National Institute for Health and Care Excellence

FINAL

Indoor air quality at home

NICE guideline: methods

NICE guideline NG149

Methods

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Final

Evidence reviews were developed by Public Health Internal Guideline Development team

Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

Local commissioners and/or providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

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Contents

Development of the guideline

What this guideline covers

This guideline covers effective ways to prevent or reduce the health impact of poor indoor air quality at home. It looks at individual or building characteristics that increase exposure to poor indoor air quality and signs and symptoms that should prompt healthcare professionals to consider exposure to poor indoor air quality in people presenting to health services. It also covers strategies for raising awareness and interventions to prevent or reduce the risks of poor indoor air quality at home.

What this guideline does not cover

This guideline does not cover areas covered by national legislation such as legislation on Radon or areas covered by other NICE guidance for example outdoor air quality, smoking: harm reduction, smoking: stopping in pregnancy and after childbirth

Methods

This guideline was developed in accordance with the process set out in 'Developing NICE guidelines: the manual' Last updated: October 2018. A booklet, 'How NICE guidelines are developed: an overview for stakeholders, the public and the NHS' is available. In instances where the guidelines manual does not provide advice, additional methods are described below. Declarations of interest were recorded according to the 2018 NICE conflicts of interest policy.

Developing the review questions and outcomes

The 4 overarching review questions (RQs) developed for this guideline were based on the key areas identified in the guideline scope. They were drafted by the NICE Public Health Internal Guideline Development team, refined and validated by the guideline committee.

The review questions were based on the following frameworks:

- population, intervention, comparator and outcome (PICO) for intervention reviews
- population (problem), exposure (prognostic factor), and outcome for prognostic and risk stratification reviews

Full literature searches, evidence tables and critical appraisal for all included studies, excluded studies and reasons for exclusion and evidence reviews were completed for all review questions.

Reviewing research evidence

The identification of evidence for evidence review in the guideline conformed to the methods set out in chapters 5 of the 'Developing NICE guidelines: the manual' (October 2018). The purpose of the search was to identify the best available evidence to address review questions without producing an unmanageable volume of results.

Relevant databases and websites, listed in indoor air quality – Search strategies, were searched systematically to identify effectiveness, prognostic, risk stratification, cost effectiveness and qualitative research evidence. The principal database search strategy is listed in Indoor air quality at home – Search strategies. The strategies have been developed in MEDLINE (Ovid interface) and will be adapted, as appropriate, for use in the other sources listed in Indoor air quality at home – Search strategies taking into account their size, search functionality and subject coverage.

Priority screening

Review questions undertaken for this guideline made use of the priority screening functionality (text mining) with the EPPI-reviewer 4 systematic reviewing software. This uses a machine learning algorithm (specifically, a stochastic gradient descent (SGD) classifier) to take information on features in the titles and abstract of papers marked as being 'includes' or 'excludes' during the title and abstract screening process, and re-orders the remaining records from most likely to least likely to be an include, based on that algorithm. This re-ordering of the remaining records occurs every time 25 additional records have been screened.

At least 10 included and 10 excluded studies were identified during the title and abstract screening process before applying the priority screening functionality Screening on title and abstracts was only terminated after a plateau was reached and priority screening did not identify any more probable new includes. As research is currently ongoing as to what are the appropriate thresholds where reviewing of abstract can be stopped, we adopted the following additional steps to ensure no studies were missed.

- the included studies list of included systematic reviews were searched to identify any papers not identified through the primary sift
- The database was also manually searched to ensure no relevant studies were missed. For example, searching for key words or intervention terms.
- We double checked with the committee to ensure all studies they were aware of were captured.

Type of studies and inclusion/exclusion criteria

- Cohort and case-control studies were included if they evaluated risk stratification and/or prognostic factors related to RQs 1 and 2.
- Randomised controlled trials (RCTs) were included if they evaluated interventions related to RQs 3.1, 3.1a, 3.2, 3.3 and 4.
- RCTs which measure health impact and economic modelling studies were included if they evaluated interventions related to RQ 3.3.

Systematic reviews of intervention studies were used as a source for primary studies but were not included in the evidence reviews as per protocol.

Papers were excluded if:

- they were not published in the English language, were not conducted in developed economies similar to the UK or not conducted from 1970[1] onwards
- only available as conference abstract, letter, opinion piece, review articles

Methods of combining evidence

Data synthesis for respiratory conditions

Respiratory conditions were reported differently within and across studies. Due to the myriad of respiratory conditions reported and measures used, the committee agreed that:

- Where 2 or more respiratory conditions are reported, to use the most sensitive outcome. For example, using Forced expiratory volume - 1 second (FEV1) over peak expiratory flow (PEF) or
- Where 2 or more respiratory conditions are reported, to use the one reported as the primary outcome for which the trial was powered. For example, reporting wheeze powered for study over cough

[1] The year 1970 was identified as a suitable start date as it would gather relevant, current evidence. It also pre-dates the national legislation on improving building structures and indoor air quality

Data synthesis for intervention reviews

Meta-analyses of intervention reviews were conducted with reference to the Cochrane Handbook for Systematic Reviews of Interventions (Higgins et al. 2011).

Data from single study was not reported in forest plots. Forest plots reported where we have pooled 2 or more studies.

Continuous data

Where different studies with continuous data measuring the same outcome but used different instruments/metrics, data were analysed using standardised mean differences

Dichotomous data

Meta-analysis of quantitative data was conducted with reference to the Cochrane Handbook for Systematic Reviews of Interventions (Higgins et al. 2011).

Where events rates were reported for both control and intervention arms, outcomes were pooled on either the odds ratio (OR) or relative risk (RR) scale using the Mantel–Haenszel method. Where events rates were not reported for both control and intervention arms and only the estimate of effects were reported, outcomes were pooled on the log odds scale using the inverse variance method. Fixed- and random-effects models were fitted for evidence review synthesis as appropriate.

Meta-analyses were performed in Cochrane Review Manager V5.3.

Minimal important difference (MID)

MIDs were not specified for this guideline so the GRADE rule of thumb (approach) for downgrading the certainty of evidence because of imprecision for dichotomous and continuous outcomes was used.

Dichotomous outcome

Outcomes were downgraded if 95% confidence interval around the pooled or best estimate of effect includes both 1) no effect and 2) appreciable benefit of 0.80 or appreciable harm of 1.25

Continuous outcome

Outcomes were downgraded if 95% confidence interval around the mean difference or pooled mean difference includes 0.5 standard deviations of the control group. For SMD, outcomes were downgraded if the upper or lower confidence limit crosses an effect size of 0.5 in either direction

Data synthesis for non-intervention reviews

Data for the non-intervention reviews were not pooled statistically (meta-analysed) as studies

- were not similar enough in terms of adjusting for the same potential confounders or variables.

- reported more than one source per pollutant
- reported more than one measure of per pollutant

The Adjusted relative effects (for example, aOR and aRR) and associated lower and upper 95% confidence interval (CI) from each study were individually reported

Appraising the quality of evidence

Critical appraisal of individual studies

The information extracted for the critical appraisal was used in two ways

- to rate the study quality for use when summarising the quality of the studies included in each review and
- as part of the GRADE assessment of the committee's confidence in the evidence base for each outcome

Intervention studies

Quality assessment for all included studies was conducted using the tools in Developing NICE guidelines: the manual. The quality of individual studies was assessed using the appropriate NICE quality assessment checklist for each study.

The critical appraisal of RCTs included for RQs 3.1, 3.2, 3.3 and 4 was conducted with the Cochrane risk of bias (ROB) tool. Bias was assessed as a judgment (high or low) for individual elements from seven domains (random sequence generation, allocation concealment performance, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other sources of bias). Each domain was given equal weight. Overall ROB was then assigned for each study as either 'high' or 'low' and was interpreted as follows:

Low overall ROB indicates low ROB for all domains or 1 high ROB for only 1 domain

High overall ROB indicates high ROB for 2 or more domains

Non-intervention studies

Quality assessment for all included studies was conducted using the tools in Developing NICE guidelines: the manual (2018). The quality of individual study was assessed using the appropriate NICE quality assessment checklist for each study.

The critical appraisal of observational studies included for RQ 1 and 2 was conducted with Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies. Bias was assessed as a judgment (high, low or moderate) for individual elements from three domains (selection, comparability and outcome assessment). Overall ROB was then assigned for each study as either 'high' 'moderate' or 'low'. The critical appraisal of modelling studies included for RQ 4 was conducted with the Philips (Philips et.al 2004) assessment checklist for decision analytic models. This checklist included 55 items across 3 domains. The 3 domains were model structure, model data and model consistency.

Certainty of the evidence for each outcome

Adoption of the GRADE approach for this guideline was confirmed during protocol development. The GRADE approach for assessing certainty of evidence across outcomes was designed using intervention studies (RCTs) as the gold standard. Where RCTs start as 'high quality' and observational studies as 'low quality'. For this guideline, it was agreed that:

- The study design that best answers our review question shall start as 'high quality' if it was determined that RCTs are not feasible or not ethical
- Where appropriate GRADE will be modified to meet the needs of the review question.

For intervention studies, RCTs were considered to be of highest quality. For the risk factor studies, cohort studies were considered to be of highest quality and case control studies as next best evidence quality

GRADE methodology for intervention and non-intervention evidence

For the non-intervention reviews (RQs 1 and 2) cohort and case control studies were included and these started as 'high and moderate quality' respectively.

For the intervention reviews (RQs 3.1, 3.2, 3.3 and 4) RCTs were included and these started as 'high quality'.

Outcomes of the included studies were rated individually to indicate the certainty around the findings, based on assessment using GRADE methodology as outlined in Table 1

Table 1: GRADE

Criterion	Reason for downgrading or not downgrading confidence
Risk of bias	The certainty of the evidence was downgraded if there were concerns about the design or execution of the study, including concealment of allocation, blinding, loss to follow up using intervention checklists in Developing NICE guidelines: the manual (2018); For example, limitations in the study design and implementation may bias the estimates of the treatment effect. Major limitations in studies decrease the confidence in the estimate of the effect. Examples of such limitations are selection bias (often due to poor allocation concealment), performance and detection bias (often due to a lack of blinding of the patient, healthcare professional or assessor) and attrition bias (due to missing data causing systematic bias in the analysis).
Indirectness	Indirectness refers to differences in study population, intervention, comparator and outcomes between the available evidence and the review question. The certainty of the evidence was downgraded if there were concerns about the population, intervention and outcome in the included studies and how directly these variables could address the specific review question.
Inconsistency	Inconsistency refers to an unexplained heterogeneity of effect estimates between studies in the same meta-analysis. The certainty of the evidence was downgraded if there were concerns about inconsistency of effects across studies: occurring when there is variability in the treatment effect demonstrated across studies (heterogeneity). This was assessed using visual inspection

Criterion	Reason for downgrading or not downgrading confidence
Imprecision	Using the recommended GRADE cut-off values for imprecision: • dichotomous outcome was downgraded if the 95% confidence interval around the effect size includes appreciable benefit of 0.80 or appreciable harm of 1.25 • continuous outcome was downgraded if the 95% confidence interval around the mean difference includes 0.5 standard deviations of the control group. For standardise mean difference (SMD), outcomes were downgraded if the upper or lower confidence limit crosses an effect size of 0.5 in either direction
Other issues	None

Reviewing economic evidence

The PHAC is required to make decisions based on the best available evidence of both general effectiveness and cost-effectiveness. Guideline recommendations should be based on the expected costs of the different options in relation to their expected benefits (that is, their 'cost-effectiveness') rather than the total implementation cost. Thus, if the evidence suggests that a strategy provides significant benefits at an acceptable cost per person treated, it should be recommended.

In order to assess the cost effectiveness of the key issues addressed in this guideline, the following actions were carried out:

- A systematic review of economic evidence in the literature was conducted, alongside the review of evidence on general effectiveness
- A de novo economic model was developed, in order to provide cost effectiveness evidence for a number of review questions

Literature review

The systematic reviewer:

- Identified potentially relevant studies for each review question from the economic search results by reviewing titles and abstracts. Full papers were then obtained.
- Reviewed full papers against pre-specified inclusion and exclusion criteria to identify relevant studies (see below for details).
- Extracted key information about the studies' methods and results into evidence tables
- Generated summaries of the evidence in NICE economic evidence profiles

Inclusion and exclusion of economic studies

Full economic evaluations (studies comparing costs and health consequences of alternative courses of action: cost-utility, cost-effectiveness, cost-benefit and cost-consequence analyses) and comparative costing studies that addressed the review

question in the relevant population were considered potentially includable as economic evidence.

As per 'Developing NICE guidelines: the manual' (2018), UK-based cost-utility studies reporting health outcomes in quality adjusted life years (QALYs) were preferred. However, due to the relatively sparse evidence for most review questions, non-UK-based cost effectiveness studies (i.e. those reporting outcomes in natural units) were also included. It was determined that such evidence may still be useful in informing the committee of the potential trade-off between costs and benefit of interventions. Similarly, cost-consequence analyses (i.e. those in which costs and benefits are reported separately) were included, as they were also determined to be potentially useful, for instance in cases where an intervention is associated with lower costs and higher benefits than the alternative.

Studies which only reported costs (without any consideration of health benefits) were excluded. Literature reviews, abstracts, posters, letters, editorials, comment articles, unpublished studies and studies not in English were excluded.

Full details can be found in the evidence review.

Appraising the quality of economic evidence

Studies that met the eligibility criteria were assessed using the quality appraisal criteria as outlined in Developing NICE guidelines: the manual (2018).

Health economic modelling

As well as reviewing the published economic literature for each review question, as described above, a de novo economic analysis was undertaken for relevant research questions. The following general principles were adhered to in developing the analysis:

- Methods were consistent with the NICE reference case.
- The committee was involved in the design of the model, selection of inputs and interpretation of the results.
- Where possible, model inputs were based on the systematic review of the clinical literature, supplemented with other published data sources identified by the committee as required.
- When published data were not available committee expert opinion was used to populate the model.
- Model inputs and assumptions were reported fully and transparently.
- The results were subject to sensitivity analysis and limitations were discussed.

Full methods for the de-novo modelling can be found in the Indoor Air Quality HE report.

Resource impact assessment

The resource impact team used the methods outlined in the Assessing resource impact process manual: guidelines

The resource impact team worked with the guideline committee from an early stage to identify recommendations that either individually or cumulatively have a substantial impact on resources. The aim was to ensure that a recommendation does not introduce a cost pressure into the health and social care system unless the committee is convinced of the benefits and cost effectiveness of the recommendation. The team gave advice to the committee on issues related to the workforce, capacity and demand, training, facilities and educational implications of the recommendations.