

# BMJ Open Healthcare costs of asthma comorbidities: a systematic review protocol

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## ABSTRACT

**Introduction** Asthma is associated with many comorbid conditions that have the potential to impact on its management, control and outcomes. These comorbid conditions have the potential to impact on healthcare expenditure. We plan to undertake a systematic review to synthesise the evidence on the healthcare costs associated with asthma comorbidity.

**Methods and analysis** We will systematically search the following electronic databases between January 2000 and January 2017: National Health Service (NHS) Economic Evaluation Database, Google Scholar, Allied and Complementary Medicine Database (AMED), Global Health, PsychINFO, Medline, Embase, Institute for Scientific Information Web of Science and Cumulative Index to Nursing and Allied Health Literature. We will search the references in the identified studies for additional potential papers. Additional literature will be identified by contacting experts in the field and through searching of registers of ongoing studies. The review will include cost-effectiveness and economic modelling/evaluation studies and analytical observational epidemiology studies that have investigated the healthcare costs of asthma comorbidity. Two reviewers will independently screen studies and extract relevant data from included studies. Methodological quality of epidemiological studies will be assessed using the Effective Public Health Practice Project tool, while that of economic evaluation studies will be assessed using the Drummond checklist. This protocol has been published in International Prospective Register of Systematic Reviews (PROSPERO) database (No. CRD42016051005).

**Ethics and dissemination** As there are no primary data collected, formal NHS ethical review is not necessary. The findings of this systematic review will be disseminated in a peer-reviewed journal and presented at relevant conferences.

**PROSPERO registration number** CRD42016051005.

## INTRODUCTION

Asthma is a highly prevalent condition that is the reason behind many morbidity and mortality cases in the world.<sup>1 2</sup> Asthma management and control can be influenced, among other things, by the presence of other comorbid conditions.<sup>3–7</sup> Our recently completed scoping review investigating the prevalence of comorbidities among patients with asthma identified a number of conditions

## Strengths and limitations of this study

- This is the first systematic review to synthesise the evidence on the healthcare costs attributable to asthma comorbidity.
- A major limitation is that it may be difficult to employ meta-analysis as we anticipate studies with different study designs, definitions of costs and time periods.
- Based on previous work, we anticipate considerable difficulties in identifying information on the indirect costs associated with asthma comorbidities such as productivity loss and social and intangible costs. This review will therefore be focused on direct healthcare costs only, we recognise that it is a subset of overall costs.

including, but not limited to depression, anxiety, rhinitis, gastro-oesophageal reflux disease (GORD) and obesity, may occur more frequently in people with asthma than in those without, leading to potential additional difficulties in asthma management.<sup>8–10</sup> It has been shown that health-related quality of life and daily-life functionality are diminished, and the use of healthcare services is increased with the presence of comorbid conditions.<sup>3 6 9–15</sup> In addition, other studies showed that controlling these conditions at an early stage may improve asthma outcomes.<sup>6 12 14 15</sup>

These international studies focused on different study samples who had different comorbid conditions, explaining the discrepancies in their findings.<sup>16–18</sup> While these have now assessed the healthcare and economic burden associated with asthma comorbidity,<sup>19–21</sup> there has hitherto been no systematic attempt to synthesise and summarise the evidence that has emanated from existing studies.

This review builds on our earlier work,<sup>8</sup> which involved a scoping review of the recent landscape of asthma comorbidity; the purpose of the current work is to identify, appraise and synthesise the evidence on healthcare costs associated with asthma comorbidity.<sup>19–21</sup>

## METHODS

This protocol has been prepared following the Preferred Reporting Items for Systematic review and Meta-Analysis Protocols (PRISMA-P) approach.<sup>22</sup> It has been published in International Prospective Register of Systematic Reviews database (no CRD42016051005).

### Types of studies

We will include economic modelling/evaluation and analytical epidemiological studies—that is, cohort, case-control and cross-sectional studies—that have investigated the healthcare costs of asthma comorbidity.

Editorials, animal studies, reviews, case studies, and case-series studies will be excluded.

### Participants

We are interested in studies on participants with evidence of clinician-diagnosed asthma. There will be no restriction concerning age or sex of participants.

### Comorbidities of interest

Comorbidity has been defined as ‘any distinct additional clinical entity that has existed or may occur during the clinical course of a patient who has the index disease under study’.<sup>23</sup> We are interested in comorbidities that are not related to natural causes such as ageing, but rather those that are pathophysiologically related to asthma and have the potential to impact on asthma control, management and/or prognosis, regardless of whether they develop before or after asthma. These include, but are not limited to allergic diseases, chronic obstructive pulmonary disease, autoimmune disorders (eg, type 1 diabetes), metabolic disorders (eg, type 2 diabetes, obesity), cardiovascular diseases, psychological dysfunction (anxiety, depression), hypertension and GORD. We grouped comorbidities according to the latest version of the International Classification of Diseases 10th Revision diagnosis codes.<sup>24</sup>

### Outcome

Healthcare costs of asthma comorbidities.

### Search methods

#### Databases

We will search for published studies, from 2007 to 2017, from the following databases: National Health Service Economic Evaluation Database, Google Scholar, Allied and Complementary Medicine Database, Global Health, Medline, Embase, Institute for Scientific Information (ISI) Web of Science, Cumulative Index to Nursing and Allied Health Literature and PsychINFO. Additional literature will be identified by searching the reference list of identified eligible studies and by searching the repositories of international conference proceedings, including ISI Conference Proceeding Citation Index and Zetoc (British Library). We will search the references in the identified studies for additional potential papers. Additional literature will be identified by contacting experts

in the field and through searching of registers of ongoing studies.

#### Search strategy

We have developed a strategy in Medline (see online supplementary appendix) to retrieve relevant literature on the topic. This search strategy will be adapted in searching other databases. There will be no language restriction and, where possible, studies in languages other than English will be translated.

The databases will be searched for the period January 2000 to January 2017. We have chosen 2000 as a start date while we are aware that there was limited work before the 2000s on the healthcare and economic burden of asthma,<sup>25</sup> these studies focused exclusively on asthma without taking any comorbid conditions into consideration.

#### Study selection

The articles retrieved from the database searches will be exported into EndNote reference management programme. Screening will be undertaken according to the inclusion and exclusion criteria. Two reviewers (KF and EV) will independently undertake the screening of the records (by title and/or abstract) for eligibility and a third reviewer (BN or AS or AP) will arbitrate in case of any disagreement to reach a consensus. Full text of eligible papers after the first screening will be reviewed again to confirm that the papers meet the inclusion and exclusion criteria. The screening process will be undertaken and reported according to the PRISMA recommendation.<sup>26</sup>

#### Data extraction

A customised data extraction form is being constructed to extract relevant data from all studies meeting our inclusion criteria. The form will first be piloted on few studies first. The data abstracted will include: author(s), publication year, geographical location of data collection, study design, aims and research questions, settings, population/participants (n, mean age, gender), comorbidities studied, time period specific costs included, cost unit(s) and estimates of total costs, currency, price year, whether discounting was applied where relevant and key findings. Data extraction will be undertaken independently by two reviewers (KF and EV). Any differences will be resolved by discussion or if necessary arbitration by a third reviewer (BN or AS or AP).

### Data assessment and synthesis

#### Quality assessment

Two reviewers (KF and EV) will independently assess the quality of included studies and the potential for risk of bias will be evaluated. We will use the Drummond checklist<sup>27</sup> for assessing the methodological quality of economic evaluation and cost studies. Although there are many economic evaluation and reporting checklists, a lot of them have overlapping aspects. The Drummond checklist focuses on the quality of the designs. Consensus will

be reached through discussion and arbitration by a third reviewer (BN or AS or AP) in event of any disagreement.

The quality of the broader study design will be evaluated using the Effective Public Health Practice Project (EPHPP) tool.<sup>28</sup> The EPHPP tool assesses different components of studies: design, biases and methods. The overall study rating will be judged as strong, moderate or weak based on the component ratings.

### Data synthesis

We anticipate considerable methodological and statistical heterogeneity across studies, which will make it hard to conduct meta-analyses of the evidence base. A narrative synthesis will thus be employed as the primary approach to synthesise the data, but we will also consider the possibility of meta-analysis using random-effects modelling if the data allow. If that is the case, then we will evaluate potential for publication bias using funnel plots and Begg and Egger tests.<sup>29 30</sup>

### Subgroup analysis

Where possible, we will conduct subgroup analyses based on the categories of relevant sociodemographic characteristics reported in the studies, particularly by age groups and gender.

- ▶ Age (will depend on how authors have reported it, but may include categorisation as follows):
- ▶ Children and young people <18 years
- ▶ Adults (≥18 years old)
- ▶ Gender
- ▶ Male
- ▶ Female

If the number of studies and data available show significant statistical heterogeneity, then we will conduct sensitivity analyses with regards to study quality by excluding studies at high risk of bias.

## CONCLUSION

Asthma comorbidities have the potential to impact on asthma management, healthcare use and outcomes. We anticipate that this systematic review will build on our previous work on the epidemiology and outcomes of asthma<sup>8 31 32</sup> and provide important insights into patterns of asthma comorbidity and the economic consequences to health systems of these comorbid disorders.

**Contributors** All authors made substantive intellectual contributions to the development of this protocol. KEF wrote this protocol. AS, AP, CG and BIN commented critically on several drafts of the manuscript. KEF, AS, AP and BIN were involved in conceptualising this review.

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**Competing interests** None declared.

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