecasting/HS: Lerner JC, Robertson DC, Goldstein SM. "Case studies on forecasting for innovative technologies: frequent revisions improve accuracy" Health Affairs 2015;34(2):311-318.

https://www.healthaffairs.org/doi/full/10.1377/hlthaff.2014.1066?url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org&rfr_dat=cr_pub%3Dpubmed

Thank you for the relevant reference, with a seemingly obvious conclusion in hindsight, but probably not at the time and nonetheless important. We were unaware of this, unfortunately, this was not picked up in the literature search process, and we feel restrained to add papers ad hoc in the results at this stage. Nevertheless, thank you very much for highlighting this.

Reviewer 3 and Responses

Reviewer Name: Patrick Saunders

Institution and Country: University of Staffordshire, UK

Please state any competing interests or state ‘None declared’: None declared

Please leave your comments for the authors below

I'm in a bit of a quandary here. I understand the importance and potential value of horizon scanning but I'm unclear about what this review adds to what we already know. Highlighting that would add value.

We believe the added value to be three-fold

1. In a relatively new and rapidly expanding field, it offers an up to date overview, which hopefully can act as an aid in the establishment and improvement of horizon scanning methods, preventing duplication and spreading good practices where possible.

2. It has a broad scope, looking at methods used beyond the health field e.g. conservation literature

3. As one could perhaps expect, it is therefore comparatively comprehensive in its nature, with 100 papers reviewed.

We have tried to explain the added value of this systematic literature review in the ‘Strengths and Limitations’ section: that it “offers an up-to-date perspective on horizon scanning methodologies – incorporating practices from a number of different fields”. As well as in the introduction: “The overall goal is to broaden and update knowledge on the methodologies used, and through mapping and evaluation, provide a useful guide for the establishment and optimisation of future horizon scanning initiatives.

Some clear examples of things that HS has identified and others that could or, accepting this is a challenge, would have been picked up if the recommended combination of scanning techniques would be useful for example.

We agree it would have been good to provide some descriptive case studies where Horizon scanning has identified important signals, or conversely, signals which were not spotted because of an unsystematic approach. In the medicines regulatory world, for example, we constantly need to update regulatory standards as science, technology and innovation evolve. Delays in reacting to foreseeable innovation cause delays for patients. Hence a small investment in horizon scanning (much of which is to do with management of existing information) can be worth it. Of course, inherently, most initiatives are funded by organisations which see them as a cost effective means to ensure that they are not blindsided. We would like to include such text as we are battling the word limit.

Nevertheless, reviewer 2 kindly provided a link which may be relevant example of the reliability of HS as a method (Lerner JC, Robertson DC, Goldstein SM. "Case studies on forecasting for innovative technologies: frequent revisions improve accuracy" Health Affairs 2015;34(2):311-318.

https://www.healthaffairs.org/doi/full/10.1377/hlthaff.2014.1066?url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org&rfr_dat=cr_pub%3Dpubmed)

Regarding the optimal combination of methods, we did not feel that there was a strong enough body of evidence to recommend a specific combination of horizon scanning methodologies, as we have written in the text:

“The range of methods used, and the limited assessment of their performance, renders recommendation of a single approach premature and explains why combining two or more techniques makes sense for validation and for improving the accuracy of predictions…”

“It is essential, therefore, that further research be performed to develop, assess and ultimately implement the most efficacious methods of scanning and to ensure their acceptance and uptake by relevant stakeholders.”

In terms of presentation there is a lot of repetition of the narrative in the supplementary information, few typos, acronym in the abstract, is collaborative/international on page and/or, Fig and Figure are used,

We have cleaned up the text, removed acronyms from the abstract and replaced figure with fig in all but the figure 1 legend. The supplementary material is duplicative but goes into more detail and therefore we feel it may be of use to readers who want to dig a little deeper into the topic or area overall. The corrections made throughout the text have, we believe, caught all the typos (highlighted in yellow).

Reviewer 4 and Responses

Reviewer Name: Jeremy Huddy

Institution and Country: Imperial College London, UK

Please state any competing interests or state ‘None declared’: None declared.

Please leave your comments for the authors below

Thank you for inviting me to review this manuscript. This review systematically reports methodology for undertaking horizon scanning in respect to medical technology. This is timely as horizon scanning is used by a variety of stakeholders to focus and plan future research activities and priorities. Giving the increasing number of reported methodologies and sources that can be used to undertake this an up to date review of the subject is highly relevant and I believe would be of interest to the wider readership of this journal. In general the article is very well written.

Thank you very much for these kind words!

The introduction is concise, defines horizon scanning, and justifies the objective of the review.

The methods are robust and well described. It would be interesting to know how the search terms were selected. Were the terms used that were synonymous with horizon scanning identified from previous experience or literature.

The search terms were chosen from previous literature to comprehensively capture horizon scanning methodology yet narrow enough to be feasible for a systematic literature review. In the end the ~100 papers approached saturation but also our capacity to conduct the review. Please see the new supplementary material which provides more detail on our search strategy.

We have amended the search strategy section in the paper to reflect this:

“The primary search terms used were derived from previous literature”

Furthermore, in the second round of article selection one of the criteria was that the paper reported an approach that was collaborative or international. I am unclear why this criterion was included. Are you suggesting that horizon scanning can only be undertaken on a collaborative basis?

We use this because of the international nature of innovation and change. We have amended the text with the following justification:

“A collaborative/international approach was sought because of the global nature of innovation and change.”

Overall, the results are extremely well written given the number and breadth of included articles and the authors should be congratulated for this. Breaking down the stages into the stages of signal detection, filtration, prioritisation, assessment and dissemination works well. A separate "full mapping section" is provided although this is very similar to the original results section. The tables included in the supplementary information I found difficult to utilise in their current form. Given the size of the tables they appear over many pages with a tiny font size and a large amount of white space. I struggled to follow these tables and I think should be amended - not including the abstract of the references may help.

We agree and we have improved the legibility and added a caption.

The conclusion summarises the study well, compares the results to the literature and provides an appropriate description of limitations.

Overall, I think this is a valuable addition to the literature surrounding horizon scanning particularly highlighting the scope of data sources and approaches to analysis that can be utilised.

Thank you again.

VERSION 2 – REVIEW

REVIEWER	Leigh-Ann Topfer CADTH, Canada
REVIEW RETURNED	17-Jan-2019

GENERAL COMMENTS	The paper is now much easier to follow and more readable.

REVIEWER	Patrick Saunders University of Staffordshire UK
REVIEW RETURNED	27-Feb-2019

GENERAL COMMENTS	Rigorous review and while there are no 'knock out' findings or recommendations the fact that none could be drawn is important in its own right. This is disappointing given that the technique has been used for many decades in industry and the authors rightly acknowledge that there is still much to do to maximise the potential of horizon scanning in healthcare and highlight some important developments and suggestions that will enable that potential. This paper will contribute to that process

REVIEWER	Jeremy Huddy Imperial College London, UK
REVIEW RETURNED	15-Mar-2019

GENERAL COMMENTS	Thank you for asking me to review the revised version of this paper. I am satisfied with the responses and amendments made in response to my comments. I have no further comments regarding the manuscript and continue to believe it represents a valuable addition to the literature regarding this subject.