

# **National Institute for Health and Care Excellence**

## **Updated Guidelines Manual**

This paper gives details of changes made to Developing NICE Guidelines: the manual following a scheduled review.

The Board is asked to approve the manual for public consultation.

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## Background

1. Developing NICE guidelines: the manual was published in October 2014, aligning for the first time process and methods across public health, social care, clinical, safe staffing and medicines practice guidelines. The manual was scheduled for review in Q3 2017, three years after publication. This paper sets out the approach taken to the review, and highlights the key changes proposed.

## Context

2. NICE has a first class international reputation for quality: our processes and methods have been iterated over time through regular review, with input from leading experts in evidence based health care and related disciplines, and from our stakeholders through public consultation.
3. While the changes proposed in this update represent further iteration, changes in the external environment are presenting new opportunities for NICE that may bring more fundamental changes to our work. Increases in the amount of data available, the development of new and efficient mechanisms for analysis, and advances in the way information is labelled, linked and shared, have the potential to significantly disrupt current ways of working. This potential is further increased by considering how these advances can be integrated. NICE has a leadership role to play in exploring these new approaches to evidence generation and interpretation, and in new ways of informing and communicating decisions.
4. The environment that NICE operates within is increasingly resource-constrained, and methods and processes will need to continue to evolve in that context. We are exploring how the use of technology can help us work efficiently, reduce uncertainty and ensure the quality of our guidance through the Transforming Guidance Development Programme and related initiatives. Current areas of focus include:
  - structured guidance authoring - benefits, user research, tools
  - evidence management - tools, workflow, connections
  - real world data for evidence generation - use cases, data sources, methods and tools, analytical expertise
  - systems for process efficiency - external consultations, identity management
  - machine learning for process efficiency - opportunities, commercial solutions, data requirements, skills and technology

5. We anticipate that significant changes will be introduced into the guidelines manual in the coming years as these initiatives mature.

## Approach

6. A number of approaches were taken to identify areas for update, including:
  - Identifying strategic drivers, chiefly the need for a sustainable surveillance process
  - Reviewing the points of process or methodological differentiation in the current manual to ensure that these remain appropriate, and to strengthen the rationale for differentiation where possible
  - Considering feedback from internal teams and external developers on issues that had arisen during implementation of the 2014 manual
  - Convening a virtual reference group of external experts (see appendix 1 for details), who reviewed the manual and made suggestions for improvement to ensure NICE methods remain at the forefront of best practice.
7. Development of new content and updates to the text have been led by a range of individuals, many from the Centre for Guidelines methods and economics team.
8. Changes were agreed with the Methods Working Group, which includes representation from all Centre for Guidelines teams, Guidance Information Services, Editorial, PIP, the Medicines practice programme and Science policy & research.
9. The updated manual was reviewed in full by teams within CfG and across NICE, and external developers, in January 2018. Further iterations were then made prior to editing.

## Changes proposed

10. A large number of changes have been made to the manual in light of the update process. A summary of the key changes proposed is included below. Other changes have been made to reflect best current practice, introduce iterative improvements to process and methods, and improve clarity.

### Scoping

11. Developers are encouraged to focus on evidence gaps during scoping, and additions to the scoping chapter prompt developers to start to compile a list of areas where evidence is missing, along with details of stakeholders who might

be able to provide information, in preparation for a call for evidence and / or early identification of expert witnesses.

12. The standard consultation period for draft scopes in the current manual is set at four weeks. The updated manual introduces the option to reduce this period to two weeks for draft scopes of partial updates.
13. The manual is now explicit that guidelines do not usually include key issues that are covered by other arms-length or government bodies such as the Department of Health, NHS England or Public Health England. In addition, developers are reminded that guidelines do not usually cover training requirements, as these are the role of the Royal Colleges and professional associations, but they may make recommendations on the need for specific knowledge and skills for a particular aspect of care.

### Service delivery guidelines and review questions

14. The 2014 manual references interim methods for service delivery, which were published to support the development of whole guidelines, and individual review questions, with a specific service focus. Our experience in this area has now been consolidated and the interim methods embedded within the main manual. This includes changes to chapters on scoping, search and evidence submission, and economics. In addition, a new appendix has been created to provide developers with detailed advice on how to develop review questions in this area.

### Committees

15. The updated manual encourages guideline developers to consider other NICE guidance in development when developing and scoping new topics. Cross-representation on committees and scoping groups of related guidelines in simultaneous development is promoted.
16. Advice is included for developers seeking to include expert testimony from children or other vulnerable groups as part of guideline development. The need to make special arrangements, such as giving testimony via video recording, or in private session, is highlighted.
17. A number of editorial changes have been made to ensure the manual is consistent with the recently updated [code of practice for declaring and dealing with conflicts of interest](#).

### Review questions and evidence review

18. Core outcome sets are agreed standardised sets of outcomes that represent the minimum that should be measured and reported in all clinical trials of a specific

condition; one source is the [COMET database](#). In a strengthening of the advice for developers on these tools, the manual now indicates that core outcome sets should be used in reviews if these are suitable, based on quality and validity. Further advice is highlighted to developers as links to external standards.

19. Clinical prediction models are developed to aid healthcare professionals in estimating the probability or risk that a specific disease or condition is present (diagnostic prediction models) or that a specific event will occur in the future (prognostic prediction models). The manual has been updated to include examples of review questions that assess and compare these models, and links out to further external sources of advice.
20. Following alignment work across the guideline programmes a standardised template for review protocols has been developed and is included as a new appendix to the updated manual. International best practice in systematic reviewing includes the registration of review protocols on the [PROSERO](#) database before the completion of data extraction. Registration is now proposed as a mandatory requirement within the updated guidelines manual.
21. Changes throughout the manual highlight that guidelines may draw on reviews that use real world evidence and data. As NICE's experience of evidence generation in response to identified evidence gaps increase through a range of ongoing initiatives, it is anticipated that the advice to developers in this area will grow in future updates of the manual.

## Searching

22. Updates to the searching chapter include new sources, tools and approaches in line with emerging best practice. In addition, a new prompt for identification of MHRA drug safety information for pharmacological effectiveness reviews has been added.

## Reviewing the evidence

23. Chapter 6 - reviewing the evidence - has been extensively rewritten during the updating process. Firstly, the clarity of the chapter has been improved by drawing a distinction between critical appraisal of individual studies and overall certainty in findings. Secondly, the manual now recommends that GRADE should be used as the first choice approach for quality assessment. One of the main differences in approach that remained between clinical and public health/social care guidelines following implementation of the 2014 manual was the approach to quality assessment. Clinical guidelines used the GRADE approach, with public health and social care developers using ++/-- or other methods, and these approaches were accepted within the 2014 manual. Following development of the GRADE-CERQual approach for application of

GRADE to qualitative evidence, and the piloting of GRADE within non-clinical guidelines, it is now accepted that the GRADE approach should be used, with other methods accepted in exceptional circumstances. GRADE-CERQual is recommended for qualitative evidence reviews, and the approaches for dealing with quantitative evidence have been better articulated.

24. In light of the standardised approach to quality assessment, the updated manual indicates that GRADE profiles should normally be provided as a way of summarising the results of the analysis and describing the confidence in the evidence. Current methods also include the development of evidence statements; these aggregated summaries of all of the relevant studies or analyses are now optional and recommended only where the GRADE approach is not used.

### Sifting

25. The 2014 manual advised developers that the gold standard approach of sifting all papers by two analysts should be undertaken. In recognition of the fact that this approach is resource-intensive, and that other mechanisms can be used to ensure relevant records are not missed, the manual has been amended to indicate that an agreed proportion of papers (not less than 10%) should be screened in duplicate. A new section has also been added to the manual highlighting the checking mechanisms that should be used.
26. The adoption of EPPI-Reviewer as a standardised tool to support systematic reviewing has given NICE staff access to functionality to improve the efficiency of the process. Priority screening refers to any technique where a machine learning algorithm is used to enhance the efficiency of the screening process. Usually this involves taking information on previously included or excluded papers, and using this to order the unscreened papers from most likely to be included to least likely. This can be used to attempt to identify a higher proportion of relevant papers earlier in the screening process, and can also be used to set a cut-off where some references are not screened, if it is decided to be sufficiently unlikely that additional relevant studies will be identified. The updated manual includes information about priority screening and, as there is currently no published guidance on setting thresholds for stopping screening where priority screening has been used, instructs developers to discuss and document their approach, taking into account specific factors to help guide their decision making.

### Network meta-analysis

27. A network meta-analysis is an analysis that includes both trials that compare the interventions of interest head-to-head, and trials that compare them indirectly via

a third intervention. Methods in this area are developing rapidly and the manual now includes advice on minimum outputs and reporting standards for NMAs. A number of approaches for assessing the quality or confidence in effect estimates derived from network meta-analysis have now been developed (Phillippo et al. in preparation, Caldwell et al 2016, Purhan et al. 2014, Salanti et al. 2014). The manual confirms that the strengths and limitations of these approaches and their application to NICE guideline development are currently being assessed. It is anticipated that this will be an area of update in the next version of the manual.

## Economic evaluation

28. Following implementation of the 2014 version of the manual, further work has been undertaken to align approaches to economic evaluation across NICE guidelines that focus on different sectors. The manual has been updated to indicate that for the base case analysis, a cost-utility analysis should be undertaken using a cost per QALY approach where possible. This change will enable more consistent application of decision rules relating to costs in future.
29. The following text has been added to the manual to clarify that the same cost per QALY threshold should be used for disinvestment as investment:

*In assessing the cost effectiveness of competing courses of action, the committee should not give particular priority to any approach that is currently offered. Therefore, in any situation where 'current practice', compared with an alternative approach, is found to generate an ICER above a level that would normally be considered cost-effective, the case for continuing to invest in it should be carefully considered. The committee should be mindful of whether the intervention is consuming more resource than its value is contributing based on NICE's cost per QALY threshold.*

This change will enable a more consistent and transparent approach to disinvestment decisions, as previously there was no clear advice in the manual.

30. The role of the newly established Guideline Recommendations Implementation Panel is also highlighted in the updated chapter as follows:

*The ability of the Health and Care System to respond to NICE guideline recommendations is also affected by their affordability and their relevance to declared priorities and ambitions at any given time. Arrangements are in place to explore the capability and willingness of the system to prioritise changes in practice proposed in NICE guidelines.*

## Links to other guidance

31. Current practice when developing a guideline where closely related technology appraisal guidance is available is for the TA team to prepare a review proposal

for each appraisal. If the proposal is to move the TA to the static list, the recommendations are incorporated verbatim into the guideline. In other cases, the TA may be updated, or links are added from the guideline to the TA. Verbatim incorporation and linking may cause issues when the TA recommendation changes, or when new recommendations are published that would also be relevant to reference. Linking to TA recommendations in the NICE Pathway is now proposed as the usual approach instead of copying them into the guideline (or adding links to the TA itself) because the Pathway is updated every time new guidance relevant to the pathway is published. This means that guideline users will see all relevant technology appraisals, including any published or updated after the guideline is published.

32. Updated text has also been included to advise developers on approaches that can be taken when similar review questions are covered in other guidelines. Options include linking to the recommendations in the other guideline, using the evidence review to make new recommendations, and undertaking a new systematic review.

### Writing the guideline

33. Information for developers on writing guidelines has been simplified in the updated manual, and a stand-alone writing guide created to enable greater detail and a greater range of examples to be included.
34. An interim update to the manual in April 2017 included a new section on supporting shared decision making. This text has been iterated following feedback from developers, and additional examples included in the stand-alone guide that is being used to support developers identify preference sensitive decision points and summarise the evidence to support a professional's discussion with the person making the decision.

### Additional consultation

35. The 2014 manual included mechanisms for engaging with users when developers identified a lack of evidence on the views and experiences of people affected by the guideline. In addition, the provision to conduct fieldwork with professional users of the guideline was included as a separate activity. These approaches have now been combined and defined as types of 'additional consultation' that can be used to inform guideline development in particular circumstances, leading to changes to appendixes, the committee, evidence review, and validation chapters of the manual.

## Implementation support

36. The chapter on implementation support has been updated in line with current ways of working and focuses on a range of tools including decision aids, visual summaries and resource impact assessments. A new section on how we work with other organisation, including endorsement of externally developed resources, has also been added.

## Surveillance

37. While the current surveillance approach is fit for purpose, the long term scenario is likely one of diminishing resources, a guideline development programme consisting mostly of updates and an ever increasing evidence base that, for some topics, changes quickly. Given resource reductions it is important that NICE can react in a timely and effective way to update guidelines.

38. The surveillance chapter of the manual has been extensively rewritten to focus the process on event-driven checks of published guidelines. NICE maintains a tracker which includes information on key events that are judged to be relevant to guideline content, such as ongoing studies, substantial changes in policy or legislation, or development of a related piece of NICE guidance. This enables a reactive approach to be employed allowing NICE to react in a timely manner to changes in the evidence base. As soon as the event has occurred or findings are available they are subject to the event-driven check.

39. In addition to event-driven checks, a standard check is proposed to be undertaken every 5 years after publication, which will include topic expert engagement, intelligence gathering and literature searching. Themed surveillance of guidelines covering similar populations or settings is planned to ensure the efficiency of the process.

## Refreshing

40. New content has been added to the manual to support developers when refreshing recommendations. Refreshing enables NICE to factually correct and improve the usability of recommendations without changing the intent and therefore without the need for an evidence review or committee input. All changes identified through a refresh are consulted on with stakeholders and signed off by NICE Guidance Executive. The new text gives examples of refreshing and confirms the process that should be followed.

## Resource impact of changes

41. A number of the changes proposed are designed to improve the efficiency of guideline development processes. These include:

- advice on sifting, including the introduction of cut-offs for priority screening
- the use of evidence statements only for the minority of topics not developed using GRADE
- proposals to link to NICE pathways rather than copying, and maintaining, TA recommendations in guidelines
- the move to event-driven and themed surveillance reviews.

42. These changes form part of a strategy to control and reduce the cost of developing guidelines, as a minimum enabling inflationary pressures to be absorbed. None of the changes proposed are anticipated to require greater resource input than the approaches described in the current manual.

## **Public consultation**

43. Subject to Board approval, public consultation on the updated Guidelines Manual is planned for a three month period from early April 2018.

44. The manual consultation will be promoted on the NICE web site at the start and end of the consultation period.

45. Existing stakeholders and committee members from all guideline programmes have been advised of the proposed consultation schedule, and will be contacted again once the manual has been approved by the Board, and when the consultation goes live.

## **Issues for decision**

46. The Board is asked to:

- approve the updated guidelines manual for public consultation.

National Institute for Health and Care Excellence

March 2018

## Appendix 1

### Virtual reference group - external members

Area of expertise	Name	Role / Organisation
Patient and Public Involvement and Experiences of Care	Dr Sophie Staniszewska	Professor of Health Research, University of Warwick Medical School
Cochrane	Dr Christopher Cates	Senior Clinical Research Fellow, SGUL; Training Fellow, Cochrane UK
	Dr Toby Lasserson	Senior Editor, Cochrane
GRADE – for complex interventions	Dr Deborah Caldwell	Senior Lecturer in Public Health Research, University of Bristol
GRADE – for public health	Dr Vittal Katikireddi	Senior Clinical Research Fellow, MRC/CSO Social & Public Health Sciences Unit, University of Glasgow
Public health guidelines	Monica Desai	Consultant Epidemiologist, Public Health England
Clinical guidelines	Dr Julian Treadwell	GP, Hindon Surgery, Wiltshire; NIHR In-Practice Fellow, Nuffield Dept Primary Care Health Sciences, Oxford.
Social care guidelines	Amanda Edwards	Retired (previously Deputy Chief Executive, SCIE)
Medicines	Jamie Hayes	Director, Welsh Medicines Resource Centre
Evidence synthesis – outcomes	Paula Williamson	Professor of Medical Statistics, University of Liverpool
Evidence synthesis	Professor Catrin Tudur-Smith	Professor of Biostatistics, University of Liverpool
Qualitative evidence - CERQual	Ruth Garside	Senior Lecturer in Evidence Synthesis, University of Exeter Medical School
Realist review, realist evaluation and qualitative reviews	Geoffrey Wong	Clinical Research Fellow, University of Oxford; GP Principal, Daleham Gardens Surgery
Service guidance	Professor Alec Morton	Professor of Management Science, University of Strathclyde

Economics	Professor Joanna Lord	Director Southampton HTA Centre, University of Southampton
Information retrieval	Julie Glanville	Associate Director of Information Services, YHEC
	Suzy Pailsey	Director of Innovation and Knowledge Transfer & Senior Research Fellow, ScHARR