Economic Plan

This document identifies the priorities for economic analysis and the proposed methods for addressing these questions as described in section 7 of the guidelines manual (2014).

1 Guideline

Full title of guideline: Asthma: The management of asthma (short: Asthma management)

2 Process for agreement

The economic plan was prepared by the guideline health economist in consultation with the rest of the National Centre for Clinical Guidelines (NCGC) technical team and the Guideline Committee. It was discussed and agreed on by the following people:

For the NCGC and Committee:

NCGC economist(s): Alexander Haines, Senior Health Economist
              Peter Rouse, Health Economist
NCGC representative(s): Bernard Higgins, Guideline Lead
Committee representative(s): John Alexander, Chair

For NICE (completed by NICE):

CCP lead: Sarah Willett
Commissioning manager: Caroline Keir
Economic lead: Paul Crosland
Costing lead: TBC

Proposals for any changes to the agreed priorities will be circulated by email to this group. If substantive revisions are agreed, they will require to be recorded as addenda to this document (section 8) or as an updated version of the document.

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This may be done by face-to-face meeting, teleconference, or email as convenient.

This may be the project manager, a systematic reviewer or research fellow and/or the centre director or manager, as appropriate for the developer and guideline. For the NCGC it will usually be the guideline lead.

This may be the Committee chair, clinical lead or other members as appropriate.

In case clinical questions are changed, for example, section 3 requires updating as well as other sections if modelling priorities are affected.
3 Topic priorities identified in the Scope

This section contains all topics, or clinical review questions as covered by the scope. These topics usually reflect selected clinical issues. Please indicate if an area is relevant for economic consideration and if modelling is deemed appropriate to address it.

<table>
<thead>
<tr>
<th>Area*</th>
<th>Relevant?</th>
<th>Appropriate for modelling?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pharmacological management of chronic asthma</strong>&lt;br&gt;In children, young people and adults with asthma who are treatment-naive, what is the most clinically and cost effective initial therapy to be started on:&lt;br&gt;- reliever therapy alone (SABA) or,&lt;br&gt;- both reliever and preventer therapy (SABA and a preventer such as ICS)</td>
<td>Yes</td>
<td>Initial scoping search found no economic or clinical evidence for the subject area. Unit costs will be presented to the GC however a research recommendation will be the most likely course of action. This question has a low priority for original economic analysis.</td>
</tr>
<tr>
<td>What is the most clinically and cost effective preventer drug (class or combination of drug classes) for the management of children, young people and adults with asthma who are uncontrolled on SABA alone (preventer-naive) or who are treatment-naive?</td>
<td>Yes</td>
<td>The question is economically important as the asthma population is large meaning any change in the cost per patient will have a large impact on the NHS. Cost-effectiveness has not been reviewed in related guidelines, such as the BTS/SIGN guideline, and could therefore lead to a change in current practice and standardisation of optimal treatment. An economic model would be built on the results of the proposed network meta-analysis (NMA), allowing the whole pharmacological pathway to be modelled. Although the current economic literature may have assessed the cost-effectiveness of one treatment compared to another we do not expect to find any economic analysis which compares all relevant comparators together. Likewise it is unlikely that any existing analysis will</td>
</tr>
<tr>
<td>What is the most clinically and cost effective drug (class or combination of drug classes) for the management of children, young people and adults with asthma who are currently taking an optimal single preventer (see previous question) when this fails to provide adequate control?</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

* This corresponds to the ‘Key clinical issues that will be covered’ section in the scope or, if available, clinical review questions.

<table>
<thead>
<tr>
<th>Relevant?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Please state if this area is deemed relevant for considering opportunity costs and likely disinvestments. Areas might pose a decision problem directly, or implicitly inform the choice between options. Categories should include information on relevance and if of high or low priority for health economic work (see below).</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Appropriate for modelling?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health economic work comprises of literature reviews, qualitative consideration of expected costs and effects or formal decision modelling. Decision modelling is particularly useful where it can reduce uncertainty over cost effectiveness or where a recommendation is likely to result in considerable changes in health or costs. For further details please see section 7 of the guidelines manual (2014). It may not be feasible or efficient to address every relevant decision problem by original work. The rationale for choosing areas for cost-effectiveness modelling should be discussed in detail in sections 3 and 4.</td>
</tr>
<tr>
<td>Question</td>
</tr>
<tr>
<td>-------------------------------------------------------------------------</td>
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<tr>
<td>young people and adults with asthma who are currently taking optimal preventer therapy according to step 3 (see previous question) when this fails to provide adequate control?</td>
</tr>
<tr>
<td>In children, young people and adults with asthma on ICS preventer therapy, is intermittent ICS more clinically and cost effective than regular ICS?</td>
</tr>
<tr>
<td>What is the clinical and cost-effectiveness of stepping down treatment in children, young people and adults who are controlled/stable on current therapy?</td>
</tr>
<tr>
<td>Question</td>
</tr>
<tr>
<td>-------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Non-pharmacological management of chronic asthma</strong></td>
</tr>
<tr>
<td>What are the most clinically and cost effective strategies to improve medicines adherence in children, young people and adults with asthma who are non-adherent to prescribed medicines?</td>
</tr>
<tr>
<td>What is the clinical and cost effectiveness of delivering asthma care stratified according to risk of asthma attacks to improve outcomes for children, young people and adults with asthma?</td>
</tr>
<tr>
<td>What is the clinical and cost effectiveness of supported self-management (including self-management education, self-monitoring and a personalised asthma action plan, PAAP) in</td>
</tr>
<tr>
<td>Question</td>
</tr>
<tr>
<td>-------------------------------------------------------------------------</td>
</tr>
<tr>
<td>comparison to standard care (asthma review only), for improving outcomes for children, young people and adults with asthma in primary care?</td>
</tr>
<tr>
<td>What is the optimal increase in preventer therapy within supported self-management when control is lost?</td>
</tr>
<tr>
<td>Are breathing exercises clinically and cost effective for children, young people and adults with asthma?</td>
</tr>
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</table>
4 Planned modelling

This section will specify modelling work prioritised by the Committee. It will provide details on how cost effectiveness will be considered for relevant, prioritised clinical areas or decision problems. Proposed modelling work should be listed in chronological order. For each decision model, please state the proposed analytical methods, including the populations, interventions and comparators, outcomes, perspective and type of economic analysis. In addition, include relevant references and any comments and justifications on, for example, possible diversions from the NHS and PSS reference case.

<table>
<thead>
<tr>
<th>Area(^h) (clinical question(s)(^i))</th>
<th>Outline proposed analysis</th>
</tr>
</thead>
</table>
| In children, young people and adults with asthma who are treatment-naïve, what is the most clinically and cost effective initial therapy to be started on:  
- reliever therapy alone (SABA) or,  
- both reliever and preventer therapy (SABA and a preventer such as ICS)  
What is the most clinically and cost effective preventer drug (class or combination of drug) | In the model there are three main outcomes that affect costs and quality of life:  
1. Exacerbations  
2. Quality of life (level of asthma control)  
3. Mortality  
The data informing these outcomes will be collected from a network meta-analysis for questions concerning the pharmacological management of asthma. The network-meta analysis should identify evidence for each step of treatment comparing all relevant comparators to enable us to populate the model. With this information, data on exacerbations and quality of life will feed into a model supplemented by costs from the NHS drug tariff for different treatment combinations and NHS reference costs for exacerbations.  
The model would be a Markov model with four states: no exacerbation, non-hospitalised exacerbation, hospitalised exacerbation and dead. In the ‘no exacerbation’ state after each cycle there would be a probability that the individual experiences an exacerbation, this could either be hospitalised or non-hospitalised. This probability would be treatment-related and be based on the clinical evidence taken from the NMA. The exacerbation would either be hospitalised leading to a high disutility and hospitalisation or non-hospitalised which would result in a smaller disutility and a lower cost, as this can be managed with oral steroids alone. The proportion of hospitalised and non-hospitalised exacerbations will be based on evidence from the clinical review. If this evidence is not available from the NMA then the proportion of severe to non-severe exacerbations will be taken from epidemiological studies and it will assumed this is the same across all treatments. Disutility values for exacerbations will be taken from Llyod et al.\(^2\) |

\(^h\) This should be the key areas relevant for considering opportunity costs and high priority for original modelling, as identified in section 3.  
\(^i\) Two or more questions may be addressed by a single analysis if appropriate.
A quality of life value would be attached to the 'no exacerbation' state based on evidence from the NMA. Depending on how the data in the clinical studies is presented there may be scope to expand the model to have more states, separating the 'no exacerbation' state into controlled and uncontrolled asthma. This strategy has been employed in previous economic assessments of asthma treatment strategies.

If EQ-5D data is unavailable from the clinical review then we would look into mapping data onto EQ-5D from AQLQ (asthma-quality of life questionnaire) for example. If mapping using published algorithms is not an option then we would explore attaching quality of life to states using published sources on how quality of life affects asthma control. This would involve a number of assumptions and therefore would undergo robust sensitivity analysis. There is one study by McTaggart et al\(^3\) which attaches an EQ-5D value to fully controlled, controlled, partially controlled and uncontrolled asthma. This will give us, at a minimum, a reference on what quality of life values would be appropriate and a range of plausible values to consider for sensitivity analyses. A recently published systematic review also looks at asthma quality of life across different levels of control which may be of use.\(^4\) One thing to note is that if an individual exacerbates then they are likely to receive a lower quality of life score anyway. Therefore adding an additional quality of life decrease every time an exacerbation occurs may overestimate the benefit of treatments that reduce exacerbations. However many of the quality of life questionnaires, such as EQ-5D, specifically ask the respondent how they feel on that particular day. Therefore they will not capture the disutility from exacerbations. This issue will be explored in sensitivity analyses.

Finally mortality would be incorporated into the model using data from the clinical review. However, given the rarity of asthma related deaths and the size of the population, it may be the case that the clinical studies identified will not be sufficiently powered to account for mortality. One way to incorporate mortality would be to attach a mortality value to exacerbations. Using epidemiological studies we could calculate the probability of death associated with exacerbations. Therefore in the model when the individual exacerbates there would be a probability attached to this that would lead to death. This would therefore assume that treatments with lower exacerbation rates would lead to fewer deaths. This could only be incorporated in the absence of mortality data from the studies as it would lead to double counting.

For pharmacological management the individual would move up treatment steps if the current line of therapy failed. In this sense ‘failing’ means that the therapy is not improving symptoms. The likelihood that a treatment was working would likely be apparent not long after the individual started taking the treatment. In this sense the ‘treatment’ failure would be a once occurring event as the model started rather than an on-going probability. Therefore when the model starts there will be a probability that the individual does not respond to the treatment and therefore moves on to the next treatment step. When this occurs the individual would move up a treatment step and the Markov model outcomes and probabilities would change to be in line with what is associated with the new, higher treatment step.
optimal preventer therapy according to step 3 (see previous question) when this fails to provide adequate control?

The probability of the line of therapy failing would be based on evidence from the clinical studies and would not be an outcome that would appear in the NMA. Therefore this would require extensive sensitivity analysis to ensure our results were robust. For this method to work first of all the cost-effectiveness of the final-line of therapy would be considered, as the cost-effectiveness of this would not be impacted by anything that preceded it and there is no therapy for the individual to move on to. Then once this is established the cost-effectiveness of the penultimate line of therapy would be considered and so on.

This model structure is similar to other asthma model’s that have appeared in the literature in the past. These previous model’s tend to have separate Markov states for level of control. However as they tend to be based on a single RCT this data is available. As we are pooling data across such a large body of evidence modelling in such a detailed way would unlikely be possible without very tenuous assumptions. However these options will be explored.

Comparators for the pharmacological review question will include:

<table>
<thead>
<tr>
<th>GINA (adult)</th>
<th>low dose</th>
<th>medium dose</th>
<th>high dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>beclometasone dipropionate (CFC)</td>
<td>200-500ug</td>
<td>&gt;500-1000ug</td>
<td>&gt;1000ug</td>
</tr>
<tr>
<td>beclometasone dipropionate (HFA)</td>
<td>100-200ug</td>
<td>&gt;200-400ug</td>
<td>&gt;400ug</td>
</tr>
<tr>
<td>budesonide (DPI)</td>
<td>200-400ug</td>
<td>&gt;400-800ug</td>
<td>&gt;800ug</td>
</tr>
<tr>
<td>ciclesonide (HFA)</td>
<td>80-160ug</td>
<td>&gt;160-320ug</td>
<td>&gt;320ug</td>
</tr>
<tr>
<td>fluticasone (DPI)</td>
<td>100-250ug</td>
<td>&gt;250-500ug</td>
<td>&gt;500ug</td>
</tr>
<tr>
<td>fluticasone (HFA)</td>
<td>100-250ug</td>
<td>&gt;250-500ug</td>
<td>&gt;500ug</td>
</tr>
<tr>
<td>mometasone furoate</td>
<td>110-200ug</td>
<td>&gt;220-440ug</td>
<td>&gt;440ug</td>
</tr>
<tr>
<td>triamcinolone acetonide</td>
<td>400-1000ug</td>
<td>&gt;1000-2000ug</td>
<td>&gt;2000ug</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>GINA (children)</th>
<th>low dose</th>
<th>medium dose</th>
<th>high dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>beclometasone dipropionate (CFC)</td>
<td>100-200ug</td>
<td>&gt;200-400ug</td>
<td>&gt;400ug</td>
</tr>
<tr>
<td>Medicine</td>
<td>Dose (ug)</td>
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</tr>
<tr>
<td>beclometasone dipropionate (HFA)</td>
<td>50-100</td>
<td>&gt;100-200</td>
<td>&gt;200</td>
</tr>
<tr>
<td>budesonide (DPI)</td>
<td>100-200</td>
<td>&gt;200-400</td>
<td>&gt;400</td>
</tr>
<tr>
<td>budesonide (nebules)</td>
<td>250-500</td>
<td>&gt;500-1000</td>
<td>&gt;1000</td>
</tr>
<tr>
<td>ciclesonide (HFA)</td>
<td>80</td>
<td>&gt;80-160</td>
<td>&gt;160</td>
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<tr>
<td>fluticasone (DPI)</td>
<td>100-200</td>
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<td>&gt;500</td>
</tr>
<tr>
<td>mometasone furoate</td>
<td>110</td>
<td>≥220≤440</td>
<td>≥440</td>
</tr>
<tr>
<td>triamcinolone acetonide</td>
<td>400-800</td>
<td>&gt;800-1200</td>
<td>&gt;1200</td>
</tr>
</tbody>
</table>

Costs and health outcomes will be discounted at 3.5%.

As mortality is an outcome, a lifetime time horizon will be used.

Probabilistic sensitivity analysis will be used to take into account uncertainty around input point estimates e.g. using standard errors. One-way / scenario sensitivity analyses will be used to explore how uncertainty about key assumptions or alternative data sources impact results. These will include setting the QALY and cost discount rate to 1.5%.

<table>
<thead>
<tr>
<th>All other review questions.</th>
<th>For other review questions, if the clinical reviews provide evidence on exacerbations, quality of life or mortality then these values could be incorporated into the above model, changing the interventions compared and their costs. Therefore this model structure could be used for multiple review questions.</th>
</tr>
</thead>
</table>
5 Clinical Guidelines Technical Support Unit

Please indicate if any of the analyses or areas suggested in section 3 require or would benefit from the Clinical Guidelines Technical Support Unit support or validation.

The network meta-analysis used to inform the economic model may need support and validation from the TSU.

6 Data access

Please indicate whether the feasibility of any of the analyses or areas suggested in section 3 will be dependent on access to data sources not publicly available, and how these will be accessed, for example, through a call for evidence.

All data needed should be publically available.

7 References


8 Addenda to economic plan

Please state any changes that have been made to the above agreed plan, together with date. If clinical questions have changed since the economic plan was signed off, include a new list with all clinical questions as part of the addendum, together with a comment where questions were inserted, deleted or altered and an explanation.

<table>
<thead>
<tr>
<th>Scope area (clinical question(s))</th>
<th>Proposed changes</th>
<th>Date agreed</th>
</tr>
</thead>
</table>

The clinical guidelines technical support unit provides academic support to guideline developers at any point in guideline development: conduct, or support the developer team in the development of advanced evidence synthesis, support complex economic analyses, conduct validation of or amendments to existing evidence syntheses used in guideline models and address concerns from stakeholder (via consultation). Please contact the senior technical adviser for further details.

This should be the key area(s) relevant for considering opportunity costs and high priority for original modelling, as identified in section 3.

Two or more questions may be addressed by a single analysis if appropriate.