

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (http://bmjopen.bmj.com).

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open

Scanning the horizon: A systematic literature review of methodologies

Journal:	BMJ Open
Manuscript ID	bmjopen-2018-026764
Article Type:	Research
Date Submitted by the Author:	24-Sep-2018
Complete List of Authors:	Hines, Philip; United Nations University-Maastricht Economic and social Research institute on Innovation and Technology; European Medicines Agency, SciRS Hiu yu, Li; European Medicines Agency, SciRS Guy, Richard; University of Bath - Department of Pharmacy and Pharmacology; European Medicines Agency, SciRS Papaluca, Marisa; European Medicines Agency, SciRS
Keywords:	HEALTH SERVICES ADMINISTRATION & MANAGEMENT, EDUCATION & TRAINING (see Medical Education & Training), PUBLIC HEALTH, QUALITATIVE RESEARCH
	-

SCHOLARONE™ Manuscripts

Scanning the horizon: A systematic literature review of methodologies

Authors:

Philip Hines^{1*},

Li hiu yu²,

Richard Guy³

Marisa Papaluca⁴

1 UNU-MERIT, Maastricht, Netherlands;

Scientific Committees Regulatory Science Strategy, the European Medicines Agency, 30 Churchill Place, Canary Wharf, London E14 5EU, United Kingdom, London, UK;

Email: Philip.hines@ema.europa.eu;

Telephone: +442036606048

- 2 Maastricht University, Maastricht, Netherlands; Scientific Committees Regulatory Science Strategy, the European Medicines Agency, London, UK
- 3 University of Bath, UK; Scientific Committees Regulatory Science Strategy, the European Medicines Agency, London, UK
- 4 Scientific Committees Regulatory Science Strategy, the European Medicines Agency, London, UK
- *Corresponding author

Word count: 3978

ABSTRACT

Objectives: Society is confronted with the rapid emergence of innovation in science and technology. To manage this, horizon scanning is being adopted globally to identify, assess and prioritise innovations and trends at an early stage of their development. This enables decision-makers to be better informed and prepare for change. The aim of this paper is to systematically identify and evaluate HS methodologies employed in healthcare and elsewhere.

Methods and Results: A systematic literature review was performed using PUBMED and EMBASE, and was supplemented with grey literature searches. The principal methodologies used in horizon scanning were extracted from approximately 100 articles, and were summarised in a literature map. The search revealed many examples of horizon scanning across disciplines. Challenges, such as the need to refine prioritisation criteria, manage uncertainty inherent in the findings, and improve the dissemination of identified issues, have been highlighted.

Conclusion: Horizon scanning, when performed appropriately, is a flexible and reliable tool. When used for the early identification of trends, horizon scanning can inform and influence decision-making, leverage opportunities and address challenges at an international level. Further research to identify the most effective methodologies available would add depth to this landscape and enable the evolution of best practice to most efficiently anticipate novel developments and innovations.

Strengths and limitations of this study

- This systematic review offers an up-to-date perspective on horizon scanning methodologies – incorporating practices from beyond the health field; however, as reviews into horizon scanning in healthcare have been undertaken previously, some duplication of findings was inevitable.(1-5)
- Resource limitations have precluded evaluation of horizon-scanning in all sectors, particularly in the private sector, and consideration of material in languages other than English and Italian.
- The paper may be subject to outcome bias as the papers reported systematic methodological aspects of horizon scanning; therefore, some ad-hoc horizon scanning methods may not be captured.

INTRODUCTION

Across organizations worldwide, the rapid emergence of high impact innovation is a major challenge faced by decision makers.(6) To respond, the identification of future innovations and trends is being undertaken in a comprehensive, systematic and sustainable manner so that policy makers, and other stakeholders, can respond appropriately and enable innovations to reach the market with minimal developmental, legal, regulatory, process or procurement bottle-necks. To catalyse the achievement of this objective, horizon scanning is emerging as a valuable and viable strategy. This is particularly true in the health sector, where the European Medicines Agency (EMA) is seeking to promote the availability of innovative medicines using horizon scanning. This foresight will in turn inform the Agency's Regulatory Science Strategy and the European medicines regulatory network strategy. (7-9) Horizon scanning has been in use for many years, initially by commercial organisations and later by public bodies; Japan was an early adopter of foresight methodologies in the 1970s.(4, 10) Since then, horizon scanning has been used across diverse sectors to aid financial, policy, process and research planning. (5, 11) 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. The approach generally targets the early lifecycle of technologies - i.e, in an early phase of adoption before their introduction on to the market - but may also scan for broader trends, challenges and opportunities. It provides an early warning of 'signals', rather than a comprehensive study of their impact.

Horizon scanning generally follows a process of signal detection, filtration, prioritisation, assessment and dissemination (Fig 1). Its use is growing across sectors,(13) and this risks the duplication of efforts (both in design and execution) as similar stretches of the horizon are scanned by many.

Fig 1. Common stages of Horizon scanning from the EuroScan network (12).

This figure is licensed under the Creative Commons Attribution-NonCommercial-ShareAlike
4.0 International License (CC BY-NC-SA 4.0)

There have been no recent reviews of horizon scanning methods used in the health sector, (12, 14) or those looking beyond the health sector sectors. As a result, the aim of this literature review is to systematically identify and evaluate HS methodologies employed in healthcare and elsewhere. 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. This includes the activities of the EMA's recently established Regulatory Science Observatory, as well as the EU Innovation offices Network and the International Coalition of Medicines Regulatory Authorities (ICMRA).(9)

METHODS

A systematic review of the literature was performed to capture and map the use of horizon scanning activity, and the widespread use of modern IT/web capabilities, with 2008 to 2018 chosen accordingly.(15) Three researchers were involved and a systematic protocol was followed to minimise inter-rater bias; this involved cross validation between two researchers, with diverging opinions then arbitrated by the third. This systematic approach also permitted gaps and inconsistencies in the field to be identified. Data collection followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines:(16) the literature was first screened and filtered using inclusion and exclusion criteria; the accepted papers then underwent data extraction and analysis; and, finally, the scanning methodologies were mapped.

Search strategy

Medline and Embase bibliographic databases were searched to identify research papers on the use of horizon scanning, and the methods used for this purpose. Grey literature and bibliographies of the most relevant research papers supplemented this search. The primary search terms and relevant MeSH terms used were: "*horizon scan*" OR "*strategic foresight*" OR "*systematic early dialogue*" OR "*early warning and alert system*". All literature, of which the title or abstract contained any of the keywords above, was flagged.

Inclusion and exclusion criteria

Only articles published in English or Italian from 2008-2018 were included,

In the first round of screening the publication abstracts had to indicate:

(a) either a methodology for horizon scanning or strategic foresight, *or* a discussion, or experience provided, of horizon scanning.

(b) It was also essential for the abstracts to indicate a breadth of horizon scanning of the relevant field level *or* address a methodological aspect which may be generally applicable across different fields.

In the second round, the full texts of the selected articles were then reviewed according to additional inclusion criteria:

- (a) the horizon scan or foresight methodology was detailed, and
- (b) the priority areas included relevant science and/or technology, and
- (c) a collaborative/international approach was used, and
- (d) the horizon scanning undertaken spanned a period of between 2 and 15 years.

Alternatively, the paper was required to demonstrate methodological aspect(s) of foresight or horizon scanning of potentially general applicability.

The foresight period of 2-15 years reflected the facts that signals suggesting impact in less than two years obviously 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.

The mapping was elaborated using the EuroScan International Information Network method, a scientific association of member organizations and individuals for the exchange of information on important emerging new drugs, devices, procedures, programs, and settings in health care (EuroScan), and novel methodological aspects from the searched literature.(12)

Patient and Public Involvement

The patients and public were not directly involved in the design or conduct of the study.

RESULTS

There were 413 papers identified through the initial database searches and grey literature, of which 252 were removed due to duplication or failing to meet the inclusion criteria. 60 papers were excluded because of language issues or lack of access to full-text. 101 publications were included in this study after reading the full text as indicated (Fig 2).

Fig 1. Literature selection process flowchart (16)

Consistency between the selection of papers by the two researchers, who undertook the screening, was fair (Cohen's unweighted Kappa =0.28).(17) A third researcher therefore screened the excluded literature according to the criteria to ensure that all relevant papers were captured (and resulting in one further publication being selected).

Most of the studies included in this review address horizon scanning as whole, following the process outlined in Figure 1, and of these, many operate in a national context. A few papers also focus on the use of specific methodological aspects such as Delphi techniques (see Table 1). Given the databases interrogated, the most prevalent priority areas identified were environmental issues,(12) gene therapy,(8) oncology(9) and clinical practice. Public sector bodies in the UK, USA, Sweden and Australia published the most on the topic. Internationally, EuroScan was repeatedly referenced for its role in harmonizing horizon scanning methodology, supporting its members and encouraging international collaboration.

Risk of bias was assessed in accordance with the BMJ guidelines and the Cochrane risk of bias tool. Most bias were not applicable to these non-clinical qualitative studies, however the following were:

- A form of publication bias was likely in which only horizon scanning undertaken in organisations with a strong background in publishing academic publications were discovered. It was not possible to correct for this.
- Outcome bias may have occurred as the papers reported systematic methodological aspects of horizon scanning, whereas some horizon scanning may occur in an ad-hoc manner e.g. a signal discovered by word of mouth.
- The competing interests of the authors were not considered beyond the standards of the source journals. This was because it was not thought highly relevant to the reporting of methodologies.

Mapping

The process outlined in the EuroScan Method toolkit was used as a basis and novel methodological aspects found in the literature added.(12) The resulting map is segmented into: signal identification and detection, criteria and methods of filtration and prioritization, assessment, dissemination and updating of information, and overall evaluation of the process. Notable references are given; the full dataset is provided in supplementary data file.

Information sources and signal detection

For more detailed results, please see the supplementary information.

Signals are detected from manifold sources in a horizon scanning exercise; Table 1 summarises the most common origins of information.

Information sources (signal detection)

- Scientific/biomedical literature review
- Patents
- Input from industry and industry associations
- Other observatories
- Media
- International institutions and forums
- Individuals, committees and expert groups
- Surveys
- Government bodies
- Meetings and conferences
- Other organisations
- Grey literature

Table 1: Information sources used for signal detection in horizon-scanning

Review of the scientific and biomedical literature is perhaps the most common place to identify innovation. Searches can be structured, using systematic and validated strategies, for broad or targeted topic areas; (18-20) a two-step approach, first to survey the field and, second, for a 'deep dive', can be used. Recently issued patents and published patent applications (e.g., the European Patent Office)(21) represent an alternative source of early

signals, particularly of innovations originating in industry (large, medium and small). Systematic and/or *ad hoc* scanning of direct or indirect information about new findings from industry or industry associations(22, 23) (such as investment of venture capital in SMEs) is also useful for monitoring of research pipelines. As are, for example, clinical trials databases(24, 25) and intelligence gathered from research infrastructures and consortia, and from university and research institute technology transfer offices.

Other observatories of potential value include repositories of innovation and trends generated from the horizon scanning outputs of international regulators and the committees and expert groups of governmental bodies, such as OECD and EuroScan(26-28). The media - print, electronic and social - generate substantial topic-specific and commercially-relevant information, available via RSS feeds(13), Twitter, Facebook, etc.(29) Social media also allow suggestions of signals from stakeholders. Workshops can also be useful to bring together diverse experts (chosen on the basis of their area of specialisation, breadth of knowledge, publications and commitment to the process) to discuss areas of novel science and technology and to collaboratively scan the horizon from different points of view.(30) These 'sand-pit' exercises can be supplemented by participants from the scanning organisation itself, appropriate stakeholder groups, external consultants and policy-makers.(31, 32) For sustainable and continuous horizon scanning, it may prove valuable to create a steering committee, think tank or "idea radar" including representatives of the aforementioned participants.(33, 34)

Delphi studies are widely used to pool knowledge and build consensus around emerging issues. There are two or more rounds involved: in the first, participants identify relevant issues, which are then pooled and ranked; the second round sees these issues discussed followed by their re-ranking. This process is iterated until a consensus is reached. Several Delphi variations have been described, from more conventional workshop formats to the use of online tools such as Nvivo (quantitative analysis of text) or Wordle.net (a word cloud

tool).(35) The design of a Delphi study should take into account the sample size and confounding factors, such as the level of conformity in the group.(5, 36, 37)

Surveys, conducted via the web or by mail,(23, 34) enable staff of an organisation, stakeholders and the public to be asked to identify new technologies or trends.(38) These may be most useful when horizon-scanning in well-defined fields.(5) Semi-structured interviews covering a standard set of questions can also be used, with similar outcomes.(19) However, public input was not found to be hugely productive.(38) Likewise, an attempt to establish a Wikipedia community has been largely unsuccessful.(39)

Finally, a number of additional sources have been identified including draft legislation and policy papers from governmental bodies, the proceedings of scientific conferences and symposia, professional and scientific societies, interest groups, think-tanks and research funders (government, charities, venture capital, etc.), the so-called grey literature where global shifts that influence society, the economy and the environment — megatrends —(40) are sometimes foreseen. Google alert queries, Google Trends, Google News Timeline, Google Insight, and blogs were mentioned.(39, 41)

Filtration criteria and methods

For more detailed and explanatory results, please see the supplementary information.

Table 2 presents the criteria and methods commonly used to discard irrelevant signals.

Filtration criteria (discarding irrelevant	Filtration methods
signals)	
Potential impact	Classification criteria
Size of affected population or global	Automated text-mining tools
relevance	Individual and group filtration
• Novelty	Peer review
Level of innovation	Expert participation
• Evidence	
Organisational impact	
• Plausibility	
Levels of stakeholder and media	
interest	
Policy priority	
Stage of development	
Ethical and social issues	
Within time-frame of 2-15 years	

Table 2: Filtration criteria and methods used in horizon-scanning to discard irrelevant signals

Several key criteria concerning a signal's potential impact were used: (20, 34, 42-44) What are the costs, and the cost-utility ratio, of resource consumption; what are the implications in terms of quality of life, burden of disease and patient safety? (44, 45)

The level of evidence is a further important criterion that has been ranked using a simple traffic light system, (46) where green denotes sufficient evidence to support the uptake of the signal, yellow indicates insufficient evidence to support uptake but the evidence may constitute useful information, and red implies unsupportive or insufficient evidence.

In terms of filtration methods, these may be separated into those which tag signals according to the criteria in a binary yes/no fashion, or those which use distinct or graduated categories, e.g., confirmed, likely, potential, unlikely, and questionable.(25) Automated text-mining tools can be used with databases to enable the identification, tagging and categorisation of signals and facilitate clustering and filtering.(5) Individual or group filtration may be performed by organisational staff, who can also undertake, up to point, peer review that ultimately requires the participation of external experts. The latter can also be responsible for weighting signals, according to the criteria, using an evidence framework.(20, 30)

Prioritisation criteria and methods for assessing signals

For more detailed and explanatory results, please see the supplementary information.

The signals which have met the filtration criteria can then be prioritised. The prioritisation criteria which must be met, and the methods used to do so, are collected in Table 3.

Prioritisation criteria (assessing	Prioritisation methods
signals)	
Potential impact on outcomes	Qualitative approach
Size make-up of the affected	Quantitative or semi-quantitative
population	approaches
Expected variation of impact	Rating and ranking
Likely time-frame	Best-worst scaling
Evidence of effectiveness	Risk analysis
Relevance to strategic and political	Standardisation of signals
priorities	Delphi approach
Effect on other related policies	Public consultation
• Desirability	Engagement of experts
Factual basis	Mixed methods
Requirement of availability of	
expertise	
 Novelty 	
Table 2. Brightigation suitaria and mathe	

Table 3: Prioritisation criteria and methods used in horizon-scanning to assess signals

Logically, the criteria consider the potential impact on outcomes, a clear example being resource consumption, and the cost of a signal.(34, 42) The size and composition of the

affected population are therefore important factors, (34, 45, 47, 48) as well as the expected variation that may be observed between different subsets. (42, 47) For the signal to be prioritised, the timeframe must be realistic, (11, 34, 49) and there must be a clear, factual indication of true novelty and desirability. In addition to evidence of effectiveness, consideration must be given to the relative added-value over current practice, (34) and whether this sufficient to satisfy strategic and/or political priorities and policies (e.g., reduction in inequality)(42).

With respect to prioritisation methods, a simple qualitative approach uses short summaries of the signals as a basis to prioritise.(50) Quantitative or semi-quantitative approaches are obviously more rigorous and typical (for details of such approaches see supplementary information).

There were several novel Delphi approaches developed, for example, to acquire expert input online in a continuous feedback forum or market place. Here, participants prioritise, or purchase, a limited number of signals which then accrue a "price" that can ultimately be used to prioritise those of greatest value.(33) Controls are possible to counteract the possibility of scoring fatigue.(51)

Finally, it should be emphasised that the engagement of experts for prioritisation must ensure diverse participation from different sectors, geographical regions, disciplines, and demographics.(29, 43, 52) Public consultation is a valuable asset to provide input and involvement from citizens and users in prioritisation, and can be achieved in person, via email or online.(34, 39)

Signal assessment and methods

For more detailed and explanatory results, please see the supplementary information.

The signals which have met the prioritisation criteria are then assessed. The factors assessed, and the methods employed to do so, are in Table 4. (e.g., in terms of resource implications and broad financial perspectives).

Signal assessment	Assessment methods
Impact, e.g., resource (financial)	ExpertLens
implications	Driver analysis
Level of innovation	Scenario planning
Expected utilisation and diffusion	Expert, user and policy-maker
Risk assessment	participation
Actions required and time to impact	Peer review
Legal and ethical issues	- :
Barriers to market	
Stakeholder perception	7

Table 4: Signal assessment and methods used in horizon-scanning

A key factor to consider in the assessment of any signal, of course, are the resource implications. The expected utilisation and availability of the innovation across different geographical regions is also important(32, 34, 45), as is a detailed risk assessment. A number of practical issues must also be considered, including actions needed to translate the signal into use (such as further research, the development of new processes, and whether complementary technology, for example, is essential to realise the value of the signal), the time and investment required to do so, the need for new or specialised training of personnel involved,(11) the cooperation and acceptance of key stakeholders, any ethical

issues, access to the necessary experts(5) and the intellectual property associated with the signal, and whether legislative or regulatory guideline changes are required. As always, impact on the market must be taken into consideration: is the innovation likely to have a disruptive effect, will it encounter reimbursement barriers, what are the timelines and milestones,(33) etc.? A consensus level of innovation can be sought (e.g., important, moderate, modest)(53).

Insofar as the methods used for signal assessment are concerned, a number of approaches are available (see supplementary information).

Dissemination and evaluation of the results of horizon scanning

For more detailed and explanatory results, please see the supplementary information.

The key elements involved in the disseminating and evaluating the results of horizon scanning are listed in Table 5.

Dissemination	Evaluation
Format	Short, medium and long-term
Methods	Process and output audit
Audience	Validation and sensitivity
Frequency	Focus groups
• Updating	Metrics
	Access to database

Table 5: Dissemination and evaluation of the results of horizon-scanning

In terms of dissemination, the assessment of an individual signal can be summarised in a document with the following elements: authors, lay summary, assessment objectives and methods, background and current practice, signal description, impacts and other issues, estimated time to impact, comparator signals (innovations), expert opinion, and declaration of any conflict of interests. It may also be beneficial to include policy recommendations which are linked to decision-making priorities, structures, and individual and cross-cutting policies.(18, 30, 38, 45, 48) Dissemination can be achieved, when a new report is available, via numerous pathways, including email, social media, notification of target groups,(39, 43) public events involving the participation of policymakers,(5, 34) publicly-accessible repositories of data or outputs that are clearly indexed, easily searchable and categorised, for example, by level of evidence and other metrics.(41, 54)

Dissemination of any new report should be made systematically through diverse platforms(43) and shared directly with relevant organisations.(41) The frequency of dissemination depends on circumstances.

A related activity that bridges dissemination and evaluation is the updating of horizon-scanning information. This comprises four essential elements: (a) continually checking and pruning sources based on their usefulness, relevance, and evolution, (b) monitoring and updating changes in signals by periodically refreshing the horizon scan, (c) reassessment of signals when sufficient new data are available or a step-change in technology has occurred, (d) validating annually, for example, the horizon-scanning update by a team of expert researchers, practitioners and journalists.

Evaluation of the results of horizon-scanning can be performed in the short, medium and long-term. A short-term evaluation may involve the following actions: survey of an appropriate audience on the usefulness of horizon-scanning in decision-making; use of metrics (e.g., provided by Google Analytics), such as number of downloads, page views, average session duration, citations in publications and funding applications; reports of

failures; consistency with other horizon scanning methods. In the medium-term, an evaluation would include the responsiveness of the horizon-scanning team to requests; the ability to keep the horizon-scanning content up-to-date; to compare findings with "gold" standards (e.g., EuroScan, The Agency for Healthcare Research and Quality); and to measure sensitivity and associated predictive value. Finally, a long-term evaluation assesses the usage of horizon-scanning information in arriving at decisions; the accuracy of projections; the timeliness with which new technologies were detected; the prioritisation criteria which best signalled the impact of the technology.

A process and output audit represents another approach to evaluation and ensures the completeness of the search record; records of external input; records of expert contact details; clear filing of information used; and a clear statement of the innovation in the briefing. 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 the database.

DISCUSSION

There were a wide variety of sources and methods used to identify new and emerging issues. However, it was common to use scientific literature, individuals, committees and expert groups, the web and Delphi methodologies. That the scientific literature dominates is expected as innovation often begins in an academic environment and because widely-accessible bibliographic databases have powerful search and filtering capabilities. The frequent use of the Delphi methodology may be explained by its ability to 'crowd-source' information and build a consensus amongst participants in a relatively short timeframe. This consensus, particularly expert consensus, adds weight to the conclusions drawn from horizon scanning.

Overall, the majority of the methods used were manual or semi-automated, with relatively few automated aspects. This could be due to the limited availability of software and budget constraints. Complex filtration, prioritisation and assessment criteria are some of the barriers to full automation that may be resolved in the not-too-distant future by the rapidly evolving fields of machine learning and artificial intelligence.

Dissemination of horizon-scanning reports appear to have rarely fed directly and systematically into policymaking. This may simply be a reflection of the unpredictable and political nature of policymaking, as well as a mismatch with the longer time-scale of horizon-scanning. Equally, it is probably fair to say that the information gathered by horizon-scanning lacks, at least to some extent, the conventional measures of credibility and authority required to influence policymaking.(30) New tools and approaches (e.g., via generation of complex scenarios and the clear weighting of evidence)(30, 55) are probably needed to enable horizon-scanning to be considered more seriously by policymakers.

The distance of the horizon scanned was also found to be a tricky balance between the need to assess signals as early as possible to inform decision makers, and the limited information

available at an early stage.(56) There were many different evaluation methods employed, covering different time-spans, reflecting *inter alia* cultural differences, resource limitations and a time-lag between horizon-scanning and its critical evaluation (for example, a high false-positive rate of horizon-scanning implied the need for tighter filtration criteria)(2). From a public policy standpoint, horizon-scanning has both informative and creative functions, alerting policy makers to emerging issues, and providing new, plausible policy options.(5) This use of horizon-scanning is well established for identification of emerging issues, both positive and negative, in global conservation and biological diversity.(57) In some contrast, however, in the biomedical field, in which this review has concentrated, horizon-scanning is biased towards identification of positive, innovative signals as those with low value inevitably have little impact.(58) Finally, in addition to its institutional value, horizon-scanning can significantly help related stakeholders, such as technology developers or civil society - it can reveal barriers to innovation and allow proactive engagement to reduce these barriers.(59)

Limitations

As systematic reviews into horizon scanning in healthcare have been undertaken previously, some duplication of findings was inevitable;(1-5) however, this review offers an up-to-date and wider perspective, and includes methodologies from beyond the health field. Resource limitations have precluded evaluation of horizon-scanning in other, related sectors, and consideration of material in languages other than English and Italian. Lastly, a fully comprehensive review of all methodologies has not been performed for practical reasons: the inconsistent reporting of the horizon-scanning details and the continually evolving approaches employed. This effort must be viewed as a 'snapshot', therefore, of a rapidly moving target.

Conclusions

To respond to accelerating innovation, horizon-scanning methodology is being adopted both nationally and internationally, particularly in the public sector. 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.(4, 5)

Undoubtedly, automation and the development of 'intelligent' horizon-scanning are short-term milestones that will significantly improve the process, enhancing the evidence base, disseminating the acquired outputs efficiently, and facilitating decision-making. Self-evidently, given the need for horizon-scanning across diverse disciplines, involving large numbers of interested stakeholders with related information needs, the process can only benefit from international collaboration. To this end an initiative is already underway within the International Coalition of Medicines Regulatory Authorities in which the EMA is taking an active role)(60, 61). Of course, scanning the horizon for signals is not an endpoint, in and of itself, but rather a window through which current and future opportunities and policies can be linked.(62) 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.

Acknowledgments

Thank you to Angela Brand, Monica Ensini and Lucia D'apote for your kind assistance.

Disclaimer

The views expressed in this article are the personal views of the authors and may not be understood or quoted as being made on behalf of or reflecting the position of the agencies or organisations with which the authors are affiliated.

Data sharing

The dataset is available in the supplementary data file or upon request.

Competing interests

We declare that no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Author contributions:

Philip Hines, Marisa Papaluca, Li hiu yu and Richard Guy all made the following contributions to the work:

- Substantial contributions to the conception or design of the work; or the acquisition,
 analysis, or interpretation of data for the work; AND
- Drafting the work or revising it critically for important intellectual content; AND
- Final approval of the version to be published; AND
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

- 1. Packer C, Simpson S, Almeida RT. EuroScan International Network Member Agencies: their structure, processes, and outputs. . *International Journal of Technology Assessment in Health Care*. 2015;31(1-2):78-85.
- 2. Packer C, Fung M, Stevens A. Analyzing 10 years of early awareness and alert activity in the United Kingdom. *International Journal of Technology Assessment in Health Care*. 2012;28(3):308-14.
- 3. Sun F, Bruening W, Uhl S, Ballard R, Tipton K, Schoelles K. Quality, Regulation and Clinical Utility of Laboratory-developed Molecular Tests. AHRQ Technology Assessments. Rockville (MD)2010.
- 4. Doos L, Packer C, Ward D, Simpson S, Stevens A. Past speculations of the future: a review of the methods used for forecasting emerging health technologies. *BMJ Open*. 2016;6(3).
- 5. Amanatidou E, Butter M, Carabias V, Könnölä T, Leis M, Saritas O, et al. On concepts and methods in horizon scanning: Lessons from initiating policy dialogues on emerging issues. *Science and Public Policy*. 2012;39(2):208-21.
- 6. Collins A. The Global Risks Report 2018. Geneva: World Economic Forum; 2018.
- 7. Bujar M MN, Liberti L. R&D Briefing 65: New drug approvals in six major authorities 2007 2016: Focus on the internationalisation of medicines. London: Centre for Innovation in Regulatory Science; 2017.
- 8. O'Dwyer L, Nolan L, Fisher C. Supporting Innovation through Regulation and Science: Ireland as an Innovation Hub for Health Products. *Biomedicine Hub*. 2017;2(Suppl. 1):3-.
- 9. ICMRA. Key Outcomes. Kyoto: International Coalition of Medicines Regulatory Authorities (ICMRA); 2017.
- 10. Stevens A, Packer C, Roberts G. Early warning and of new health care technologies in the United Kingdom. *International Journal of Technology Assessment in Health Care*. 1998;14(4):680-6.
- 11. Plüddemann A, Heneghan C, Thompson M, Roberts N, Summerton N, Linden-Phillips L, et al. Prioritisation criteria for the selection of new diagnostic technologies for evaluation. *BMC health services research*. 2010;10(1):109.
- 12. EuroScan. A toolkit for the identification and assessment of new and emerging health technologies. Birmingham; 2014.
- 13. Urquhart GJ, Saunders P. Wider horizons, wiser choices: horizon scanning for public health protection and improvement. *Journal of public health (Oxford, England)*. 2017;39(2):248-53.
- 14. Sun F, Schoelles K. A systematic review of methods for health care technology horizon scanning. . *Agency for Healthcare Research and Quality*. 2013.
- 15. Mulrow CD. Systematic Reviews: Rationale for systematic reviews. *BMJ*. 1994;309(6954):597-9.
- 16. Moher D, Liberati A, Tetzlaff J, Altman DG, The PG. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLOS Medicine*. 2009;6(7):e1000097.
- 17. McHugh ML. Interrater reliability: the kappa statistic. *Biochemia Medica*. 2012;22(3):276-82.
- 18. CADTH. CADTH Environmental Scan Process. 2015.
- 19. Jones MM, Hall A, Brooker D, Castle-Clarke S, Winpenny E, Jahagirdar D, et al. The future of public health: a horizon scan. *Rand health quarterly*. 2014;4(3).
- 20. Varela-Lema L, De La Fuente-Cid R, López-García M. Developing a prioritized list of innovative technologies: the Spanish experience. *International Journal of Technology Assessment in Health Care*. 2014;30(6):626-33.

- 21. Office TEP. 2018 [Available from: https://www.epo.org/index.html.
- 22. Working together to improve NHS planning for new medicines: UK PhramaScan;
- 2018 [Available from: https://www.ukpharmascan.org.uk/static/about.
- 23. Smith J, Ward D, Michaelides M, Moore AT, Simpson S. New and emerging technologies for the treatment of inherited retinal diseases: a horizon scanning review. *Eye*. 2015;29:1131.
- 24. Jackson GMDMGTKAHJCM, Michael N, Deidre B, E CH, Andrew M, Deborah S, et al. Trans Tasman Radiation Oncology Group: Development of the Assessment of New Radiation Oncology Technology and Treatments (ANROTAT) Framework. *Journal of Medical Imaging and Radiation Oncology*. 2015;59(3):363-70.
- 25. Noorlander CW, Kooi MW, Oomen AG, Park MV, Vandebriel RJ, Geertsma RE. Horizon scan of nanomedicinal products. *Nanomedicine*. 2015;10(10):1599-608.
- 26. Clyne M, Schully SD, Dotson WD, Douglas MP, Gwinn M, Kolor K, et al. Horizon scanning for translational genomic research beyond bench to bedside. *Genetics in Medicine*. 2014;16(7):535.
- 27. Saunders PJ, Middleton JD, Rudge G. Environmental Public Health Tracking: a cost-effective system for characterizing the sources, distribution and public health impacts of environmental hazards. *Journal of Public Health*. 2017;39(3):506-13.
- 28. Varela-Lema L, Punal-Riobóo J, Acción BC, Ruano-Ravina A, García ML. Making processes reliable: a validated pubmed search strategy for identifying new or emerging technologies. *International journal of technology assessment in health care*. 2012;28(4):452-9.
- 29. Sutherland WJ, Broad S, Caine J, Clout M, Dicks LV, Doran H, et al. A Horizon Scan of Global Conservation Issues for 2016. *Trends in Ecology & Evolution*. 2016;31(1):44-53.
- 30. Garnett K, Lickorish FA, Rocks SA, Prpich G, Rathe AA, Pollard SJ. Integrating horizon scanning and strategic risk prioritisation using a weight of evidence framework to inform policy decisions. *The Science of the total environment*. 2016;560-561:82-91.
- 31. Sutherland WJ, Freckleton RP. Making predictive ecology more relevant to policy makers and practitioners. *Philosophical Transactions of the Royal Society B: Biological Sciences*. 2012;367(1586):322-30.
- 32. Veenstra DL, Piper M, Haddow JE, Pauker SG, Klein R, Richards CS, et al. Improving the efficiency and relevance of evidence-based recommendations in the era of whole-genome sequencing: an EGAPP methods update. *Genetics in medicine*. 2013;15(1):14.
- 33. Masum H, Ranck J, Singer PA. Five promising methods for health foresight. *Foresight*. 2010;12(1):54-66.
- 34. Sun F, Schoelles K. A systematic review of methods for health care technology horizon scanning. *AHRQ Publication*. 2013:1-82.
- 35. Dawson MN, Algar AC, Antonelli A, Dávalos LM, Davis E, Early R, et al. An horizon scan of biogeography. *Frontiers of biogeography*. 2013;5(2).
- 36. Birko S, Dove ES, Özdemir V. Evaluation of Nine Consensus Indices in Delphi Foresight Research and Their Dependency on Delphi Survey Characteristics: A Simulation Study and Debate on Delphi Design and Interpretation. *PLOS ONE*. 2015;10(8).
- 37. Birko S, Dove ES, Özdemir V. A Delphi Technology Foresight Study: Mapping Social Construction of Scientific Evidence on Metagenomics Tests for Water Safety. *PLOS ONE*. 2015;10(6):e0129706.
- 38. Kark S, Sutherland WJ, Shanas U, Klass K, Achisar H, Dayan T, et al. Priority Questions and Horizon Scanning for Conservation: A Comparative Study. *PLOS ONE*. 2016;11(1).
- 39. Simpson S, Cook A, Miles K. Patient and public involvement in early awareness and alert activities: an example from the United Kingdom *International Journal of Technology Assessment in Health Care*. 2018;34(01):10-7.
- 40. Reimers-Hild C. Strategic foresight, leadership, and the future of rural healthcare staffing in the United States. *Jaapa*. 2018;31(5):44-9.

- 41. Gwinn M, Grossniklaus DA, Yu W, Melillo S, Wulf A, Flome J, et al. Horizon scanning for new genomic tests. *Genetics in Medicine*. 2011;13(2):161.
- 42. Ciani O, Jommi C. The role of health technology assessment bodies in shaping drug development. *Drug design, development and therapy*. 2014;8:2273.
- 43. Nachtnebel A, Breuer J, Willenbacher W, Bucsics A, Krippl P, Wild C. Looking back on 5 years of horizon scanning in oncology. *International journal of technology assessment in health care*. 2016;32(1-2):54-60.
- 44. Stafinski T, Topfer L-A, Zakariasen K, Menon D. The role of surgeons in identifying emerging technologies for health technology assessment. *Canadian Journal of Surgery*. 2010;53(2):86-92.
- 45. Eriksson I, Wettermark B, Persson M, Edström M, Godman B, Lindhé A, et al. The Early Awareness and Alert System in Sweden: History and Current Status. *Frontiers in Pharmacology*. 2017;8(674).
- 46. RANZCR. Position Paper Techniques and Technologies in Radiation Oncology 2015 Sydney: The Royal Australian and New Zealand College of Radiologists; 2015.
- 47. Nachtnebel A, Geiger-Gritsch S, Hintringer K, Wild C. Scanning the horizon—Development and implementation of an early awareness system for anticancer drugs in Austria. *Health Policy*. 2012;104(1):1-11.
- 48. Raman G, Wallace B, Patel K, Lau J, Trikalinos TA. Update on horizon scans of genetic tests currently available for clinical use in cancers. In: Quality AfHRa, editor. Rockville (MD)2011.
- 49. Wild C, Simpson S, Douw K, Geiger-Gritsch S, Mathis S, Langer T. Information service on new and emerging health technologies: Identification and prioritization processes for a European Union–wide newsletter. *International Journal of Technology Assessment in Health Care*. 2009;25(S2):48-55.
- 50. Maddern G, Boult M, Ahern E, Babidge W. ASERNIP-S: International trend setting. *ANZ journal of surgery*. 2008;78(10):853-8.
- 51. Chapman AM, Taylor CA, Girling AJ. PRM22 The Headroom Method of Early Economic Evaluation of Medical Devices: A Useful Tool for Device Developers? *Value in Health*. 2012;15(7):A463-A4.
- 52. Rudd MA, Moore AFP, Rochberg D, Bianchi-Fossati L, Brown MA, D'Onofrio D, et al. Climate research priorities for policy-makers, practitioners, and scientists in Georgia, USA. *Environmental management*. 2018.
- 53. Joppi R, Demattè L, Menti AM, Pase D, Poggiani C, Mezzalira L, et al. The Italian Horizon Scanning Project. *European journal of clinical pharmacology*. 2009;65(8):775-81.
- 54. Khoury MJ, Gwinn M, Dotson WD, Schully SD. Knowledge integration at the center of genomic medicine. *Genetics in Medicine*. 2012;14(7):643.
- 55. Gale P, Breed AC. Horizon scanning for emergence of new viruses: from constructing complex scenarios to online games. *Transboundary and Emerging Diseases*. 2012;60(5):472-4.
- 56. Wild C, Langer T. Emerging health technologies: informing and supporting health policy early. *Health Policy*. 2008;87(2):160-71.
- 57. Sutherland WJ, Butchart SH, Connor B, Culshaw C, Dicks LV, Dinsdale J, et al. A 2018 horizon scan of emerging issues for global conservation and biological diversity. *Trends in Ecology & Evolution*. 2018;33(1):47-58.
- 58. Mundy L, Hiller J, Merlin T. The true role of horizon scanning in Australia: who it informs and why. . *international Journal of Technology Assessment in Health Care*. 2011;27(1):95-6.
- 59. Ciani O, Jommi C. The role of health technology assessment bodies in shaping drug development. *Drug Des Devel Ther*. 2014;8:2273-81.
- 60. ICMRA. ICMRA strategic strategic priority on innovation. 2017 [Available from: http://www.icmra.info/drupal/sites/default/files/2017-12/ICMRA%20Innovation%20Concept%20Note 0.pdf.

- 61. HMA, EMA. Mandate of the European Innovation Network. 2016.
- 62. Wettermark B, Persson ME, Wilking N, Kalin M, Korkmaz S, Hjemdahl P, et al. Forecasting drug utilization and expenditure in a metropolitan health region. *BMC Health Services Research*. 2010;10(1).



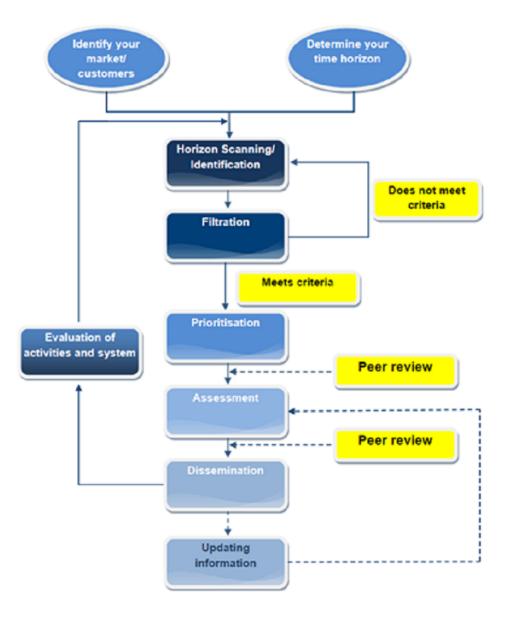
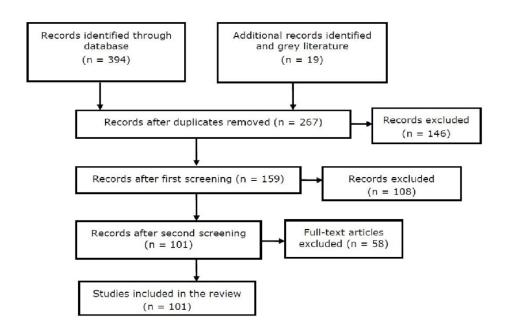


Fig 1. Common stages of Horizon scanning from the EuroScan network (12). This figure is licensed under the Creative Commons Attribution-NonCommercial-ShareAlike4.0 International License (CC BY-NC-SA 4.0)

97x113mm (300 x 300 DPI)



Caption : Fig 2. Literature selection process flowchart (16) $150 \times 102 \text{mm}$ (300 x 300 DPI)

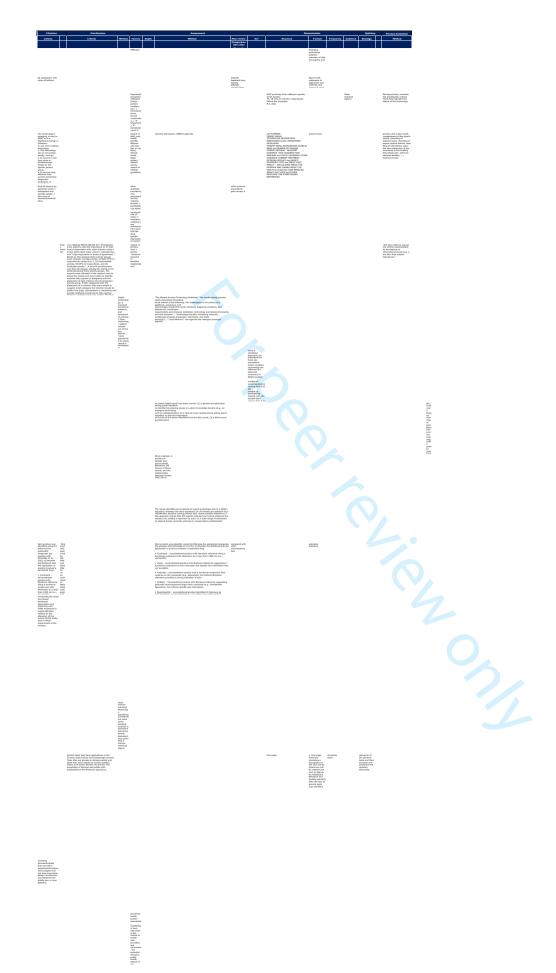


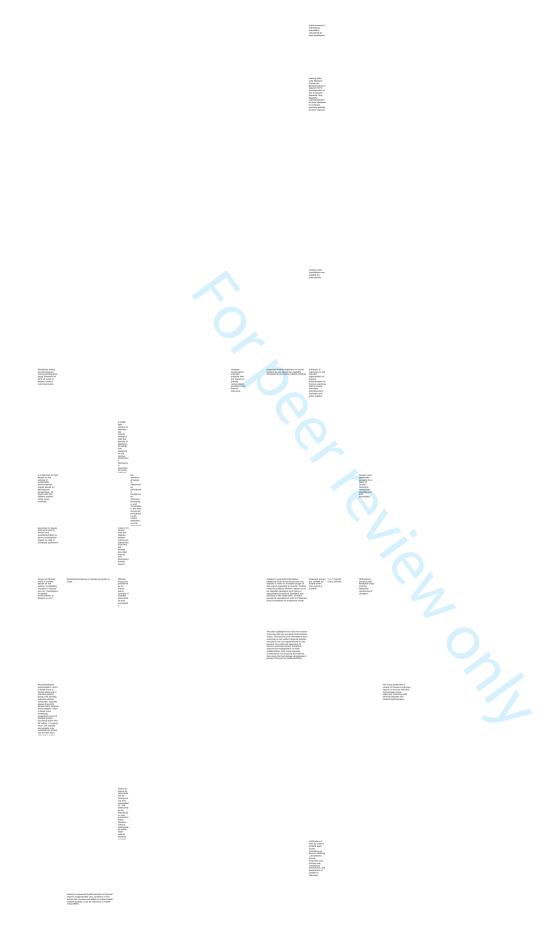


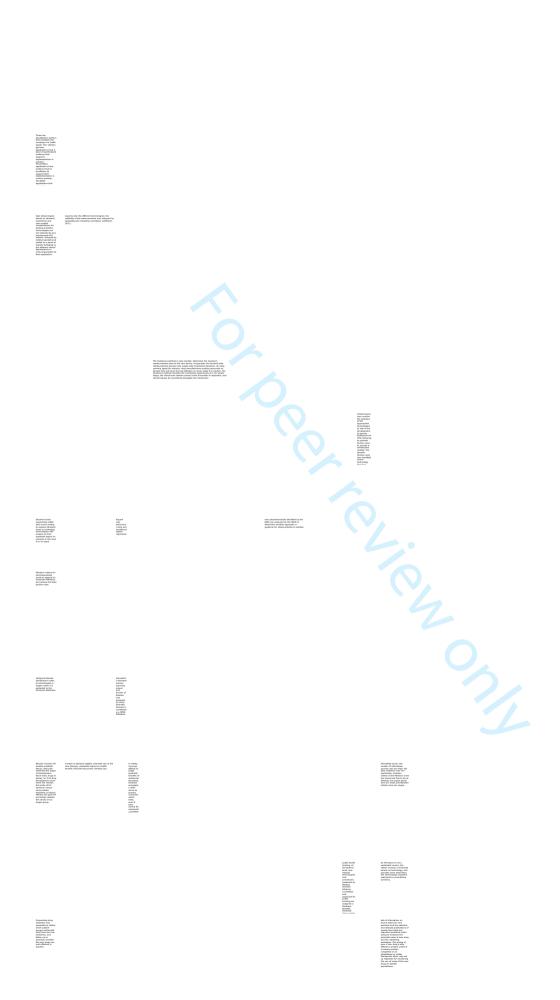
















Full Mapping

The process outlined in the EuroScan Method toolkit was used as a basis and novel methodological aspects found in the literature added (9). The resulting map is segmented into: signal identification and detection, criteria and methods of filtration and prioritization, assessment, dissemination and updating of information, and overall evaluation of the process. Notable references are given; the full dataset is provided in S1 Appendix.

Information sources and signal detection

Signals are detected from manifold sources in a horizon scanning exercise; Table 1 summarises the most common origins of information.

Information sources (signal detection)

- · Scientific/biomedical literature review
- Patents
- Input from industry and industry associations
- Other observatories
- Media
- International institutions and forums
- Individuals, committees and expert groups
- Surveys
- Government bodies
- Meetings and conferences
- Other organisations
- Grey literature

Table 1: Information sources used for signal detection in horizon-scanning

Review of the scientific and biomedical literature is perhaps the most common place to identify innovation and novel methodologies emerging (primarily) from academic research laboratories. Searches can be structured, using systematic and validated strategies, for broad or targeted topic areas (17-19); a two-step approach, first to survey the field and, second, for a 'deep dive', can be used. Recently issued patents and published patent applications (e.g., the European Patent Office (20)) represent an alternative source of early signals, particularly of innovations originating in industry (large, medium and small). Systematic and/or *ad hoc* scanning of direct or indirect information about new findings from industry or industry associations (21, 22) (such as investment of venture capital in SMEs) is also useful for monitoring of research pipelines. As are, for example, clinical trials databases (23, 24) and intelligence gathered from research infrastructures and consortia, and from university and research institute technology transfer offices.

Other observatories of potential value include repositories of innovation and trends generated from the horizon scanning outputs of international regulators and the committees and expert groups of governmental bodies, such as OECD and EuroScan (25-27). The media - print, electronic and social - generate substantial topic-specific and commercially-relevant information, available via RSS feeds (10), Twitter, Facebook, etc. (28). They also allow suggestions of signals from stakeholders. Workshops can also be useful to bring together diverse experts (chosen on the basis of their area of specialisation, breadth of knowledge, publications and commitment to the process) to discuss areas of novel science and technology and to collaboratively scan the horizon from different points of view (29). These 'sand-pit' exercises can be supplemented by participants from the scanning organisation itself, appropriate stakeholder groups, external consultants and policy-makers (30, 31). For sustainable and continuous horizon scanning, it may prove valuable to create a steering committee, think tank or "idea radar" including representatives of the aforementioned participants (32, 33).

Delphi studies are widely used to pool knowledge and build consensus around emerging issues. There are two or more rounds involved: in the first, participants identify relevant issues, which are then pooled and ranked; the second round sees these issues discussed followed by their re-ranking. This process is iterated until a consensus is reached. Several Delphi variations have been described, from more conventional workshop formats to the use of online tools such as Nvivo (quantitative analysis of text) or Wordle.net (a word cloud tool) (34). The design of a Delphi study should take into account the sample size and confounding factors, such as the level of conformity in the group (7, 35, 36).

Surveys, conducted via the web or by mail (22, 33), enable staff of an organisation, stakeholders and the public to be asked to identify new technologies or trends (37). These have proved most useful when horizon-scanning in well-defined fields (7). Semi-structured interviews covering a standard set of questions can also be used, with similar outcomes (18). However, public input was not found to be hugely productive (38).

Likewise, an attempt to establish a Wikipedia community has been largely unsuccessful (38).

Finally, a number of additional sources have been identified including draft legislation and policy papers from governmental bodies, the proceedings of scientific conferences and symposia, professional and scientific societies, interest groups, think-tanks and research funders (government, charities, venture capital, etc.), the so-called grey literature where global shifts that influence society, the economy and the environment — megatrends — (39) are sometimes foreseen. Google alert queries, Google Trends, Google News Timeline, Google Insight, and blogs were mentioned (38, 40).

Filtration criteria and methods

Table 2 presents the criteria and methods commonly used to discard irrelevant signals.

Filtra	tion criteria (discarding irrelevant	Filtration methods
signa	ls)	
•	Potential impact	Classification criteria
•	Size of affected population or global	Automated text-mining tools
	relevance	Individual and group filtration
•	Novelty	Peer review
•	Level of innovation	Expert participation
•	Evidence	
•	Organisational impact	
•	Plausibility	
•	Levels of stakeholder and media	
	interest	
•	Policy priority	
•	Stage of development	
•	Ethical and social issues	
•	Within time-frame of 2-15 years	· 4

Table 2: Filtration criteria and methods used in horizon-scanning to discard irrelevant signals

Several key criteria concerning a signal's potential impact were used (19, 33, 41-43): What are the costs, and the cost-utility ratio, of resource consumption; what are the implications in terms of quality of life, burden of disease and patient safety (43, 44)?

Next, to pursue the signal, it was asked what is the size of the affected population, and is this an issue of global relevance (45)? Is the signal truly novel, for which a legislative basis does not exist (8)? What is the level of the innovation based on factors such as design, function and materials? For example, is this a new drug class or a novel treatment paradigm?

The level of evidence is a further important criterion that has been ranked using a simple traffic light system (46), where green denotes sufficient evidence to support the uptake of the signal, yellow indicates insufficient evidence to support uptake but the evidence may constitute useful information, and red implies unsupportive or insufficient evidence. Additional criteria include (a) potential organisational impact: is this a technology that will require service reorganisation (33, 44), for example?; (b) plausibility – is uptake feasible?; (c) the level of interest of relevant stakeholders; (d) policy priority; (e) stage of development (e.g., clinical trials initiated?) (22, 42); (f) ethical and social issues; and (g) time-frame within the horizon-scanning period.

In terms of filtration methods, these may be separated into those which tag signals according to the criteria in a binary yes/no fashion, or those which use distinct or graduated categories, e.g., confirmed, likely, potential, unlikely, and questionable (24). Automated text-mining tools can be used with databases to enable the identification, tagging and categorisation of signals and facilitate clustering and filtering (7). Individual or group filtration may be performed by organisational staff, who can also undertake, up to point, peer review that ultimately requires the participation of external experts. The latter can also be responsible for weighting signals, according to the criteria, using an evidence framework (19, 29).

Prioritisation criteria and methods for assessing signals

The signals which have med the filtration criteria can then be prioritised. The prioritisation criteria which must be met, and the methods used to do so, are collected in Table 3.

Prioritisation criteria (assessing	Prioritisation methods
signals)	

- Potential impact on outcomes
- Size make-up of the affected population
- Expected variation of impact
- Likely time-frame
- Evidence of effectiveness
- Relevance to strategic and political priorities
- Effect on other related policies
- Desirability
- Factual basis
- Requirement of availability of expertise
- Novelty

- Qualitative approach
- Quantitative or semi-quantitative approaches
- · Rating and ranking
- Best-worst scaling
- Risk analysis
- Standardisation of signals
- Delphi approach
- Public consultation
- Engagement of experts
- Mixed methods

Table 3: Prioritisation criteria and methods used in horizon-scanning to assess signals

Logically, the criteria consider the potential impact on outcomes, a clear example being resource consumption, and the cost of a signal (33, 41). The size and composition of the affected population are therefore important factors (33, 44, 47, 48), as well as the expected variation that may be observed between different subsets (41, 47). For the signal to be prioritised, the timeframe must be realistic (8, 33, 49), and there must be a clear, factual indication of true novelty and desirability. In addition to evidence of effectiveness, consideration must be given to the relative added-value over current practice (33), and whether this sufficient to satisfy strategic and/or political priorities and policies (e.g., reduction in inequality (41)).

With respect to prioritisation methods, a simple qualitative approach uses short summaries of the signals as a basis to prioritise (50). Quantitative or semi-quantitative approaches are obviously more rigorous and typical. A straightforward rating and ranking can be undertaken using readily available online statistical tools; for example, according to median scores (28, 37), or by rating signals as gold, silver or bronze (51), or by application of a 7-point Likert scale. Prioritisation groupings (e.g., high, medium, low) can be extracted from the rankings and reliability of the results can be assessed using the intra-class correlation coefficient (19).

Another technique, best-worst scaling allows the views of experts to be ranked, via calculation of best-worst scores, square root estimates and conditional Logistic Regression (52). Risk prioritization, risk analysis, and multi-criteria decision analysis are further, more quantitative methods. The latter, for example, assigns objective weightings to different aspects of probability, impact, and other criteria, which can be used separately in rating signals (53). These ratings can then be used to rank and rerank the signals in an iterative and discursive process taking into account and trading off weightings based on stakeholder preferences (as identified, for example, in symposia or workshops) (54).

Signal scores from different raters can be standardised via the Z-statistic and agreement (or divergence) between the resulting values can be assessed using Kendall's coefficient of concordance (W), a non-parametric statistic that has values from 0 (no agreement) to 1 (complete agreement) (55).

A Delphi approach has been developed to acquire expert input online in a continuous feedback forum or market place. Participants prioritise, or purchase, a limited number of signals which then accrue a "price" that can ultimately be used to prioritise those of greatest value (32). Controls are possible to counteract the possibility of scoring fatigue (56).

Clustering and Likert-scale scoring has been used as a mixed qualitative and quantitative method (57). Wordle.net has also been applied to the prioritisation of signals based on the frequency with which they appear in cloud-based searches.

Finally, it should be emphasised that the engagement of experts for prioritisation must ensure diverse participation from different sectors, geographical regions, disciplines, and demographics (28, 42, 53). Public consultation is a valuable asset to provide input and involvement from citizens and users in prioritisation, and can be achieved in person, via email or online (33, 38).



Signal assessment and methods

The signals which have met the prioritisation criteria are then assessed. The factors assessed, and the methods employed to do so, are in Table 4. (e.g., in terms of resource implications and broad financial perspectives).

Signal assessment	Assessment methods	

- Impact, e.g., resource (financial)
 implications
- Level of innovation
- Expected utilisation and diffusion
- Risk assessment
- Actions required and time to impact
- Legal and ethical issues
- Barriers to market
- Stakeholder perception

- ExpertLens
- Driver analysis
- Scenario planning
- Expert, user and policy-maker participation
- Peer review

Table 4: Signal assessment and methods used in horizon-scanning

A key factor to consider in the assessment of any signal, of course, are the resource implications. The expected utilisation and availability of the innovation across different geographical regions is also important (31, 33, 44), as is a detailed risk assessment. A number of practical issues must also be considered, including actions needed to translate the signal into use (such as further research, the development of new processes, and whether complementary technology, for example, is essential to realise the value of the signal), the time and investment required to do so, the need for new or specialised training of personnel involved (8), the cooperation and acceptance of key stakeholders, any ethical issues, access to the necessary experts (7) and the intellectual property associated with the signal, and whether legislative or regulatory guideline changes are required. As always, impact on the market must be taken into consideration: is the innovation likely to have a disruptive effect, will it encounter reimbursement barriers, what are the timelines and milestones (32), etc.? A consensus level of innovation can be sought (e.g., important, moderate, modest (58)).

Insofar as the methods used for signal assessment are concerned, a number of approaches are available. ExpertLens (Rand Corporation), for example, is an iterative,

online system that permits a large group of people with different levels of expertise in different areas to independently, or collaboratively, identify, rate, prioritise, review and revise their opinions on important issues (59). Driver analysis is a process to identify and group trends, to determine the drivers of these trends, and to characterise the relationship between the drivers (60, 61). Multiple linear regression is used to find the probable links between causes and effects and other tools, such as spidergrams, can generate new perspectives (57). Scenario planning involves the creation of scenarios (e.g., best and worst cases) to assess the impact of signals (33). The headroom method can be applied to the determination of the maximum value of an emerging innovation (56). Methods should ensure the use of discounting and sensitivity analysis (62). Leveraging the participation of experts, users and policy-makers is an additional and valuable method by which to reach consensus about the value of a particular signal (e.g., via face-to-face workshops, remotely, or online (33)). A typical approach might involve a working group of experts that provides oversight and rotates responsibility for assessment (44) using, perhaps, tools such as ExpertLens, Delphi, the Nominal Group Technique and crowdsourcing (36). With respect to users of the potential innovation, their views are recognised as important: patients' assessment of impact on quality of life being an example (38). Finally, peer review and the early and ongoing involvement of experts with policymakers and stakeholders (7) can clearly facilitate both the communication and comparison against other horizon-scanning results (37, 44) and the translation of the signals into actions (7).

Dissemination and evaluation of the results of horizon scanning

The key elements involved in the disseminating and evaluating the results of horizon scanning are listed in Table 5.

Dissemination	Evaluation
---------------	------------

• Format	Short, medium and long-term
 Methods 	Process and output audit
• Audience	Validation and sensitivity
 Frequency 	Focus groups
 Updating 	• Metrics
	Access to database

Table 5: Dissemination and evaluation of the results of horizon-scanning

In terms of dissemination, the assessment of an individual signal can be summarised in a document with the following elements: authors, lay summary, assessment objectives and methods, background and current practice, signal description, impacts and other issues, estimated time to impact, comparator signals (innovations), expert opinion, and declaration of any conflict of interests. It may also be beneficial to include policy recommendations which are linked to decision-making priorities, structures, and individual and cross-cutting policies (17, 29, 37, 44, 48). Dissemination can be achieved, when a new report is available, via numerous pathways, including email, social media, notification of target groups (38, 42), public events involving the participation of policymakers (7, 33), publicly-accessible repositories of data or outputs that are clearly indexed, easily searchable and categorised, for example, by level of evidence and other metrics (40, 63).

The audience for dissemination is self-evident: internal staff and management; local and/or central government; institutions, agencies and relevant committees (42, 48, 58); research funding bodies (64); practitioners and (e.g.) healthcare system managers (37, 42); industry and other stakeholders (65). Dissemination of any new report should be made systematically through diverse platforms (42) and shared directly with relevant organisations (40). The frequency of dissemination depends on circumstances and examples available include on a quarterly basis (48) or the release of up to 1 to 3 reports per quarter (42); alternatively, information may be released at set time-points,

such as those corresponding to the accomplishment of milestones towards (or the time until) the expected introduction of an innovation (19).

A related activity that bridges dissemination and evaluation is the updating of horizon-scanning information. This comprises four essential elements: (a) continually checking and pruning sources based on their usefulness, relevance, and evolution, (b) monitoring and updating changes in signals by periodically refreshing the horizon scan, (c) reassessment of signals when sufficient new data are available or a step-change in technology has occurred, (d) validating annually, for example, the horizon-scanning update by a team of expert researchers, practitioners and journalists.

Evaluation of the results of horizon-scanning can be performed in the short, medium and long-term. A short-term evaluation may involve the following actions: survey of an appropriate audience on the usefulness of horizon-scanning in decision-making; use of metrics (e.g., provided by Google Analytics), such as number of downloads, page views, average session duration, citations in publications and funding applications; reports of failures; consistency with other horizon scanning methods. In the medium-term, an evaluation would include the responsiveness of the horizon-scanning team to requests; the ability to keep the horizon-scanning content up-to-date; to compare findings with "gold" standards (e.g., EuroScan, The Agency for Healthcare Research and Quality); and to measure sensitivity and associated predictive value. Finally, a long-term evaluation assesses the usage of horizon-scanning information in arriving at decisions; the accuracy of projections; the timeliness with which new technologies were detected; the prioritisation criteria which best signalled the impact of the technology.

A process and output audit represents another approach to evaluation and ensures the completeness of the search record; records of external input; records of expert contact details; clear filing of information used; and a clear statement of the innovation in the briefing. 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 the database.



Page 55 of 57

BMJ Open



PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary 3 4 5	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	N/A
8 Eligibility criteria 9 0	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	6
7 Study selection 8	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6-7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and yany assumptions land com/site/about	9 (guidelines.xhtml



PRISMA 2009 Checklist

3 [4			simplifications made.	
5 6 7 8 9 10 11	Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	Risk of bias was assessed in accordance with the BMJ guidelines and the Cochrane risk of bias tool. Most bias were not applicable to these non-clinical qualitative studies, however the following were: - A form of publication bias was likely in which only horizon scanning undertaken in organisations with a
13 14				strong background in publishing academic publications were discovered. It was not possible to correct for this.
16 17 18 19 20			Deert	- Outcome bias may have occurred as the papers reported systematic methodological aspects of horizon scanning, whereas some horizon scanning may occur in an ad-hoc manner e.g. a signal discovered by word of mouth.
21 22 23 24 25 26			Chich	- The competing interests of the authors were not considered beyond the standards of the source journals. This was because it was not thought highly relevant to the reporting of methodologies.
28 29	Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	9
31 32	Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	9
33			Page 1 of 2	

Page 1 of 2

35	Section/topic	#	Checklist item	Reported on page #
38 38	Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	9
40 41	Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
42 43	RESULTS			
45	Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, really with a from diagram propen by com/site/about/guidelines.xhtml	8
46)			



PRISMA 2009 Checklist

Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	N/A
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	9 (See point 12)
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	N/A
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	9
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	21-22
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	22
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	23
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	24

29 From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. 30 doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.

BMJ Open

Scanning the horizon: A systematic literature review of methodologies

Journal:	BMJ Open
Manuscript ID	bmjopen-2018-026764.R1
Article Type:	Research
Date Submitted by the Author:	15-Jan-2019
Complete List of Authors:	Hines, Philip; European Medicines Agency, SciRS; United Nations University-Maastricht Economic and social Research institute on Innovation and Technology Hiu yu, Li; European Medicines Agency, SciRS Guy, Richard; University of Bath - Department of Pharmacy and Pharmacology; European Medicines Agency, SciRS Papaluca, Marisa; European Medicines Agency, SciRS
Primary Subject Heading :	Health policy
Secondary Subject Heading:	Qualitative research
Keywords:	HEALTH SERVICES ADMINISTRATION & MANAGEMENT, EDUCATION & TRAINING (see Medical Education & Training), PUBLIC HEALTH, QUALITATIVE RESEARCH

SCHOLARONE™ Manuscripts

SCANNING THE HORIZON: A SYSTEMATIC LITERATURE REVIEW OF METHODOLOGIES

Authors:

Philip Hines^{1*},

Li hiu yu²,

Richard H. Guy³

Marisa Papaluca-Amati⁴

1 Scientific Committees Regulatory Science Strategy, the European Medicines Agency, 30 Churchill Place, Canary Wharf, London E14 5EU, United Kingdom, London, UK; United Nations University - Maastricht Economic and Social Research Institute on Innovation and Technology (UNU-MERIT); Department of International Health, Faculty of Health, Medicine and Life Sciences (FHLM), Maastricht University UNU-MERIT, Maastricht, Netherlands;

Email: Philip.hines@ema.europa.eu;

Telephone: +442036606048

- 2 Maastricht University, Maastricht, Netherlands; Scientific Committees Regulatory Science Strategy, the European Medicines Agency, London, UK
- 3 University of Bath, UK; Scientific Committees Regulatory Science Strategy, the European Medicines Agency, London, UK
- 4 Scientific Committees Regulatory Science Strategy, the European Medicines Agency, London, UK

*Corresponding author

Word count: 4102

ABSTRACT

Objectives: Society is confronted with the rapid emergence of innovation in science and technology. To manage this, horizon scanning is being adopted globally to identify, assess and prioritise innovations and trends at an early stage of their development. This enables decision-makers to be better informed and to prepare for change. The aim of this paper is to systematically identify and evaluate horizon scanning methodologies employed in the healthcare and biomedical fields.

Methods: A systematic literature review was performed using PubMed and Embase, and was supplemented with grey literature searches (2008 to 2018). The principal methodologies used in horizon scanning were extracted.

Results: Approximately 100 articles were summarised in a literature map. The search revealed many examples of horizon scanning across disciplines. Challenges, such as the need to refine prioritisation criteria, manage uncertainty inherent in the findings, and improve the dissemination of identified issues, have been highlighted.

Conclusion: 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. Further research to identify the most effective methodologies available would add depth to this landscape and enable the evolution of best practice to most efficiently anticipate novel developments and innovations.

Strengths and limitations of this study

- This systematic review offers an up-to-date perspective on horizon scanning methodologies – incorporating practices from a number of different fields; however, as reviews into horizon scanning in healthcare have been undertaken previously, some duplication of findings was inevitable.
- A detailed evaluation, and a more practical guide to all the methodologies, could not be performed for practical reasons; specifically, the inconsistent reporting of the horizon-scanning details and their efficacy, and the continually evolving approaches employed.
- The paper may be subject to omission bias as the literature reported systematic methodological aspects of horizon scanning; therefore, some ad-hoc horizon scanning methods may not be captured.

INTRODUCTION

Across organizations worldwide, the rapid emergence of high impact innovation is a major challenge faced by decision makers 1. To respond, the identification of future innovations and trends is being undertaken in a comprehensive, systematic and sustainable manner so that policy makers, and other stakeholders, can respond appropriately and enable innovations to reach the market with minimal developmental, legal, regulatory, process or procurement bottle-necks. To catalyse the achievement of this objective, horizon scanning is emerging as a valuable and viable strategy. This is particularly true in the health sector, where the European Medicines Agency (EMA) is seeking to promote the availability of innovative medicines using horizon scanning. This foresight will in turn inform the Agency's Regulatory Science Strategy and the European medicines regulatory network strategy 2-4. Horizon scanning has been in use for many years, initially by commercial organisations and later by public bodies; Japan was an early adopter of foresight methodologies in the 1970s ⁵ 6. Since then, horizon scanning has been used across diverse sectors to aid financial, policy, process and research planning 78. There are many definitions of horizon scanning 910, but most can be captured by its generic characterisation as a systematic examination of information sources to detect early signs of important developments. The approach generally targets the early lifecycle of technologies – i.e., in an early phase of adoption before their introduction onto the market - but may also scan for broader trends, challenges and opportunities. It provides an early warning of 'signals', rather than a comprehensive study of their impact.

Horizon scanning generally follows a process of signal detection, filtration, prioritisation, assessment and dissemination (Fig 1). Its use is growing across sectors ¹¹, and this risks the duplication of efforts (both in design and execution) as similar stretches of the horizon are scanned by many.

Fig 1. Common stages of Horizon scanning from the EuroScan network 9.

This figure is licensed under the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License (CC BY-NC-SA 4.0).

There have been no recent reviews of horizon scanning methods used in the health sector ⁹ ¹², or those looking at broader biomedical sectors ⁶ ⁷ ¹²⁻¹⁴. As a result, the aim of this literature review is to systematically identify and evaluate horizon scanning methodologies employed in the healthcare and biomedical fields. 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. This includes the activities of the EMA's recently established Regulatory Science Observatory, as well other international efforts to reduce duplication including the EU Innovation offices Network, the European Network for Health Technology Assessment, and the International Coalition of Medicines Regulatory Authorities (ICMRA) ⁴ ¹⁵.

METHODS

A systematic review of the literature was performed to capture and map the use of horizon scanning activity, and the widespread use of modern IT/web capabilities, over the period from 2008 to 2018 (see supplementary file 1) ¹⁶. Three researchers were involved and a systematic protocol was followed to minimise inter-rater bias; this involved cross validation between two researchers, with diverging opinions then arbitrated by the third. This systematic approach also permitted gaps and inconsistencies in the field to be identified. Data collection followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines ¹⁷: the literature was first screened and filtered using inclusion and exclusion criteria; the accepted papers then underwent data extraction and analysis; and, finally, the scanning methodologies were mapped.

Search strategy

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. The primary search terms used were derived from previous literature: "horizon scan*" OR "strategic foresight*" OR "systematic early dialogue*" OR "early warning and alert system*". All literature, of which the title or abstract contained any of the keywords above, was flagged.

Inclusion and exclusion criteria

Only articles published in English or Italian from 2008-2018 were included. In the first round of quality appraisal and screening (see supplementary file 1), the publication abstracts or title had to indicate:

- (a) either a methodology for horizon scanning or strategic foresight, or a discussion, or experience provided, of horizon scanning;
- (b) a breadth of horizon scanning of the relevant field or address a methodological aspect which may be generally applicable across different fields.

In the second round, the full texts of the selected articles were then reviewed according to additional inclusion criteria:

- (a) the horizon scan or foresight methodology was detailed, and
- (b) the priority areas included relevant science and/or technology, and
- (c) a collaborative/international approach was used, and
- (d) the horizon scanning undertaken spanned a period of between 2 and 15 years.

Alternatively, the paper was required to demonstrate methodological aspect(s) of foresight or horizon scanning of potentially general applicability.

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.

The mapping was elaborated using the EuroScan International Information Network method, a scientific association of member organizations and individuals for the exchange of information on important emerging new drugs, devices, procedures, programs, and settings in health care (EuroScan), and novel methodological aspects from the searched literature ⁹.

Patient and Public Involvement

The patients and public were not directly involved in the design or conduct of the study.

RESULTS

were three exceptions:

There were 413 papers identified through the initial database searches and grey literature, of which 252 were removed due to duplication or failing to meet the inclusion criteria. 60 papers were excluded because of language issues or lack of access to full-text. 101 publications were included in this study after reading the full text as indicated (Fig. 2).

Fig 2. Literature selection process flowchart ¹⁷

Consistency between the selection of papers by the two researchers, who undertook the screening, was fair (Cohen's unweighted Kappa = 0.28) 18 . A third researcher therefore screened the excluded literature according to the criteria to ensure that all relevant papers were captured (and resulting in one further publication being selected).

Most of the studies included in this review address horizon scanning as whole, following the process outlined in Fig. 1, and of these, many operate in a national context. A few papers also focus on the use of specific methodological aspects such as Delphi techniques (see Table 1). Given the databases interrogated, the most prevalent priority areas identified were environmental issues (9), gene therapy (8), oncology (9) and clinical practice. Public sector bodies in the UK, USA, Sweden and Australia published most often on the topic. Internationally, EuroScan was repeatedly referenced for its role in harmonizing horizon scanning methodology, supporting its members and encouraging international collaboration. Risk of bias was assessed in accordance with the BMJ guidelines and the Cochrane risk of

bias tool ¹⁹. While bias was not typically found in these non-clinical qualitative studies, there

- 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.
- Omission bias may have occurred as the papers reported systematic methodological aspects of horizon scanning; however, some horizon scanning may occur in an ad-hoc manner, e.g., a signal discovered by word-of-mouth.
- The competing interests of the authors were not considered beyond the standards of the source journals. This was because it was not thought highly relevant to the reporting of methodologies.

Mapping

The process outlined in the EuroScan Method toolkit was used as a basis and novel methodological aspects found in the literature were added ⁹. The resulting map is segmented into: signal identification and detection, criteria and methods of filtration and prioritisation, assessment, dissemination and updating of information, and overall evaluation of the process. Notable references are given and the full dataset is provided in the supplementary file 2.

Information sources and signal detection

Signals are detected from manifold sources in a horizon scanning exercise; Table 1 summarises the most common.

Review of the scientific and biomedical literature is perhaps the most common place to identify innovation. Searches can be structured, using systematic and validated strategies, for broad or targeted topic areas ²⁰⁻²²; a two-step approach, first to survey the field and, second, for a 'deep dive', can be used. Recently issued patents and published patent applications (e.g., the European Patent Office) ²³ represent an alternative source of early

signals, particularly of innovations originating in industry (large, medium and small). Systematic and/or ad hoc scanning of direct or indirect information about new findings from industry or industry associations ²⁴ ²⁵ (such as investment of venture capital in SMEs) is also useful for monitoring research pipelines. Similarly, other sources, such as clinical trials databases ²⁶ ²⁷ and intelligence gathered from research infrastructures and consortia, and from university and research institute technology transfer offices, are valuable.

Information sources (signal detection)

- Scientific/biomedical literature review
- Patents
- Input from industry and industry associations
- Other observatories
- Media
- · International institutions and forums
- Individuals, committees and expert groups
- Surveys
- Government bodies
- Meetings and conferences
- Other organisations
- Grey literature

Table 1: Information sources used for signal detection in horizon-scanning

Additional observatories of potential value include repositories of innovation and trends generated from the horizon scanning outputs of international regulators and the committees and expert groups of governmental bodies, such as OECD and EuroScan ²⁸⁻³⁰. The media -

print, electronic and social - generate substantial topic-specific and commercially-relevant information, available via RSS feeds ¹¹, Twitter, Facebook, and so on ³¹. Social media also provide signal suggestions from stakeholders. Workshops can also be useful to bring together diverse experts (chosen on the basis of their area of specialisation, breadth of knowledge, publications and commitment to the process) to discuss areas of novel science and technology and to collaboratively scan the horizon from different points of view ³². These 'sand-pit' exercises can be supplemented by participants from the scanning organisation itself, appropriate stakeholder groups, external consultants and policy-makers ³³ ³⁴. For sustainable and continuous horizon scanning, it may prove valuable to create a steering committee, think tank or "idea radar" including representatives of the aforementioned participants ¹² ³⁵.

Delphi studies are widely used to pool knowledge and build consensus around emerging issues. There are two or more rounds involved. In the first, participants identify relevant issues, which are then pooled and ranked; the second round sees these issues discussed followed by their re-ranking. This process is iterated until a consensus is reached. Several Delphi variations have been described, from more conventional workshop formats to the use of online tools such as Nvivo (quantitative analysis of text) or Wordle.net (a word cloud tool) ³⁶. The design of a Delphi study should take into account the sample size and confounding factors, such as the level of conformity in the group ^{7 37 38}.

Surveys, conducted via the web or by mail ¹² ²⁵, enable staff of an organisation, stakeholders and the public to be asked to identify new technologies or trends ³⁹. These may be most useful when horizon-scanning in well-defined fields ⁷. Semi-structured interviews covering a standard set of questions can also be used, with similar outcomes ²¹. However, public input was not found to be hugely productive in topic identification ⁴⁰. Likewise, an attempt to establish a Wikipedia community has been largely unsuccessful ⁴⁰.

Finally, a number of additional sources have been identified including draft legislation and policy papers from governmental bodies, the proceedings of scientific conferences and symposia, professional and scientific societies, interest groups, think-tanks and research funders (government, charities, venture capital, etc.), the so-called grey literature where global shifts that influence society, the economy and the environment - megatrends - ⁴¹ are sometimes foreseen. Google alert queries, Google Trends, Google News Timeline, Google Insight, and blogs were also mentioned ⁴⁰ ⁴².

Filtration criteria and methods

Table 2 presents the criteria and methods commonly used to discard irrelevant signals.

Several key criteria concerning a signal's potential impact were used ¹² ²² ⁴³⁻⁴⁵ including what are the costs, and the cost-utility ratio, of resource consumption, and what are the implications in terms of quality of life, burden of disease and patient safety ⁴⁵ ⁴⁶?

The level of evidence is a further important criterion that has been ranked using a simple traffic light system ⁴⁷, where green denotes sufficient evidence to support the uptake of the signal, yellow indicates insufficient evidence to support uptake but the evidence may constitute useful information, and red implies unsupportive or insufficient evidence.

In terms of filtration methods, these may be separated into those which tag signals according to the criteria in a binary yes/no fashion, or those which use distinct or graduated categories, e.g., confirmed, likely, potential, unlikely, and questionable ²⁷. Automated textmining tools can be used with databases to enable the identification, tagging and categorisation of signals and facilitate clustering and filtering ⁷. Individual or group filtration may be performed by organisational staff, who can also undertake some initial peer review that is ultimately performed in-depth by external experts. The latter can also contribute to, or determine, the weighting of signals, according to the criteria, using an evidence framework ²² ³².

Filtration criteria (discarding irrelevant	Filtration methods
signals)	
Potential impact	Classification criteria
Size of affected population or global	Automated text-mining tools
relevance	Individual and group filtration
• Novelty	Peer review
Level of innovation	Expert participation
• Evidence	
Organisational impact	
 Plausibility 	
Levels of stakeholder and media	
interest	
Policy priority	4.
Stage of development	
Ethical and social issues	1
Within time-frame of 2-15 years	O ₂

Table 2: Filtration criteria and methods used in horizon-scanning to discard irrelevant signals

Prioritisation criteria and methods for assessing signals

The signals which have met the filtration criteria can then be prioritised. The prioritisation criteria which must be met, and the methods used to do so, are collected in Table 3.

Prioritisation criteria (assessing	Prioritisation methods
signals)	
Potential impact on outcomes	Qualitative approach
Size make-up of the affected	Quantitative or semi-quantitative
population	approaches
Expected variation of impact	Rating and ranking
Likely time-frame	Best-worst scaling
Evidence of effectiveness	Risk analysis
Relevance to strategic and political	Standardisation of signals
priorities	Delphi approach
Effect on other related policies	Public consultation
• Desirability	Engagement of experts
Factual basis	Mixed methods
Requirement of availability of	
expertise	12
• Novelty	

Table 3: Prioritisation criteria and methods used in horizon-scanning to assess signals

Logically, the criteria consider the potential impact on outcomes, a clear example being resource consumption, and the cost implications ^{12 43}. The size and composition of the affected population are therefore important factors ^{12 46 48 49}, as well as the expected variation that may be observed between different subsets ^{43 48}. For the signal to be prioritised, the timeframe must be realistic ^{8 12 50}, and there must be a clear, factual indication of true novelty and desirability. In addition to evidence of effectiveness,

consideration must be given to the relative added-value over current practice 12 , and whether this sufficient to satisfy strategic and/or political priorities and policies (e.g., reduction in inequality) 43 .

With respect to prioritisation methods, a simple qualitative approach uses short summaries of the signals as a basis to prioritise ⁵¹. Quantitative or semi-quantitative approaches are obviously more rigorous and typical.

There were several novel Delphi approaches developed, for example, to acquire expert input online in a continuous feedback forum or market place. Here, participants prioritise, or purchase, a limited number of signals which then accrue a "price" that can ultimately be used to prioritise those of greatest value ³⁵. Controls are possible to counteract the possibility of scoring fatigue ⁵².

Finally, it should be emphasised that the engagement of experts for prioritisation must ensure diverse participation from different sectors, geographical regions, disciplines, and demographics ³¹ ⁴⁴ ⁵³. Public consultation is a valuable asset to provide input and involvement from citizens and users in prioritisation, and can be achieved in person, via email or online ¹² ⁴⁰.

Signal assessment and methods

The signals which have met the prioritisation criteria are then assessed. The factors assessed, and the methods employed to do so, are in Table 4 (e.g., in terms of resource implications and broad financial perspectives).

Signal assessment	Assessment methods
Impact, e.g., resource (financial)	ExpertLens
implications	Driver analysis
Level of innovation	Scenario planning
Expected utilisation and diffusion	Expert, user and policy-maker
Risk assessment	participation
Actions required and time to impact	Peer review
Legal and ethical issues	
Barriers to market	4.
Stakeholder perception	

Table 4: Signal assessment and methods used in horizon-scanning

A key factor to consider in the assessment of any signal, of course, is the resource implications. The expected utilisation and availability of the innovation across different geographical regions is also important ^{12 34 46}, as is an assessment of risk. A number of practical issues must also be considered, including actions needed to translate the signal into use (such as further research, the development of new processes, and whether complementary technology, for example, is essential to realise the value of the signal), the time and investment required to do so, the need for new or specialised training of personnel involved ⁸, the cooperation and acceptance of key stakeholders, any ethical issues, access to the necessary experts ⁷ and the intellectual property associated with the signal, and

whether legislative or regulatory guideline changes are required. As always, impact on the market must be taken into consideration. Is the innovation likely to have a disruptive effect, will it encounter reimbursement barriers, what are the timelines and milestones ³⁵, etc.? A consensus level of innovation can be sought (e.g., important, moderate, modest) ⁵⁴.

Insofar as the methods used for signal assessment are concerned, a number of approaches are available.

Dissemination and evaluation of the results of horizon scanning

The key elements involved in the disseminating and evaluating the results of horizon scanning are listed in Table 5.

Dissemination	Evaluation
Format	Short, medium and long-term
 Methods 	Process and output audit
Audience	Validation and sensitivity
Frequency	Focus groups
• Updating	Metrics
	Access to database

Table 5: Dissemination and evaluation of the results of horizon-scanning

In terms of dissemination, the assessment of an individual signal can be summarised in a document with the following elements: authors, lay summary, assessment objectives and methods, background and current practice, signal description, impacts and other issues, estimated time to impact, comparator signals (innovations), expert opinion, and declaration of any conflict of interests. It may also be beneficial to include policy recommendations which are linked to decision-making priorities, structures, and individual and cross-cutting

policies ^{20 32 39 46 49}. Dissemination can be achieved, when a new report is available, via numerous pathways, including email, social media, notification of target groups ^{40 44}, public events involving the participation of policymakers ^{7 12}, publicly-accessible repositories of data or outputs that are clearly indexed, easily searchable and categorised, for example, by level of evidence and other metrics ^{42 55}.

Dissemination of any new report should be made systematically through diverse platforms ⁴⁴ and shared directly with relevant organisations ⁴². The frequency of dissemination depends on circumstances.

A related activity that bridges dissemination and evaluation is the updating of horizon-scanning information. This comprises four essential elements: (a) continually checking and pruning sources based on their usefulness, relevance, and evolution ¹², (b) monitoring and updating changes in signals by periodically refreshing the horizon scan ⁴⁹, (c) reassessment of signals when sufficient new data are available or a step-change in technology has occurred ⁵⁶, and (d) validating annually, for example, the horizon-scanning update by a team of expert researchers, practitioners and journalists ³¹.

Evaluation of the results of horizon-scanning can be performed in the short, medium and long-term ¹². A short-term evaluation may involve the following actions: survey of an appropriate audience on the usefulness of horizon-scanning in decision-making; use of metrics (e.g., provided by Google Analytics), such as number of downloads, page views, average session duration, citations in publications and funding applications ⁵⁷; reports of failures; consistency with other horizon scanning methods. In the medium-term, an evaluation would include the responsiveness of the horizon-scanning team to requests, the ability to keep the horizon-scanning content up-to-date, comparing findings with other horizon scanning agencies/databases (e.g. EuroScan,), and measuring sensitivity and associated predictive value. Finally, a long-term evaluation assesses the usage of horizon-scanning information in arriving at decisions, the accuracy of projections, the timeliness

with which new technologies were detected, and the prioritisation criteria which best signalled the impact of the technology ⁵⁴.

A process and output audit represents another approach to evaluation and ensures the completeness of the search record, records of external input and expert contact details, clear filing of information used, and a clear statement of the innovation in the briefing 58. 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

There was a wide variety of sources and methods used to identify new and emerging issues. However, it was common to use scientific literature, individuals, committees and expert groups, the web and Delphi methodologies. That the scientific literature dominates is expected as innovation often begins in an academic environment and because widely-accessible bibliographic databases have powerful search and filtering capabilities. The frequent use of the Delphi methodology may be explained by its ability to 'crowd-source' information and build a consensus amongst participants in a relatively short timeframe. This consensus, particularly expert consensus, adds weight to the conclusions drawn from horizon scanning.

Overall, the majority of the methods used were manual or semi-automated, with relatively few automated aspects. This could be due to the limited availability of software and budget constraints. Complex filtration, prioritisation and assessment criteria are some of the barriers to full automation that may be resolved in the not-too-distant future by the rapidly evolving fields of machine learning and artificial intelligence ⁶⁰.

Dissemination of horizon-scanning reports appear to have rarely fed directly and systematically into policymaking. This may simply be a reflection of the unpredictable and political nature of policymaking, as well as a mismatch with the longer time-scale of horizon-scanning. Equally, it is probably fair to say that the information gathered by horizon-scanning lacks, at least to some extent, the conventional measures of credibility and authority required to influence policymaking ³². New tools and approaches (e.g., via generation of complex scenarios and the clear weighting of evidence) ³² ⁶¹ are probably needed to enable horizon-scanning to be considered more seriously by policymakers.

The distance of the horizon scanned was also found to be a tricky balance between the need to assess signals as early as possible to inform decision makers, and the limited information

available at an early stage ⁶². There were many different evaluation methods employed, covering different time-spans, reflecting *inter alia* cultural differences, resource limitations and a time-lag between horizon-scanning and its critical evaluation (for example, a high false-positive rate of horizon-scanning implied the need for tighter filtration criteria) ¹⁴.

From a public policy standpoint, horizon-scanning has both informative and creative functions, alerting policy makers to emerging issues, and providing new, plausible policy options ⁷. This use of horizon-scanning is well established for identification of emerging issues, both positive and negative, in global conservation and biological diversity ⁶³. In some contrast, however, in the biomedical field, in which this review has concentrated, horizon-scanning is biased towards identification of positive, innovative signals as those with low value inevitably have little impact.⁶⁴ Finally, in addition to its institutional value, horizon-scanning can significantly help related stakeholders, such as technology developers or civil society - it can reveal barriers to innovation and allow proactive engagement to reduce these barriers ⁴³.

Limitations

As systematic reviews into horizon scanning in healthcare have been undertaken previously, some duplication of findings was inevitable ^{6 7 13 14 65}; however, this review offers an up-to-date and wider perspective, and includes methodologies from beyond the health field, e.g., conservation. Resource limitations have precluded evaluation of horizon-scanning in other, related sectors, and consideration of material in languages other than English and Italian. Lastly, 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. This effort must be viewed as a 'snapshot', therefore, of a rapidly moving target.

Conclusions

To respond to accelerating innovation, horizon-scanning methodology is being adopted both nationally and internationally, particularly in the public sector. 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 ⁶⁷.

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. Self-evidently, given the need for horizon-scanning across diverse disciplines, involving large numbers of interested stakeholders with related information needs, the process can only benefit from international collaboration. To this end, initiatives are underway, including within the International Coalition of Medicines Regulatory Authorities in which the EMA is taking an active role ^{15 66-68}. Of course, scanning the horizon for signals is not an endpoint, in and of itself, but rather a window through which current and future opportunities and policies can be linked ⁶⁹. 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.

Acknowledgments

The authors are grateful to Angela Brand, Monica Ensini and Lucia D'apote for their input and assistance.

Disclaimer

The views expressed in this article are the personal views of the authors and may not be understood or quoted as being made on behalf of or reflecting the position of the agencies or organisations with which the authors are affiliated.

Data sharing

The dataset is available in the supplementary file 2 or upon request.

Competing interests

We have read and understood BMJ policy on declaration of interests and declare that we have no competing interests, specifically no financial relationships with any organisations that might have an interest in the work presented here, and no other relationships or activities that could appear to have influenced the results and conclusions drawn.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Author contributions:

Philip Hines, Marisa Papaluca-Amati, Li hiu yu and Richard Guy all contributed to the work as follows:

- Substantial contributions to the conception or design of the work; or the acquisition,
 analysis, or interpretation of data; and
- Drafting and revising the paper for intellectual content; and
- Final approval of the version to be published; and
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.



REFERENCES

- 1. Collins A. The Global Risks Report 2018. Geneva: World Economic Forum, 2018.
- 2. Bujar M MN, Liberti L. R&D Briefing 65: New drug approvals in six major authorities 2007
 2016: Focus on the internationalisation of medicines. London: Centre for Innovation in Regulatory Science, 2017.
- O'Dwyer L, Nolan L, Fisher C. Supporting Innovation through Regulation and Science:
 Ireland as an Innovation Hub for Health Products. Biomedicine Hub 2017;2(Suppl. 1):3.
- ICMRA. Key Outcomes. ICMRA Summit October. Kyoto: International Coalition of Medicines Regulatory Authorities (ICMRA), 2017.
- 5. Stevens A, Packer C, Roberts G. Early warning and of new health care technologies in the United Kingdom. International Journal of Technology Assessment in Health Care 1998;14(4):680-86.
- 6. Doos L, Packer C, Ward D, et al. Past speculations of the future: a review of the methods used for forecasting emerging health technologies. BMJ Open 2016;6(3)
- 7. Amanatidou E, Butter M, Carabias V, et al. On concepts and methods in horizon scanning:

 Lessons from initiating policy dialogues on emerging issues. Science and Public Policy
 2012;39(2):208-21. doi: 10.1093/scipol/scs017
- Plüddemann A, Heneghan C, Thompson M, et al. Prioritisation criteria for the selection of new diagnostic technologies for evaluation. BMC health services research 2010;10(1):109.
- EuroScan. A toolkit for the identification and assessment of new and emerging health technologies. Birmingham, 2014.
- Thorne M. Sense-Making With Strategic Foresight: Scanning for Future Disruptions,
 2018.

- 11. Urquhart GJ, Saunders P. Wider horizons, wiser choices: horizon scanning for public health protection and improvement. J Public Health (Oxf) 2017;39(2):248-53. doi: 10.1093/pubmed/fdw039
- 12. Sun F, Schoelles K. A systematic review of methods for health care technology horizon scanning. AHRQ Publication. Rockville (MD), 2013:1-82.
- 13. Packer C, Simpson S, Almeida RT. EuroScan International Network Member Agencies: their structure, processes, and outputs. . International Journal of Technology Assessment in Health Care 2015;31(1-2):78-85.
- 14. Packer C, Fung M, Stevens A. Analyzing 10 years of early awareness and alert activity in the United Kingdom. International Journal of Technology Assessment in Health Care 2012;28(3):308-14.
- 15. EUnetHTA. Horizon Scanning, Topic Identification, Selection and Prioritisation for European cooperation on HTA Draft recommendations Brussels, 2018.
- 16. Mulrow CD. Systematic Reviews: Rationale for systematic reviews. BMJ 1994;309(6954):597-99. doi: 10.1136/bmj.309.6954.597
- 17. Moher D, Liberati A, Tetzlaff J, et al. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLOS Medicine 2009;6(7):e1000097.

 doi: 10.1371/journal.pmed.1000097
- 18. McHugh ML. Interrater reliability: the kappa statistic. Biochem Med (Zagreb) 2012;22(3):276-82.
- 19. Higgins JP, Altman DG, Gotzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011;343:d5928. doi: 10.1136/bmj.d5928
- 20. CADTH. CADTH Environmental Scan Process. Ottawa, 2015.
- 21. Jones MM, Hall A, Brooker D, et al. The Future of Public Health: A Horizon Scan. Rand Health Q 2014;4(3):18.

- 22. Varela-Lema L, De La Fuente-Cid R, Lopez-Garcia M. Developing a prioritized list of innovative technologies: the Spanish experience. Int J Technol Assess Health Care 2014;30(6):626-33. doi: 10.1017/S0266462314000774 [published Online First: 03/30]
- 23. EPO. The European Patent Office 2018 [Available from: https://www.epo.org/index.html accessed 06/08/2018.
- 24. Pharmascan U. Working together to improve NHS planning for new medicines: UK

 PhramaScan; 2018 [Available from: https://www.ukpharmascan.org.uk/static/about.
- 25. Smith J, Ward D, Michaelides M, et al. New and emerging technologies for the treatment of inherited retinal diseases: a horizon scanning review. Eye (Lond) 2015;29(9):1131-40. doi: 10.1038/eye.2015.115
- 26. Duchesne GM, Grand M, Kron T, et al. Trans Tasman Radiation Oncology Group: Development of the Assessment of New Radiation Oncology Technology and Treatments (ANROTAT) Framework. J Med Imaging Radiat Oncol 2015;59(3):363-70. doi: 10.1111/1754-9485.12255
- 27. Noorlander CW, Kooi MW, Oomen AG, et al. Horizon scan of nanomedicinal products.

 Nanomedicine (Lond) 2015;10(10):1599-608. doi: 10.2217/nnm.15.21
- 28. Clyne M, Schully SD, Dotson WD, et al. Horizon scanning for translational genomic research beyond bench to bedside. Genet Med 2014;16(7):535-8. doi: 10.1038/gim.2013.184
- 29. Saunders PJ, Middleton JD, Rudge G. Environmental Public Health Tracking: a cost-effective system for characterizing the sources, distribution and public health impacts of environmental hazards. J Public Health (Oxf) 2017;39(3):506-13. doi: 10.1093/pubmed/fdw130
- 30. Varela-Lema L, Punal-Rioboo J, Accion BC, et al. Making processes reliable: a validated pubmed search strategy for identifying new or emerging technologies. Int J Technol Assess Health Care 2012;28(4):452-9. doi: 10.1017/S0266462312000578

- 31. Sutherland WJ, Broad S, Caine J, et al. A Horizon Scan of Global Conservation Issues for 2016. Trends Ecol Evol 2016;31(1):44-53. doi: 10.1016/j.tree.2015.11.007
- 32. Garnett K, Lickorish FA, Rocks SA, et al. Integrating horizon scanning and strategic risk prioritisation using a weight of evidence framework to inform policy decisions. The Science of the total environment 2016;560-561:82-91. doi: 10.1016/j.scitotenv.2016.04.040 [published Online First: 2016/04/20]
- 33. Sutherland WJ, Freckleton RP. Making predictive ecology more relevant to policy makers and practitioners. Philos Trans R Soc Lond B Biol Sci 2012;367(1586):322-30. doi: 10.1098/rstb.2011.0181
- 34. Veenstra DL, Piper M, Haddow JE, et al. Improving the efficiency and relevance of evidence-based recommendations in the era of whole-genome sequencing: an EGAPP methods update. Genet Med 2013;15(1):14-24. doi: 10.1038/gim.2012.106
- 35. Masum H, Ranck J, Singer PA. Five promising methods for health foresight. Foresight 2010;12(1):54-66.
- 36. Dawson MN, Algar AC, Antonelli A, et al. An horizon scan of biogeography. Front Biogeogr 2013;5(2)
- 37. Birko S, Dove ES, Ozdemir V. Evaluation of Nine Consensus Indices in Delphi Foresight
 Research and Their Dependency on Delphi Survey Characteristics: A Simulation
 Study and Debate on Delphi Design and Interpretation. PLoS One
 2015;10(8):e0135162. doi: 10.1371/journal.pone.0135162
- 38. Birko S, Dove ES, Ozdemir V. A Delphi Technology Foresight Study: Mapping Social

 Construction of Scientific Evidence on Metagenomics Tests for Water Safety. PLoS

 One 2015;10(6):e0129706. doi: 10.1371/journal.pone.0129706
- 39. Kark S, Sutherland WJ, Shanas U, et al. Priority Questions and Horizon Scanning for Conservation: A Comparative Study. PLoS One 2016;11(1):e0145978. doi: 10.1371/journal.pone.0145978

- 40. Simpson S, Cook A, Miles K. Patient and Public Involvement in Early Awareness and Alert Activities: An Example from the United Kingdom. Int J Technol Assess Health Care 2018;34(1):10-17. doi: 10.1017/S0266462317004421
- 41. Reimers-Hild C. Strategic foresight, leadership, and the future of rural healthcare staffing in the United States. JAAPA 2018;31(5):44-49. doi: 10.1097/01.JAA.0000532119.06003.12
- 42. Gwinn M, Grossniklaus DA, Yu W, et al. Horizon scanning for new genomic tests. Genet Med 2011;13(2):161-5. doi: 10.1097/GIM.0b013e3182011661
- 43. Ciani O, Jommi C. The role of health technology assessment bodies in shaping drug development. Drug Des Devel Ther 2014;8:2273-81. doi: 10.2147/DDDT.S49935
- 44. Nachtnebel A, Breuer J, Willenbacher W, et al. Looking Back on 5 Years of Horizon

 Scanning in Oncology. Int J Technol Assess Health Care 2016;32(1-2):54-60. doi: 10.1017/S0266462316000052
- 45. Stafinski T, Topfer LA, Zakariasen K, et al. The role of surgeons in identifying emerging technologies for health technology assessment. Can J Surg 2010;53(2):86-92.
- 46. Eriksson I, Wettermark B, Persson M, et al. The Early Awareness and Alert System in Sweden: History and Current Status. Front Pharmacol 2017;8(674):674. doi: 10.3389/fphar.2017.00674
- 47. RANZCR. Position Paper Techniques and Technologies in Radiation Oncology 2015 Sydney: The Royal Australian and New Zealand College of Radiologists, 2015.
- 48. Nachtnebel A, Geiger-Gritsch S, Hintringer K, et al. Scanning the horizon: development and implementation of an early awareness system for anticancer drugs in Austria.

 Health Policy 2012;104(1):1-11. doi: 10.1016/j.healthpol.2011.11.003
- 49. Raman G, Wallace B, Patel K, et al. Update on horizon scans of genetic tests currently available for clinical use in cancers. In: Quality AfHRa, ed. Rockville (MD), 2011.
- 50. Wild C, Simpson S, Douw K, et al. Information service on new and emerging health technologies: identification and prioritization processes for a European union-wide

- newsletter. Int J Technol Assess Health Care 2009;25 Suppl 2(S2):48-55. doi: 10.1017/S0266462309990687 [published Online First: 12/23]
- 51. Maddern G, Boult M, Ahern E, et al. ASERNIP-S: international trend setting. ANZ J Surg 2008;78(10):853-8. doi: 10.1111/j.1445-2197.2008.04679.x
- 52. Chapman AM, Taylor CA, Girling AJ. PRM22 The Headroom Method of Early Economic Evaluation of Medical Devices: A Useful Tool for Device Developers? Value in Health 2012;15(7):463-64. doi: 10.1016/j.jval.2012.08.1486
- 53. Rudd MA, Moore AFP, Rochberg D, et al. Climate research priorities for policy-makers, practitioners, and scientists in Georgia, USA. Environ Manage 2018;62(2):190-209. doi: 10.1007/s00267-018-1051-4
- 54. Joppi R, Dematte L, Menti AM, et al. The Italian Horizon Scanning Project. Eur J Clin Pharmacol 2009;65(8):775-81. doi: 10.1007/s00228-009-0666-z
- 55. Khoury MJ, Gwinn M, Dotson WD, et al. Knowledge integration at the center of genomic medicine. Genetics in Medicine 2012;14(7):643.
- 56. Wild C, Langer T. Emerging health technologies: informing and supporting health policy early. Health Policy 2008;87(2):160-71. doi: 10.1016/j.healthpol.2008.01.002
- 57. Gomes PT, Teixeira Vidal A, Souza A. Radar An Important Tool for Horizon Scanning

 Dissemination in Brazil. Value in Health 2017;20(9):906.
- 58. Doos L, Packer C, Ward D, et al. Past speculations of the future: a review of the methods used for forecasting emerging health technologies. BMJ Open 2016;6(3):e010479. doi: 10.1136/bmjopen-2015-010479
- 59. Sun F, Bruening W, Uhl S, et al. Quality, regulation and clinical utility of laboratory-developed molecular tests. Rockville (MD), 2010.
- 60. Observatory I. Who We Are And What We Do Newcastle upon Tyne, United Kingdom:

 National Institute for Health Research (NIHR); 2018 [Available from:

 http://www.io.nihr.ac.uk/what-we-do/.

- 61. Gale P, Breed AC. Horizon scanning for emergence of new viruses: from constructing complex scenarios to online games. Transboundary and Emerging Diseases 2012;60(5):472-74.
- 62. Wild C, Langer T. Emerging health technologies: informing and supporting health policy early. Health Policy 2008;87(2):160-71.
- 63. Sutherland WJ, Butchart SH, Connor B, et al. A 2018 horizon scan of emerging issues for global conservation and biological diversity. Trends in Ecology & Evolution 2018;33(1):47-58.
- 64. Mundy L, Hiller J, Merlin T. The true role of horizon scanning in Australia: who it informs and why. . international Journal of Technology Assessment in Health Care 2011;27(1):95-96.
- 65. Sun F, Bruening W, Uhl S, et al. Quality, Regulation and Clinical Utility of Laboratory-developed Molecular Tests. Rockville (MD)2010.
- 66. ICMRA. ICMRA strategic strategic priority on innovation. 2017 [Available from: http://www.icmra.info/drupal/sites/default/files/2017-12/ICMRA%20Innovation%20Concept%20Note_0.pdf.
- 67. HMA, EMA. Mandate of the European Innovation Network, 2016.
- 68. Lepage-Nefkens I DK, Mantjes G, de Graaf G, Leroy R, Cleemput I. Horizon scanning for pharmaceuticals: Proposal for the BeNeLuxA collaboration. Brussels: Health Services Research (HSR) Brussels: Belgian Health Care Knowledge Centre (KCE), 2017.
- 69. Wettermark B, Persson ME, Wilking N, et al. Forecasting drug utilization and expenditure in a metropolitan health region. BMC Health Services Research 2010;10(1)

Fig 2. Literature selection process flowchart 17

Flow diagram depicting the different stages of the systematic literature review according to the PRISMA format.



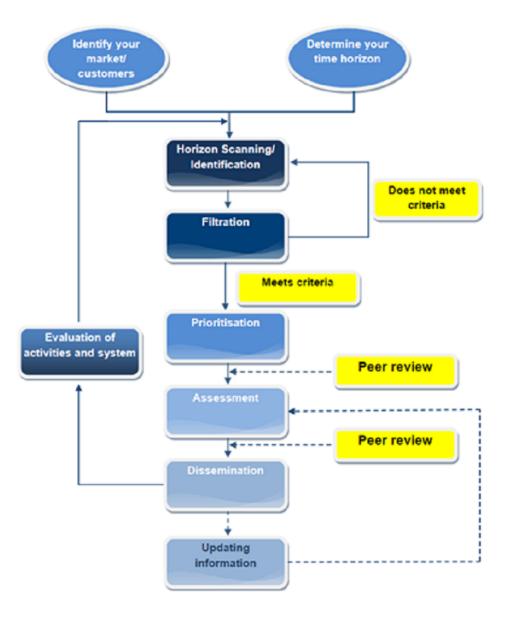
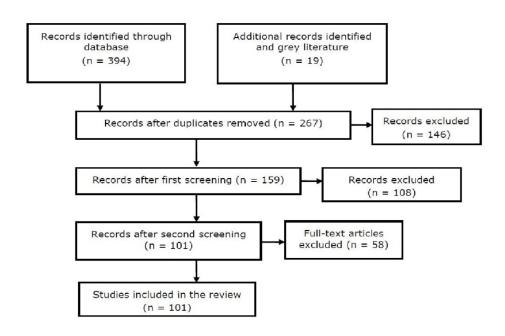


Fig 1. Common stages of Horizon scanning from the EuroScan network (12). This figure is licensed under the Creative Commons Attribution-NonCommercial-ShareAlike4.0 International License (CC BY-NC-SA 4.0)

97x113mm (300 x 300 DPI)



Caption : Fig 2. Literature selection process flowchart (16) $150 \times 102 \text{mm}$ (300 x 300 DPI)

Search strategy

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.

The primary search terms used were: "horizon scan*" OR "strategic foresight*" OR "systematic early dialogue*" OR "early warning and alert system*". All literature, of which the title or abstract contained any of the keywords above, was flagged.

In the database searches, a single set of entry terms were applied:

('horizon scan*':ab,ti OR 'strategic foresight*':ab,ti OR 'systematic early dialogue*':ab,ti OR (('early awareness' NEXT/2 'alert system*'):ab,ti))

In Fields:

horizon scan* in Abstract
horizon scan* in Title
strategic foresight* in Abstract
strategic foresight* in Title
systematic early dialogue* in Abstract
systematic early dialogue* in Title
'early awareness' NEXT/2 'alert system*' in Abstract
'early awareness' NEXT/2 'alert system*' in Title

Quality appraisal

The appraisal was conducted at the screening stage as part of the inclusion/exclusion criteria. The questions regarding internal and external validity are indicated in Table 1.

To ensure that the quality appraisal and screening were being applied harmoniously, a third researcher appraised and screened the excluded literature according to the same criteria to ensure that all relevant papers were captured (resulting in one further publication being selected).

Table 1. Quality appraisal items and inclusion/exclusion criteria for screening

	Internal validity	External validity
First round	(a) either a methodology	(b) It was also essential for the abstracts to
of appraisal	for horizon scanning or	indicate a breadth of horizon scanning of
and	strategic foresight, or a	the relevant field level <i>or</i> address a
screening	discussion, or experience	methodological aspect which may be
(108	provided, of horizon	generally applicable across different fields.
excluded)	scanning.	
Second	(a) the horizon scan or	(b) the priority areas included relevant
round of	foresight methodology	science and/or technology, and
appraisal	was detailed, and	(c) a collaborative/international approach
and		was used, and
screening		(d) the horizon scanning undertaken
(58		spanned a period of between 2 and 15
excluded)		years.
		Alternatively, the paper was required to
		demonstrate methodological aspect(s) of
		foresight or horizon scanning of potentially
		general applicability.

Risk of bias was assessed in accordance with the BMJ guidelines and the Cochrane risk of bias tool. While bias was not typically found in these non-clinical qualitative studies, there were three exceptions:

- 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.
- Omission bias may have occurred as the papers reported systematic methodological aspects of horizon scanning; some horizon scanning, however, may occur in an ad-hoc manner, e.g., a signal discovered by word-of-mouth.
- The competing interests of the authors were not considered beyond the standards of the source journals. This was because it was not thought highly relevant to the reporting of methodologies.

Page 38 of 46

Literature Map - Work		luded papers and info					Internati		mation sources (proactive and passive)	it (ton tiens tiens tiens ton			Time horizon Filtrati	on		oritisation			Assessment	Borr		Dissemination		Programme Progra
Title	Full Text Link ("-" if unnavailable; or explanation of non- inclusion)	Abstract	Scientific literature	Clinical trial registers	Commercial sources	Patents Other observatories	Media onal institution and Fora	ns.	Individuals, Committees and expert groups Survey techniques	Popularian Page Page Page Page Page Page Page Page	Interest group profiles	Annications Meeting and conferences literature of the part of the	g Critoria		Criteria	Method	Factors	Depth	Method	Comparison with other HS results		Structure Format Frequency	Audience	Methy
Australia and New Zealand Horizon Scanning Network, Australia and New Zealand (ANZHSN, Including Adelaide Health Technology Assessment [AHTA])																						Control of the contro		
Basque Office for Health Technology Assessment, Basque Country (OSTEBA)	The second secon							24																
Canadian Agency for Drugs and Technologies in Health, Canada (CADTH)	The second secon		Magnini Records (width										* 0000 0000							adole hading his		Man rolls Man rolls		
Supporting Innovation through Regulation and Science: Ireland as an Innovation Hub for Health Products																								
Italian Horizon Scanning Project, Servizio Farmaceutico Territoriale, Italy (IHSP)																	especial manufacture of a property of the second of a second of the seco				The state of the s	Commission space and Commissio	The second species	And opening to comment of the commen
National Horizon Scanning Centre, England (NHSC) + (Their research paper: Past speculations of the future: a review of the methods used for forecasting emerging health technologies)									(0)				The second secon				age of the last half hand hand to the last hand hand to the last hand to t	And the second				and the control of th		among and any day of the control of
Swedish Council on Technology Assessment in Health Care, Sweden (SBU)							Paragraphic and			76							And a second seco			der videren generalen gene				
UK PharmaScan												10												
Oxford Centre for Monitoring and Diagnosis in Primary Care													10/		Author language and the Author and t		Separation of the second speed when							The designation below the designation of the design
Masum H, Ranck J, Singer PA. Five promising methods for health foresight. Foresight 2010;12:54–66. doi:10.1108/14636 681011020182/ors sRefGoogle Scholar								60						0,				The control of the second of t						
Evaluation of nine consensus indices in delphi foresight research and their dependency on delphi survey characteristics: A simulation study and delphi design and interpretation			many desirables of the control of th												1	>				Ample of Manager of Ma	THE RESERVE OF THE PROPERTY OF			
A Delphi technology foresight study: Mapping social construction of scientific evidence on metagenomics tests for water safety			An and additional and additional and addition and subject of the s															- Among San Andrews (Among San Andrews Among San	in his way go di subaggi dan pa di supagni dan panggan					with the control of t
Using strategic foresight to assess conservation opportunity	The same and the s		And the control of th															Similar of the second of the s						
Strategic foresight: how planning for the unpredictable can improve environmental decision-making																		The department of the second o						
Horizon scan of nanomedicinal products			to hong to send the send to se	And the process and the process of t			agent of walk and a	in a second						Annual An				- Collection - American - America		response of the later and the later of the l		Manage Ma		
Trans Tasman Radiation Oncology Group: Development of the Assessment of New Radiation Oncology Technology and Treatments (ANROTAT) Framework			in the following as and a second of the seco	manufacture design desi										_										
Horizon scanning for translational genomic research beyond bench to bedside			COMPANY PROPERTY OF THE PROPER			personal agency of the second																		

BMJ Open

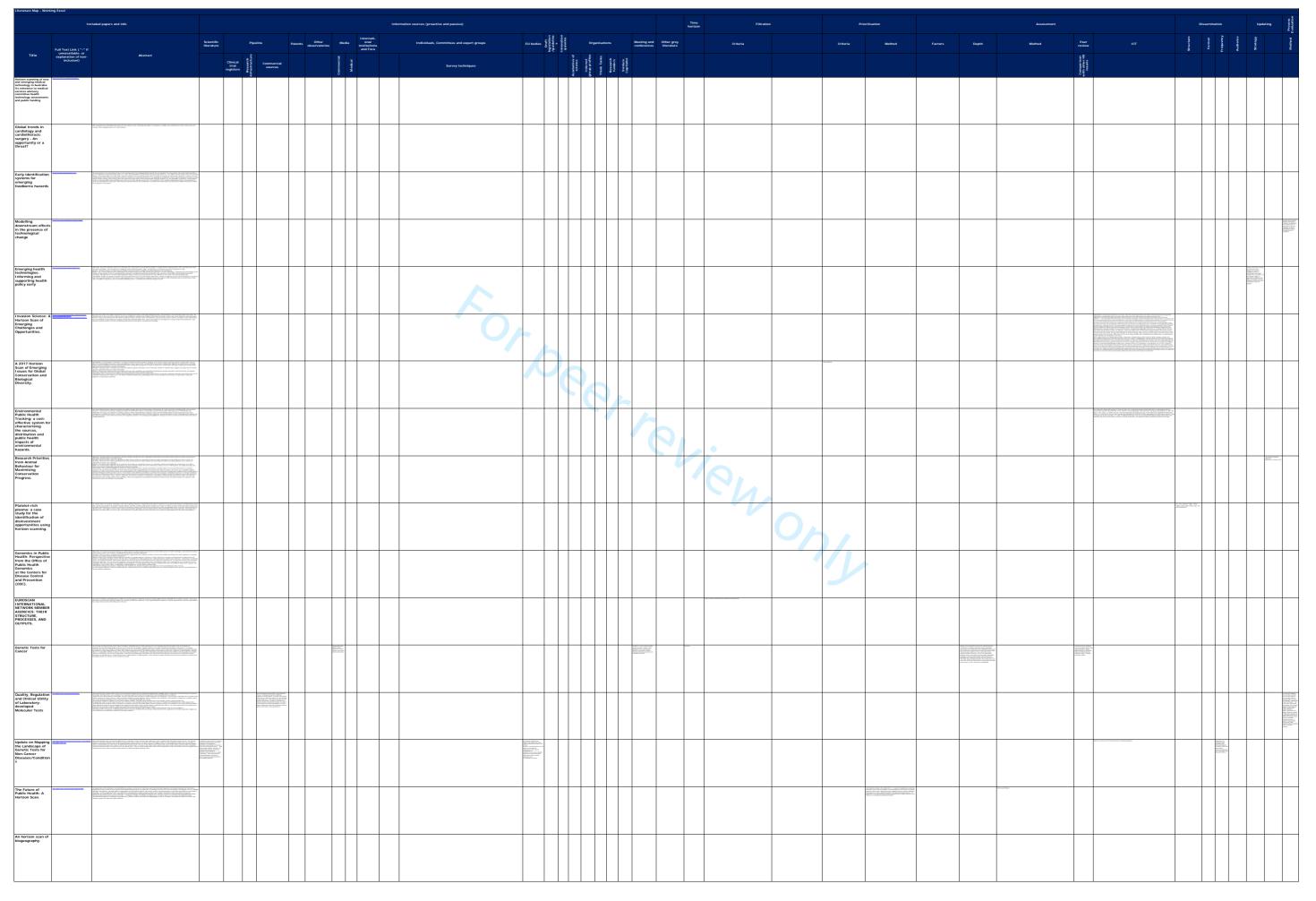
Literature Map - Worki		luded papers and info	Scientific literature	Pip	eline	Patents Other observator	ir Medi.	Internati- ia onal	tion sources (proactive and p		oups	EU bodies di Si	deline Services erries	Organisati	tions	Meeting and Other go	Time horizon	Criteria	Filtration		P	vioritisation Method	Factors	Depth	M	Assessment	Peer review	ict		Dissemination Southeast Superior State Superior	Updating	Process thod Evaluation
Title	Full Text Link ("-" if unnavailable; or explanation of non- inclusion)	Abstract	Ci	Sinical Sinical Straight Strai	Commercial sources	observate	Commercial	and Fora		urvey techniques		4 6	Academies of science	Interest group profiles Think Tanks	Research funders Venture Capitalist	Meeting and Other gr conferences literatur	•										Comparison with other HS results			Sire Free	215	Me
ASERNIP-S: International trend setting																							was allowed									
Update on Horizon Scans of Genetic Tests Currently Available for Clinical Use in Cancers [Internet].	and the second		Fred Control of Contro				-														And the second sec								No. Prop.	The state of the s	Security of the property of the control of the property of the control of the con	
Horizon scanning for invasive allen species with the potential to threaten blodiversity in Great Britain.	-		And a place of the state of the																													
Making processes reliable: a validated pubmed search strategy for identifying new or emerging technologies.			N. L. C.			and comment of the co	of patients or											The second seco	Antonio del monte depo													
Improving the efficiency and relevance of evidence-based recommendations in the era of whole-genome sequencing: an EGAPP methods update.																							American with the control of an analysis of the control of the con	or and a second of the second								
Knowledge integration at the center of genomic medicine.											0,	-																		Section of the sectio		
Horizon scanning for new genomic tests.			any to																											water to said. When the said of the said		
Evaluating new surgical techniques in Australia: the Australian Safety and Efficacy Register of New Interventional Procedures- Surgical experience.																10																
The Australian Safety and Efficacy Register of New Interventional Procedures - Surgical (ASERNIP- S) assesses new surgeries.																		0/	1													
Report from the World Health Organization's third Product Development for Vaccines Advisory Committee (PDVAC) meeting, Geneva, 8-10th June 2016			mental me																	0/												
A knowledge base for tracking the impact of genomics on population health						And control returns and co	or community of the com														1									Contraction of the Contraction o		
Challenges and priorities for modelling livestock health and pathogens in the context of climate change			Company of the Compan																													
Priority questions and horizon scanning for conservation: A comparative study																											internal paper Note and a contract of paper No		And the second s	Office and the control of the contro		
Techniques and technologies in radiation oncology: The RANZCR faculty of radiation oncology horizon scan																						Section 2 and a factor of the control of the contro	Private Communication of the C									
A Horizon Scan of Global Conservation Issues for 2016								Michael Canada Michael Canada Michae											alan ingan sawa inganingang panganan				See the state of t	enter de la constante de la co							Section And proceeding working to the con- cept of the con- traction of the con- traction of the con- position of the con- traction of	
A horizon scan of future threats and opportunities for pollinators and pollination			Company Compan															Sample Service of the purple Service S	Antonia i additional region en del el			and of the control of	No. of the latest and									
Looking back on 5 years of horizon scanning in oncology			man and a second a																			managan a palama, a nay pan man a nay							early control of the	William and the second of the	with place process of a second	

Page 40 of 46

Literature Map - Working Excel	Included papers and info					Informatio	on sources (proactive and passi	ive)						ime rizon	Filtration	Pric	ritisation			Assessment	ıt		dissemination	Updating	Process Evaluation
Full Test L umayal Title explanatic exclusi	ink (^ - * If babbles or on of non- sion)	Scientific literature Clinical trial registers	Pipeline Commercial sources	Patents Other observatories	Media institution and For	rii ra	Individuals, Committees ar Survey I	nd expert groups	EU bodies	legislation /guideline /guideline guideline quideline	Organic Organi	irek Tanks Research funders	Meeting and conferences Other grey literature	Criteria		Critoria	Method	Factors	Depth	Method	Peer review SH Julio u SH Julio u	Structure	Frequency	Audiense	Method
CHANGING HEALTH TECHNOLOGY ASSESSMENT PARADIGMS7			110		8						0.6	-									o Maria	And the highlight date must be hanging and the state of t			
New and emerging technologies for the treatment of inherited retinal diseases: A horizon scanning review			when the second section of the second section of the second section se			Sec. 37.								And a second control of the second control o	on part of the second s										The study production of the st
Results from a horizon scan on with associated with associated with transplantation of human organs, tissues and cells: from donor to patient																									
Preparedness for merging the m																	States from the Application States (Section 2) and according to the Control of Section 2) and according to the	7							
I dentifying and selecting new procedures for our procedures for our procedures for assessment: A decade of nice experience in the United Kingdom								<u> </u>															And Control of the Co		
The role of health technology assessment bodies in shaping drug development								0	-				200	PARAMETER CONTRACTOR C											
A horizon scan for species conservation by zoos and aquartums																									
Stratogic for esight, how planning for the unpredictable can improve environmental decision-making													101												
Evolutionary rescue in a changing world														10/	,										
Identifying the science and schoology dimensions of omerging public through horizon scanning															0,										
Prioritizing genomic applications for action by level of action by level of action in the action by level of action in the action of action of action														Secretary and the design of the secretary of the secretar	Security of the Control of the Contr	J	>								
A horizon- prioritizing method can identify gaps among genomic application guidelines																									
DEVELOPING A PRIORITIZED LIST OF INNOVATIVE TECHNOLOGIES: THE SPANISH EXPERIENCE														Secretary of page 19 and page 19 and	in companies. In companies of the compa	Application in Security Security (Security Security Secur									
Eu pharmaceutical expenditure forecast				The state of the s						Market and				magnetic de service de la constant de service de servic											
Horizon scanning for emergence of more constructing complex scenarios to online games						The state of the s																			
The headroom method of early economic or medical devices: A useful tool for device developers?																			100 min 100 mi		Andrew Angles Andrew Angles An				
Horizon scanning in radiation encology Considerations and future trends																								the control of the co	

BMJ Open

Literature Map - Working Excel	Included papers and info			Information sources (proactive and passive)				ine Filtration	Prio	ritisation		Assessment			emination	Opdating Spring
Full Text Li umavail explanation inclusi	is ("-" if Bile; or an Abstract of non- Abstract on)	Scientific Pipeline Illerature Clinical trial registers & Supplementation of the Commercial Sources r	Patents Other observatories Media International Institution and Fora		EU bodies of a constant to con	Academies of soleme of interest group profiles O. Think Tanks	Meeting and Other grey Elferature	Critoria	Criteria	Method	Factors Depth		eer ICT	Structure	Frequency Audience	Strategy
The 'Assessment of New Radiation Oncology Technology and Treatments' (ANROTAT) project: Update on progress		<u>5</u>	Control of the Contro	Survey techniques		Acadas sole Inte group 1	south services and services are services and services are					nuos	o estivo			
Using best-worst scaling in horizon scanning for scanning for scanning to reaction scanning technologies		in the second se												and principles in advantage in the baseline of the contract of		
Analyzing 10 years of early awareness the United Kingdom		20 20 20 20 20 20 20 20 20 20 20 20 20 2														
Implementing a national early awareness and removed removed and emerging health technologies in Italy: The COTE project																
Innovation and the burden of disease: Retrospective observational study of new and emerging health technologiste reported by the EuroScan network from 2000 to 2009										ang mananan ma						
Making predictive ecology more relevant to policy makers and practitioners					2/4											
Scanning the horizon- Development and implementation of a system for areness of anticancer drugs in Austria						96		and the second and the second are second as the second are second are second as the second are second as the second are second as the second are s	and a special		A reason formed and applications control of the con					And the state of t
identification of immediate involves to public health. The true role of Australia. Who is informs and why								ie,							The state of the s	The state of the s
Regly to the letter by Mundy, Hiller, and Marrin on the second of the second of the scanning in Australia For exacting drug utilization and expenditure in a networkiture in a networkiture in a networkiture in a		<u>.</u>						0,	4	•						Common of the co
Issues facing the Australian health successment review of medical technology funding																
Evaluation criteria to assess the value of identification sources for horizon scanning																was a common or
The role of surgeons in identifying emerging the state of								SPECIFICATION OF THE PROPERTY								
Information service on new and emerging health care from the service of the servi														An analysis was and an interface of the control of	g Greener In The Tay of the Control	
The Italian Horizon Canning Project									State of the state							



	ing Excel	luded papers and info					Information s	sources (preactive and passive						Time horizon	Fittra	ion		Prioritisation			Assessment			Dissemination	Solution Sol
Title	Full Text Link ("-" if umavailable; or explanation of non- inclusion)	Abstract		Pipeline	Patents Other observatories	Media International institutions and Fora		Individuals, Committees and	d expert groups	En poques De di maria de la constanta de la co	0	Organisations	Meeting and conferences literat	grey	Criteria		Criteria	Method	Factors	Depth	Method	Peer review	Structure	Format Frequency Audience	Strategy Method EV
Wiser horizons, wiser choices:	ELIGENATY		Clinical trial registers	Commercial sources		Commerc		Survey to	chniques		Acadamie solenze Imbres group pro	Thirk Tanks Thirk Tanks Research funders	Venturi		Mengy rag jabo ram hadi da badi yan hadi hanggaya hari Mengah da sahan sahan sasah sasah sasah da sigil ang salah saha Mengah da sahan sahan sasah sasah sahan da sigil ang saha sahan mahari da saha saha saha saha saha saha saha s	-		make the trade of probability and object represents all response of				Comparity with other results			
Wiser horizons, wiser choices: horizon scanning for public health protection and improvement.		Chicken in the Section of Artifact Management	was not show any show and show any show any show any show any show any show any show and show any show and show any show any show any show any show any show any show and show any show																						
PATIENT and PUBLIC INVOLVEMENT IN EARLY AWARENESS and ALERT ACTIVITIES: AN EXAMPLE from the UNITED KINGDOM			organisms of the state of the s				Amount of the common of the co											Control and contro	and the second			The American of the Con- ception of the Con- ception of the Con- tention of the Con- t	The state of the s	one on the state of the state o	A more part of a comment of the comm
A transatlantic perspective on 20 emerging issues in biological engineering			or company																						
The Early Awareness and Alert System in Sweden: History and Current Status			and											=======================================		and				1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		Charles account of the control of th	Annual control of the	-	
Radar-an importan tool for horizon scanning dissemination in Brazil			Section of the Control of the Contro						<u> </u>														No. status		County of the co
Horizon scanning is oncology-rapid scanning approach in Slovakla			or an analysis of the second o						0,																
Climate research priorities for policy makers, practitioners, and scientists in Georgia, USA.											9	9,						Annual content of the	words Water of the control of the c						
Strategic foresight, leadership, and the future of rural healthcare staffing in the United States.													Spring Street	State	•										
Toward sustainable environmental quality: Identifying priority research questions for Latin America.			CONTRACTOR OF THE CONT												94										
A 2018 Horizon Scan of Emerging Issues for Global Conservation and Biological Diversity.																0,	The second secon	1							
Integrating horizor scanning and strategic risk prioritisation using a weight of evidence framework to inform policy decisions														Section (Control Section) plants of the Control Section (Control Section) and (Control Section) and (Control Section)			1						Services and second of the Con- centration of the Con- tentration of	3	
How can health systems prepare for new and emerging health technologies? The role of horizon scanning revisited			Section 1.	See Name			The second secon	per and per system describe a special described and	n sa mana sana a kana sanaya ma			State of the State											The state of the s	77 A TOTAL OF THE PARTY OF THE	
EMA Sources			Continue and a second a second and a second and a second and a second and a second																				Section of the sectio		
Reviewing the effectiveness of UK drug horizon scanning efforts & the production of nice commentary along therapeutic specialties			money — management of the control of																						
The multi-criteria decision analysis in the priority setting of emerging medicines			and the second s																						



47

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	N/A
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	6
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6-7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and yarry assumptions land com/site/about	9 /guidelines.xhtml



PRISMA 2009 Checklist

		simplifications made.	
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	Risk of bias was assessed in accordance with the BMJ guidelines and the Cochrane risk of bias tool. Most bias were not applicable to these non-clinical qualitative studies, however the following were: - A form of publication bias was likely in which only horizon scanning undertaken in organisations with a strong background in publishing academic publications
4 5 6 7 8 9		10eer	were discovered. It was not possible to correct for this. - Outcome bias may have occurred as the papers reported systematic methodological aspects of horizon scanning, whereas some horizon scanning may occur in an ad-hoc manner e.g. a signal discovered by word of mouth.
2 3 4 5 6		i e Lieu	- The competing interests of the authors were not considered beyond the standards of the source journals. This was because it was not thought highly relevant to the reporting of methodologies.
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	9
9 Synthesis of results 1 2	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I ²) for each meta-analysis.	9
3		Page 1 of 2	

35 36	Section/topic	#	Checklist item	Reported on page #
38 39	Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	9
40 41	Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
42 43	RESULTS			
44 45	Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, reasons for exclusions at each stage, reasons for exclusions at each stage, reasons for exclusions at each stage.	8

PRISMA 2009 Checklist

Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	N/A	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	9 (See point 12	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	N/A	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	9	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A	
DISCUSSION				
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	21-22	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	22	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	23	
UNDING				
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	24	

29 From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. 30 doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.