NICE National Institute for Health and Care Excellence

Research recommendations process and methods guide

NICE process and methods
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Contents

1 Introduction

1.1 The foundation of NICE guidance is the synthesis of evidence primarily through the process of systematic reviewing and, if appropriate, modelling and cost effectiveness decision analysis. The results of these analyses are then discussed by independent committees. These committees include NHS staff, healthcare professionals, social care practitioners, commissioners and providers of care, patients, service users and carers, industry and academics. Stakeholders have the opportunity to comment on draft recommendations before they are finalised. Not only does this process explicitly describe the evidence base, it also identifies where there are gaps, uncertainties or conflicts in the existing evidence.

1.2 Many of these uncertainties, although interesting to resolve, are unlikely to affect people's care or NICE's ability to produce guidance. However, if these uncertainties may have an effect on NICE's recommendations it is important for NICE to liaise with the research community to ensure they are addressed. NICE does this by making recommendations for research, which are communicated to researchers and funders. At the time guidance is issued, NICE's staff and committees have a thorough understanding of the current evidence and valuable insights into uncertainties that need to be resolved. It is important that these are capitalised on.

1.3 To undertake its national role effectively, NICE needs to ensure that:

- the process of developing the research recommendations is robust, transparent and involves stakeholders
- we identify research priorities
- we make all research recommendations clearly identifiable in the guidance
- the research recommendations provide the information necessary to support research commissioning
- the research recommendations are available to researchers and funders by promoting them (for example through the research recommendations database)

- the research recommendations are relevant to current practice
- we communicate well with the research community.

1.4 This process and methods guide has been developed to help guidance-producing centres make research recommendations. It describes a step-by-step approach to identifying uncertainties, formulating research recommendations and research questions, prioritising them and communicating them to the NICE Science Policy and Research (SP&R) team, researchers, and funders. It has been developed based on the SP&R team's interactions with research funders and researchers, as well as with guidance developers.

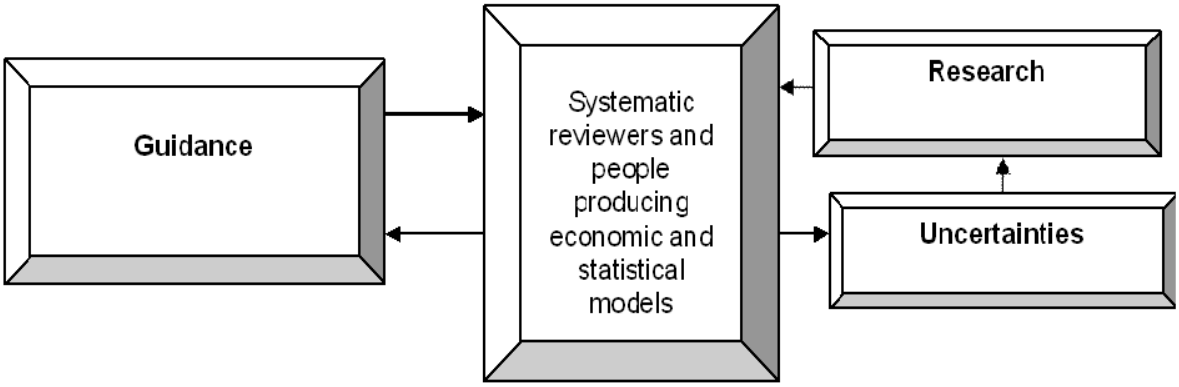
1.5 NICE works closely with the National Institute for Health Research (NIHR) Evaluation, Trials and Studies Coordinating Centre (NETSCC) to prioritise research recommendations. NICE and NETSCC interaction includes an annual meeting to review progress on carrying out and funding research from NICE research recommendations (both those given NICE key priority designation and those identified from the research recommendations database directly). This includes monitoring progress and the total spend on all research activities directly related to NICE research recommendations.

1.6 NETSCC reviews the recommendations from the NICE research recommendation database and other sources and explores their suitability for funding. This is generally either through the NIHR Health Technology Assessment (HTA), NIHR Public Health Research (PHR) or the NIHR Health Services & Delivery Research (HS&DR) programmes. If they are found to be suitable a vignette is drafted for the NIHR HTA AdvisoryPanels to consider.

1.7 The NICE SP&R team also liaises with other researchers and research funders to make them aware of the most important uncertainties or resulting research recommendations that are prioritised during guidance production. This includes national organisations such as the UK Research Councils and research charities (for example, Cancer Research UK), and industry.

1.8 The process used to develop final research recommendations may vary between NICE guidance-producing centres and is described in the process or methods manuals for each type of guidance.

Figure 1: The role of research recommendations in the guidance production cycle

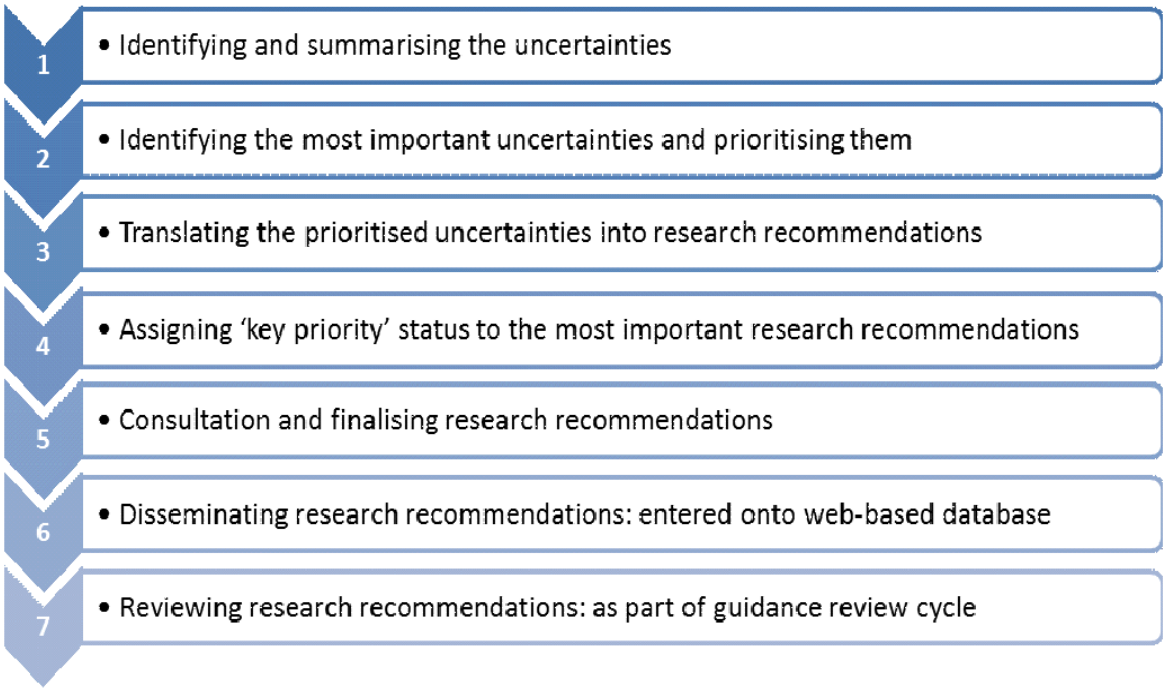


1.9 Creating research recommendations is part of the guidance production cycle (evidence synthesis through to funding opportunities, surveillance decisions and updating guidance), see figure 1. Guidance producers (including those conducting systematic reviews and producing economic models) should:

- identify any uncertainties that may affect people's care or NICE's ability to produce guidance
- develop research recommendations using an appropriate technique to frame research question development, for example PICO (population, intervention, comparator, outcome) or EPICOT (evidence, population, intervention, comparator, outcome, time)
- undertake consultation on research recommendations integral to the guidance (see the programmes' process or methods guides)
- review whether research has addressed the gaps or uncertainties as part of the guidance review and update cycle.

2 NICE research recommendations process

Figure 2: summary of the process



2.1 Step 1: identifying and summarising the uncertainties

2.1.1 The evidence synthesis, modelling and decision making processes may identify uncertainties and gaps in the evidence base. Summarise these in a clearly identifiable 'uncertainties' section in the guidance. The summary is not intended to be exhaustive, but is used to help select the most important uncertainties (step 2) for prioritisation.

2.1.2 There are different types of uncertainties, and they may relate to any aspect of clinical, health, public health, or social care practice. Examples include clinical- and cost-effectiveness, diagnosis, test accuracy, prognosis, modes of delivery, optimal service design, quality of life, outcomes that are important to users, and user preferences and values.

2.1.3 Uncertainties may arise for many reasons. The 2 primary reasons are that there is no published evidence available, or the available evidence is not sufficient, robust, or conflicting (see box 1 for more detailed examples).

Box 1 Examples of reasons for uncertainties

There is no evidence available because:

- the relevant research has not been done
- the relevant research has been done, but not published
- the relevant research has been done and published, but it has not been identified Evidence is available but:
- there is insufficient information on which to base a recommendation (for example, due to
- inadequate reporting)
- there are methodological limitations (for example, the study enrolled too few participants to be sure statistically that the results were not due to chance alone)
- the results were inconclusive or inconsistent
- the results cannot be applied to the population in question (for example, the setting or social and cultural context is not comparable, the user population differs, or a different dosage has been used)
- it concerns a related but different question (for example, the comparator differs)
- the research is out of date (for example, a systematic review needs updating with recent trials or practice has changed)

2.2 Step 2: identifying the most important uncertainties and prioritising them

2.2.1 NICE reviews the summarised list of uncertainties and identifies and documents the most important ones. The uncertainties deemed most important are those

that the NICE committees consider need to be resolved to inform future updates of guidance recommendations, and that will also give clear benefits and added value to the NHS, public health, social care and voluntary sectors. For example, uncertainties related to aspects of care or services that providers need to address as a priority. There are no limits to the number of important uncertainties identified and prioritised, and it may be that none are identified at all.

2.2.2 NICE committees lead the process of identifying and prioritising the most important uncertainties, with input from clinicians, researchers, patients and carers, service users or the target population, reviewers, health economists and NICE technical staff.

2.2.3 The committees may use any modelling that has been done to help select the most important uncertainties. For example, the results of an economic modelling exercise may be sensitive to specific parameter or structural assumptions that could be clarified by research.

2.2.4 Additional analysis (for example, 'value-of-information' methods) using the same models as in the decision-making are a possible method for establishing the value for money of additional research to reduce evidence gaps and help prioritise future research. There is no requirement to routinely undertake such evaluations, but they may help identify the most important uncertainties.

2.3 Step 3: translating the prioritised uncertainties into research recommendations

2.3.1 Translate prioritised uncertainties into a research recommendation applying a framework with 2 components (see box 2 for an example):

- a structured stand-alone statement that sets out the questions that need to be answered (see table 1 for an example format)
- a structured rationale explaining why the research is important and is being recommended to research funders and researchers (see table 2 for an example format).

Table 1 Example format for research recommendation statements

Criterion	Explanation
Population	Define the population that the research needs to be undertaken in. Where appropriate, specify any of the following: • diagnosis • disease stage • comorbidities • risk factors • gender • age • ethnic group • specific inclusion criteria • specific exclusion criteria • determinants of health • health status or setting (for example, community or secondary care)

Criterion	Explanation
Intervention	Specify the intervention that needs to be evaluated. This can be: • a drug • a device • a treatment • a management strategy • a psychological intervention • a behavioural intervention • a community intervention • an organisational or population intervention • a clinical prediction rule or prognostic factors. For public health this may also refer to risk factors that the service user or population is exposed to. Also consider providing information on: • the type, frequency, dose, and duration (for intervention or exposure) • any prognostic factors or any diagnostic or screening tests that might be needed. For public health interventions, the context, setting and method of delivery of the intervention may also need to be specified.
Comparators	If appropriate, state what the intervention needs to be compared with. For example, placebo, routine care, alternative treatment, or management strategy. Also consider providing information on: • the type, frequency, dose, and duration (for intervention or exposure) • any prognostic factors or any diagnostic or screening tests that might be needed.

Criterion	Explanation
Outcome	What will the researcher need to measure, improve, influence, or accomplish to assess whether the intervention is effective? What clinical outcomes or patient or user-related outcomes of the intervention should be measured to demonstrate this? Consider providing information on: • Outcomes to be measured (for example, mortality, morbidity, quality of life, patient or user perception, other outcomes that are important to patients or users). Any surrogate outcomes must be validated. • Method and process of measurement (type, frequency, or timing of measure). • Length of follow-up needed. For public health interventions, specify whether the causal pathway leads to individual or population level outcomes.
Study design	In some cases, it may be appropriate to specify the study design to address the proposed question, but be aware that there may be several alternatives depending on timescale and context. In many cases, it may be more appropriate for the study design to be considered by the research funder after the research recommendation has been made by the NICE Committee.
Timeframe	Is there a timeframe in which the study needs to be completed? For example, to inform a guidance review, or if the technology might be superseded before any studies are complete.

Table 2 Example format for research recommendation rationale, to support prioritisation

Potential criterion	Explanation
Importance to patients, service users or the population	What would be the impact of any new or altered guidance on the population (for example, acceptability to patients or service users, quality of life, morbidity or disease prevalence, severity of disease, or mortality)?

Potential criterion	Explanation
Relevance to NICE guidance	How would the answer to this question change future NICE guidance (that is, generate new knowledge or evidence)? How important is the question to the overall guidance? • High: the research is essential to inform future updates of key recommendations in the guidance. • Medium: the research is relevant to the recommendations in the guidance, but the research recommendations are not essential to future updates. • Low: the research is of interest and will fill existing evidence gaps.
Relevance to the NHS, public health, social care and voluntary sectors	What would be the impact on the NHS, public health, social care and voluntary sector and (if relevant) the public sector of any new or altered guidance (for example, financial advantage, or effect on staff, strategic planning, or service delivery)?
National priorities	Is the question relevant to a national priority area (such as a national policy or parliamentary paper)? If so, specify the document.
Current evidence base	What are the problems with the current evidence base? (That is, why is further research needed?) Is there any relevant ongoing research that may resolve the uncertainty?
Equality	Does the research recommendation have any relevance to equality? For example, does it focus on groups needing special consideration, or on a technology, intervention or service that is not available for use by people with certain disabilities? What is known about the impact of the intervention on the health gradient?

Potential criterion	Explanation
Feasibility	Can the proposed research be carried out within a realistic timescale? Would the sample size needed to resolve the question be feasible? Would the expense needed to resolve the question be warranted? Are there any ethical or technical issues?
Other comments	Any other important issues that should be mentioned, such as potential funders, outcomes of previous attempts to address this issue, or methodological problems.

Box 2 Example of structured statement and explanation

Structured standalone statement:

- A randomised-controlled trial should be undertaken to determine whether benzoyl peroxide or adapalene is more clinically and cost-effective at reducing the number of non-inflammatory lesions in the treatment of acne vulgaris in adolescents. The study should also consider the impact of treatments on quality of life.

Structured rationale:

- Retinoids such as adapalene are currently recommended by many experts as first-line treatment for acne. The systematic review undertaken by NICE in 2009 did not identify any robust evidence comparing them with generic treatments, such as benzoyl peroxide, which have been demonstrated to be clinically and cost effective. Acne has a significant impact on quality of life. Acne is highly prevalent amongst teenagers, and therefore the preferential use of retinoids could have significant budgetary implications for the NHS. No ongoing trials have been identified.

2.3.2 The research recommendations need to be stand-alone statements because they will be abstracted into a database and may not be read in the context of the guidance. The recommendation must characterise the research that needs to be undertaken and convey why it is important, to ensure that readers will pick up the recommendation for further exploration.

2.3.3 Research recommendations can propose primary and secondary quantitative and qualitative research, for example, formative and summative evaluations, trials, longitudinal studies, secondary analysis and scoping papers of research needs. They may also recommend methodological research, epidemiological studies, and data collection exercises.

2.3.4 Some NICE committees make 'only in research' recommendations if the adoption of a technology should be considered only in the context of research. See the Guide to the methods of technology appraisal 2013 for details.

2.3.5 During guidance development the NICE committee may invite a research funding body to support the development of research recommendations. The funding body advises on the structure of clear and actionable research recommendations that fall within the remit of its specific research programmes. For example, NICE guidelines in public health increasingly apply this approach, working with the NETSCC. The research funding body can also ensure that the NICE committee is aware of any relevant ongoing research it is commissioning.

2.3.6 If a committee contacts a research funding body to support the development of research recommendations, it should do this at an early stage, before the guidance is sent for consultation, and before it is finalised and published. The NICE SP&R team can support this.

2.4 Step 4: assigning 'key priority' status to the most important research recommendations

2.4.1 If NICE believes that a research recommendation is particularly important it has a special arrangement with NETSCC that enables the recommendation to be given, by agreement, a 'key priority' status.

2.4.2 A NICE key priority is a research recommendation that can be progressed rapidly through an identified research commissioning route. NICE key

2.4.3 priority research recommendations may bypass the NIHR HTA Advisory Panels and go directly to the NIHR HTA Prioritisation Group, which meets 3 times a year.

Processes for other NETSCC programmes may vary.

2.4.4 The aim of the key priority designation is to resolve important uncertainties as rapidly as possible through research. The intended outcome is that the commissioned research will provide evidence that can be used to inform an update to the guidance or related guidance. This process can take place outside of formal guidance update timelines depending on the relevance and importance of the findings from the research evidence, which may require NICE to update the guidance as soon as possible.

2.4.5 The NICE key priority designation is made only if the NICE Committee Chair and Centre Director agree that special priority needs to be signalled. The designation should be made before the guidance is finalised and the SP&R team should be notified to facilitate discussion with NETSCC. This ensures that the final research recommendation is clear and actionable and takes account of any research started or commissioned since the systematic reviews were carried out for the NICE Committee. The details of the research in progress can then be added to the final guidance.

2.4.6 It has been agreed that NETSCC will accept for consideration up to 10 NICE key priority research recommendations each year. NICE's SP&R team maintains and manages the list across NICE and liaises with NETSCC and the NICE guidance producing centres.

2.5 Step 5: consultation and finalising research recommendations

2.5.1 Always include all research recommendations in the draft guidance for consultation in a separate 'Research recommendations' section. For guidelines, include this section in both the full and short versions. The recommendations may also be included in the body of the text.

2.5.2 NICE committees (with input from professionals and practitioners, researchers, patients, users of services, carers, the target population, reviewers, health economists and NICE technical staff) may be aware of research in progress that

would support a research recommendation. Do not put information about these research activities in the 'Research recommendations' section, but in a separate 'Ongoing research' section.

2.5.3 Revise the draft research recommendations in light of any consultation comments and publish the final recommendations in the guidance.

2.6 Step 6: disseminating research recommendations

2.6.1 The NICE SP&R team extracts all the important research recommendations that are published and adds them to the online NICE research recommendation database. The database is searchable and is monitored by research funders. For example, NETSCC actively reviews all NICE research recommendations and considers those that are within the remit of the programmes they manage.

2.7 Step 7: reviewing research recommendations

2.7.1 It is important to check research recommendations as part of the guidance-review cycle to see if research has been undertaken that could feed into the updated guidance.

2.7.2 Carry out this check in conjunction with developing a review scope. The literature searches for the review scope process may identify whether research has been undertaken or is in progress. If the research has been undertaken, notify the NICE SP&R team so they can record the uptake of the research recommendation, and if necessary, remove the recommendation from the research recommendation database.

2.7.3 As part of the review process, guidance development teams may also be able to advise if partially updated guidance confirms amendments to, replacement or removal of existing research recommendations.

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