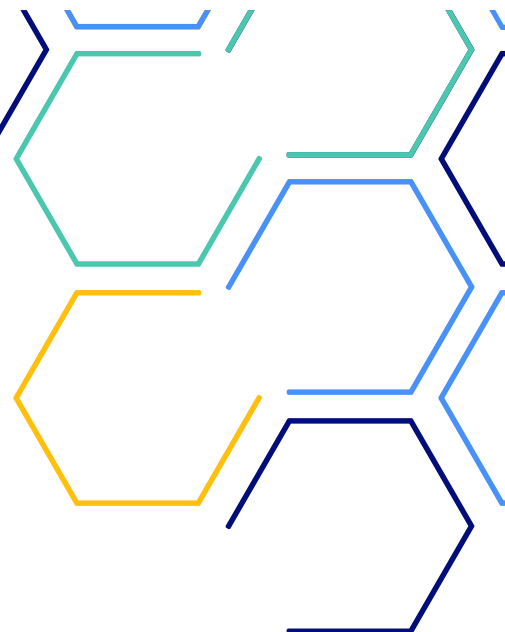


# CICER

Tacaíocht don Treoirlíne Chliniciúil  
Clinical Guideline Support



## Anti-interleukin-5, specialist assessment, and self-management for acute asthma: Protocol for systematic reviews

**November 2025**



**Health  
Information  
and Quality  
Authority**

An tÚdarás Um Fhaisnéis  
agus Cáilíocht Sláinte



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## About CICER

In 2016, the Department of Health requested that the Health Research Board (HRB) fund an evidence synthesis service to support the activities of the Ministerially-appointed National Clinical Effectiveness Committee (NCEC). Following a competitive process, the Health Information and Quality Authority (HIQA) was awarded research funding spanning the period from 2017 to 2024 to produce the evidence to support the development of National Clinical Guidelines. This funding was renewed through a competitive process to support the work of the Centre in Ireland for Clinical guideline support and Evidence Reviews (CICER) from 2024 to 2028. CICER comprises a dedicated multidisciplinary research team supported by staff from the Health Technology Assessment team in HIQA, the Discipline of Public Health and Primary Care in the School of Medicine in Trinity College Dublin, as well as national and international clinical and methodological experts.

With regard to clinical guidelines, the role of the CICER team is to independently review evidence and provide scientific support for the development (by guideline development groups (GDGs)), of National Clinical Guidelines for the NCEC. The CICER team undertakes systematic reviews of the clinical effectiveness and cost effectiveness of interventions included in the guidelines, as well as estimating the budget impact of implementing the guidelines. The CICER team also works closely with the GDGs and provides tailored training sessions; assists in the development of clinical questions and search strategies; performs systematic reviews of international clinical guidelines and supports the assessment of their suitability for adaptation to Ireland; and supports the development of evidence-based recommendations informed within the National Clinical Guidelines.

### How to cite this report:

Molly Mattsson, Celine Larkin, Shelley O'Neill, Ruth Martin, Marie Carrigan, Susan M. Smith, Máirín Ryan. Anti-interleukin-5, specialist assessment, and self-management for acute asthma: Protocol for systematic reviews. Cork. CICER, HIQA, 2025.

This research is funded by the Health Research Board under grant number ESCG-2024-002. The authors have no conflicts of interest to declare.

## Table of Contents

|                                                                          |           |
|--------------------------------------------------------------------------|-----------|
| <b>About CICER .....</b>                                                 | <b>2</b>  |
| <b>Table of Contents .....</b>                                           | <b>3</b>  |
| <b>List of Tables .....</b>                                              | <b>4</b>  |
| <b>List of abbreviations that appear in this protocol .....</b>          | <b>5</b>  |
| <b>1 Background .....</b>                                                | <b>7</b>  |
| 1.1 Description of the condition .....                                   | 7         |
| 1.2 Description of the interventions.....                                | 8         |
| 1.2.1 Anti-interleukin-5 therapy in asthma .....                         | 8         |
| 1.2.2 Specialist care for asthma.....                                    | 9         |
| 1.2.3 Self-management education and support for people with asthma ..... | 10        |
| 1.3 Purpose of these reviews.....                                        | 11        |
| <b>2 Methods.....</b>                                                    | <b>11</b> |
| 2.1 Review questions .....                                               | 12        |
| 2.2 PICOs (Population, Intervention, Comparison, Outcome).....           | 12        |
| 2.3 Health economic studies.....                                         | 15        |
| 2.3.1 Types of studies .....                                             | 15        |
| 2.3.2 Types of outcomes.....                                             | 15        |
| 2.4 Search strategy .....                                                | 16        |
| 2.5 Selection of eligible publications .....                             | 16        |
| 2.6 Data extraction and management.....                                  | 16        |
| 2.7 Quality appraisal .....                                              | 17        |
| 2.8 Data synthesis .....                                                 | 17        |
| <b>References .....</b>                                                  | <b>18</b> |
| <b>Appendices .....</b>                                                  | <b>22</b> |
| Appendix 1: Search strategy .....                                        | 22        |
| Appendix 2: Data extraction template .....                               | 26        |

## List of Tables

|                                                                                                                                                     |           |
|-----------------------------------------------------------------------------------------------------------------------------------------------------|-----------|
| <b>Table 1. PICO – Anti-IL-5 drugs for acute exacerbations of asthma.....</b>                                                                       | <b>11</b> |
| <b>Table 2. PICO – Specialist assessment and self-management educational interventions after attending hospital for an acute exacerbation .....</b> | <b>14</b> |

## List of abbreviations that appear in this protocol

|                 |                                                                          |
|-----------------|--------------------------------------------------------------------------|
| <b>ACT</b>      | Asthma Control Test                                                      |
| <b>ACQ</b>      | Asthma Control Questionnaire                                             |
| <b>AQLQ</b>     | Asthma Quality of Life Questionnaire                                     |
| <b>BTS/SIGN</b> | British Thoracic Society and Scottish Intercollegiate Guidelines Network |
| <b>CHEC</b>     | Consensus Health Economic Criteria                                       |
| <b>CICER</b>    | Centre in Ireland for Clinical guideline support and Evidence Reviews    |
| <b>ED</b>       | emergency department                                                     |
| <b>EQ-5D-5L</b> | EuroQoL 5-Dimension 5-Level                                              |
| <b>GDG</b>      | guideline development group                                              |
| <b>GINA</b>     | Global Initiative for Asthma                                             |
| <b>GP</b>       | general practitioner                                                     |
| <b>GRADE</b>    | Grading of Recommendations Assessment, Development and Evaluation        |
| <b>HIQA</b>     | Health Information and Quality Authority                                 |
| <b>HRB</b>      | Health Research Board                                                    |
| <b>HSE</b>      | Health Service Executive                                                 |
| <b>ICER</b>     | incremental cost-effectiveness ratio                                     |
| <b>IL-5</b>     | interleukin-5                                                            |
| <b>ISPOR</b>    | International Society for Pharmacoeconomics and Outcomes Research        |
| <b>KASE-AQ</b>  | Knowledge Attitude Self-Efficacy Asthma Questionnaire                    |
| <b>mOCS</b>     | maintenance oral corticosteroid                                          |
| <b>NCEC</b>     | National Clinical Effectiveness Committee                                |
| <b>NOS</b>      | Newcastle Ottawa scale                                                   |
| <b>nRCT</b>     | non-randomised controlled trial                                          |

|                 |                                                                             |
|-----------------|-----------------------------------------------------------------------------|
| <b>PCRS</b>     | Primary Care Reimbursement Service                                          |
| <b>PICO</b>     | population, intervention, comparison, outcome                               |
| <b>PRISMA-P</b> | Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols |
| <b>PRESS</b>    | Peer Review of Electronic Search Strategies                                 |
| <b>PROSPERO</b> | International Prospective Register of Systematic Reviews (PROSPERO)         |
| <b>QALY</b>     | quality-adjusted life year                                                  |
| <b>RCT</b>      | randomised controlled trial                                                 |
| <b>RoB</b>      | risk of bias                                                                |
| <b>ROBINS-I</b> | Risk Of Bias In Non-randomised Studies of Interventions                     |
| <b>TFA</b>      | Theoretical Framework of Acceptability                                      |

## 1 Background

### 1.1 Description of the condition

Asthma is defined as a chronic inflammatory disorder, in which the bronchial airways in the lungs become narrow and swollen, making it difficult to breathe.<sup>(1, 2)</sup> Asthma can range in severity from mild to severe, with typical symptoms including wheezing, coughing, shortness of breath, and chest tightness.<sup>(3)</sup> The causes of asthma vary: it is a “complex genetic disorder with strong environmental influence”, whose risk factors include air pollution, smoking, atopy (a genetic tendency to develop an exaggerated immune response), stress, and obesity.<sup>(4, 5)</sup> Asthma is associated with an increased risk of accompanying health conditions, including rhinitis, sinusitis, gastroesophageal reflux, and obstructive sleep apnoea.<sup>(6, 7)</sup> Asthma can develop at any age, and risk factors and comorbidities appear to vary by age of onset.<sup>(8, 9)</sup> In childhood, more boys than girls have asthma, while in adulthood, women have higher rates of asthma than men.<sup>(10-12)</sup> In Ireland, approximately 5-10% of the adult population has been diagnosed with asthma.<sup>(13-15)</sup>

Routine management of asthma usually involves monitoring for signs and symptoms, avoiding triggers, and taking medications.<sup>(16)</sup> Bronchodilator inhalers (such as salbutamol, terbutaline, and ipratropium bromide) can help to relax the lung muscles and open up the air passages to relieve symptoms,<sup>(17)</sup> while steroid inhalers (such as fluticasone, beclomethasone, and budesonide) work by reducing inflammation in the airway. More severe chronic asthma may require management with oral medicines, such as leukotriene receptor antagonists or steroid tablets, or with injectable biologic therapies<sup>(18)</sup>.

Occasionally, individuals with asthma may experience a sudden worsening of their symptoms, also known as an asthma exacerbation or an asthma attack. Asthma attacks are characterised by rapid breathing, difficulty speaking, faster heart rate, and low oxygen saturation.<sup>(19)</sup> They can be triggered by viral respiratory infections, like the common cold, or by exposure to allergens.<sup>(20, 21)</sup> Asthma attacks are typically treated with a combination of inhaled short-acting bronchodilators and systemic corticosteroids.<sup>(18)</sup> Asthma attacks can sometimes become acute and or life-threatening, requiring emergency medical intervention. Emergency treatment for an acute asthma attack may include nebulised

bronchodilators (such as short-acting beta-2 agonists and ipratropium bromide), corticosteroids, and supplementary oxygen, and in very severe cases, mechanical ventilation.<sup>(22)</sup> Experiencing repeated severe asthma attacks can lead to an accumulation of risk for patients, including increased likelihood of further attacks.<sup>(23)</sup> The repeated use of systemic steroids in particular is problematic, with adverse events arising in half of patients treated,<sup>(24)</sup> treatment failure occurring in at least 30% of exacerbations,<sup>(25, 26)</sup> and frequent courses of systemic glucocorticoids associated with an increased risk of mortality.<sup>(27)</sup>

In 2023, there were 3,495 discharges from inpatient care with a principal diagnosis of asthma in Ireland, 98% (n=3,427) of which were “emergency admissions”, meaning that they were unplanned admissions requiring immediate care and treatment and were likely admitted through the emergency department.<sup>(28, 29)</sup> Asthma was the registered cause of death in 86 fatalities in 2023, all among people aged 15 years and older.<sup>(30)</sup>

## **1.2 Description of the interventions**

### **1.2.1 Anti-interleukin-5 therapy in asthma**

There are many inflammatory pathways involved in asthma, but eosinophils, a type of white blood cell, plays a critical role in the pathogenesis and severity of the disease.<sup>(31)</sup> Asthma is associated with tissue eosinophilia, defined as the presence of an excessive amount of eosinophils in the blood, in 40–60% of patients,<sup>(32)</sup> and the intensity of eosinophilia has been correlated with asthma severity.<sup>(33)</sup> Interleukin (IL)-5 is the key cytokine (signalling protein) in the maturation, activation, proliferation, migration and survival of eosinophils.<sup>(34)</sup> Eosinophilic asthma is often therapeutically responsive to corticosteroids due to their effective ability to induce eosinophils apoptosis (cell death).<sup>(35)</sup> However, severe eosinophilic asthma may be resistant to both inhaled and systemic corticosteroids, partly because of an excessive bronchial amount of IL-5.<sup>(36, 37)</sup> IL-5 has therefore become a therapeutic target for eosinophilic asthma and, in recent years, two monoclonal antibodies (mepolizumab and reslizumab) directed against IL-5 and one monoclonal antibody directed against the alpha-subunit of the IL-5 receptor (benralizumab) have been developed.<sup>(38)</sup> Mepolizumab, reslizumab, and benralizumab received initial European Medicines Agency approval between 2015 and 2018 and are currently licensed as an add-on maintenance treatment for

patients with severe eosinophilic asthma.<sup>(39)</sup> In Ireland, these drugs must be initiated by a consultant respiratory physician and are currently recommended as an add-on maintenance treatment in adult patients with severe eosinophilic asthma that is inadequately controlled despite high-dose inhaled corticosteroids plus long-acting beta-agonist.<sup>(40)</sup> Mepolizumab and benralizumab are administered as a subcutaneous injection and are reimbursable through the Health Service Executive (HSE) Primary Care Reimbursement Service (PCRS), while reslizumab is administered as an intravenous infusion in a hospital-setting only.<sup>(40)</sup> A recent systematic review and meta-analysis found that administering anti-IL-5 drugs in severe chronic asthma as an add-on maintenance treatment was associated with a 62% reduction in severe exacerbations and a 54% reduction in hospitalisations at 12 months following treatment initiation, compared to pre-treatment, and was associated with a 51% reduction in oral corticosteroid use.<sup>(41)</sup>

While much of the research on the use of anti-IL-5 therapy is focused on the maintenance treatment of severe eosinophilic asthma,<sup>(41)</sup> not much is known about its potential role in the management of acute exacerbations and how it may be associated with future exacerbations and other outcomes, with no recent clinical guidelines recommending the use of anti-IL-5 therapy for this indication.

### **1.2.2 Specialist care for asthma**

Specialist assessment and management for severe and difficult-to-control asthma, defined as care provided by healthcare providers with specialised training and expertise in asthma, including respiratory consultants, clinical nurse specialists, and specialist physiotherapists, has been found to be associated with improved asthma control, reduced exacerbations, and a planned lowering of maintenance oral corticosteroid (mOCS) dose.<sup>(42-44)</sup> Similarly, there is evidence that follow-up by specialist services after an asthma-related emergency department (ED) presentation is associated with fewer subsequent ED visits and hospitalisations, as well as improved asthma control.<sup>(45)</sup> Guidelines regarding specialist assessment and management vary. Global Initiative for Asthma (GINA) guidelines from 2024 suggest that the optimal frequency and location of reviews (primary care versus specialist) for patients with severe asthma will depend on the patient's asthma control, risk factors, and comorbidities and that referral for expert advice should be considered for patients who

have been hospitalised for asthma.<sup>(1)</sup> According to the British Thoracic Society and Scottish Intercollegiate Guidelines Network (BTS/SIGN) guideline from 2019, all patients hospitalised with an acute exacerbation of asthma should be reviewed by a respiratory nurse specialist or respiratory consultant within a month of discharge.<sup>(46)</sup>

In Ireland, the National Framework for the Integrated Prevention and Management of Chronic Disease in Ireland in 2020-2025<sup>(47)</sup> and End to End Model of Care for Asthma<sup>(48)</sup> outline how specialist respiratory care should be provided in the context of the Chronic Disease Community Specialist team, which includes a Respiratory Nursing Service, Respiratory Physiotherapy Service, and Integrated Care Respiratory Consultant. Eligibility for referral includes anyone with clinically-confirmed asthma with more than two unplanned asthma-related attendances in 12 months at a GP practice or anyone attending an out-of-hours service or ED with an acute asthma exacerbation.<sup>(49)</sup> Since 2020, the HSE has been rolling out Chronic Disease Community Speciality Teams in all areas of the country, with each team covering approximately 150,000 of the population. All 30 teams are, at the time of writing, initiated at various levels of operation, with the HSE envisioning that all teams will be fully operational by 2027.<sup>(50)</sup>

### **1.2.3 Self-management education and support for people with asthma**

A self-management intervention is broadly defined as “an intervention primarily designed to develop the abilities of patients to undertake management of health conditions through education, training and support to develop patient knowledge, skills or psychological and social resources.”<sup>(51)</sup> Self-management has been well-established as a core component of all models of care for people with chronic disease,<sup>(52, 53)</sup> including in the context of asthma.<sup>(54)</sup> Optimal self-management for asthma has previously been described as including a written action plan for self-management of drugs for exacerbations, together with self-monitoring and regular medical review.<sup>(55)</sup> International guidelines (for example from GINA and BTS/SIGN) have recommended the use of self-management interventions for people with asthma for decades,<sup>(1, 46)</sup> and there is evidence that supported self-management can reduce hospitalisations, ED presentations, and unscheduled consultations, and improve markers of control and quality of life for people with asthma across a range of cultural, demographic and healthcare settings.<sup>(56)</sup> Despite this, asthma self-management remains poorly

implemented in clinical practice, with international evidence estimating that less than one third of people with asthma have personal asthma action plans.<sup>(57)</sup> A 2014 UK National Review of Asthma Deaths found that, of all asthma mortalities, only 23% had documented evidence of having been provided with self-management education.<sup>(58)</sup> Self-management support and or education specifically aimed at patients who have been hospitalised for an acute exacerbation may be an important aspect of asthma care. Such interventions might include education about the condition, its triggers, and day-to-day management, exacerbation management strategies, goal-setting, skills training, and or psychosocial support. The intervention could be delivered by a range of different clinical roles and the format could be in-person or online, individual, family, or group-based, live or asynchronous, and could be of varying durations.

### **1.3 Purpose of these reviews**

The purpose of these systematic reviews is to identify and evaluate the clinical and economic evidence relating to:

1. anti-IL-5 therapy for acute asthma
2. specialist assessment post hospitalisation for acute asthma
3. self-management education or support post hospitalisation for acute asthma, to help inform the recommendations of the updated NCEC National Clinical Guideline on Management of an Acute Asthma Attack in Adults (aged 16 years and older).

This will take the form of six systematic reviews, three on the clinical effectiveness and three on the cost-effectiveness of the included interventions, summarised within two reports.

## **2 Methods**

This protocol outlines the proposed approach to conducting systematic reviews of the clinical and cost-effectiveness of three interventions and adheres to the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) criteria.<sup>(59)</sup> The identification and synthesis of economic evidence will follow the HIQA national guidelines for the retrieval and interpretation of economic literature.<sup>(60)</sup> Each review question will be

registered on the International Prospective Register of Systematic Reviews (PROSPERO) [database](#) of systematic reviews and meta-analyses (record numbers: CRD420251105241, CRD420251122370, and CRD420251122376 ).<sup>(61)</sup> The six systematic reviews will result in two reports, to be completed sequentially.

## **2.1 Review questions**

This review will consider the following questions:

1. What is the clinical and cost-effectiveness of anti-IL-5 drugs for the management of asthma symptoms in adults presenting to hospital with an acute exacerbation of asthma, either as an add-on to or instead of usual treatment?
2. What is the clinical and cost-effectiveness of:
  - a. outpatient specialist assessment
  - b. outpatient self-management educational interventions, for the management of asthma symptoms in adults following an attendance at hospital for an acute asthma exacerbation?

## **2.2 PICOs (Population, Intervention, Comparison, Outcome)**

The review questions were formulated in line with the PICO framework, as presented in Tables 1 and 2.

**Table 1. PICO framework for anti-IL-5 drugs for acute exacerbations of asthma**

|                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|----------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Population</b>    | Patients aged 16 years or older with an acute exacerbation of asthma in the acute care setting (urgent care, emergency department, inpatient, or intensive care unit).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| <b>Intervention</b>  | <p><b>Include:</b></p> <ul style="list-style-type: none"> <li>treatment with an anti-IL-5 drug (including reslizumab, mepolizumab or benralizumab) during an acute exacerbation that requires presentation to emergency department and or hospital admission for treatment.</li> </ul> <p><b>Exclude:</b></p> <ul style="list-style-type: none"> <li>use of anti-IL-5 drugs as an ongoing maintenance treatment.</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| <b>Comparator</b>    | Usual care or other treatment or no other treatment.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| <b>Outcome</b>       | <p><b>“Critical” outcomes:</b></p> <ul style="list-style-type: none"> <li>death during current visit</li> <li>intensive care admission during current visit</li> <li>ventilation during current visit</li> <li>subsequent severe asthma exacerbations requiring emergency department visit/inpatient admission within a timeframe of up to 90 days (number of events and or proportion of patients experiencing events).</li> </ul> <p><b>“Important” outcomes:</b></p> <ul style="list-style-type: none"> <li>subsequent asthma exacerbation (any severity, defined as an exacerbation requiring a change in treatment), within a timeframe of up to 90 days (number of events and or proportion of patients experiencing events)</li> <li>length of current stay in hospital, if admitted</li> <li>adverse events within a timeframe of up to 90 days (for example nasopharyngitis, headache, upper respiratory tract infection, bronchitis, hypersensitivity) (number of events and or proportion of patients experiencing events)</li> <li>serious adverse events requiring hospitalisation within a timeframe of up to 90 days (number of events and or proportion of patients experiencing events)</li> <li>asthma control (for example Asthma Control Test (ACT), Asthma Control Questionnaire (ACQ), within a timeframe of up to 90 days)</li> <li>asthma-related quality of life (for example Asthma Quality of Life Questionnaire (AQLQ), EuroQoL 5-Dimension 5-Level (EQ-5D-5L), within a timeframe of up to 90 days).</li> </ul> <p>Any relevant measures of costs and benefits which may be applicable to the Irish setting, see section 2.3.</p> |
| <b>Study design</b>  | <p><b>Include:</b></p> <ul style="list-style-type: none"> <li>randomised controlled trials</li> <li>economic evaluation studies.</li> </ul> <p><b>Exclude:</b></p> <ul style="list-style-type: none"> <li>observational studies</li> <li>costing studies.</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| <b>Search period</b> | All time for evaluating clinical effectiveness, 10 years for cost-effectiveness.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |

**Table 2. PICO framework for specialist assessment and self-management educational interventions after attending hospital for an acute exacerbation**

|                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|---------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Population</b>   | Patients 16 years of age or older who have attended the emergency department or been admitted to hospital for an exacerbation of asthma.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| <b>Intervention</b> | <p><b>Include:</b></p> <ul style="list-style-type: none"> <li>Intervention 1: assessment by an outpatient specialist service (for example respiratory consultant, respiratory specialist hub, respiratory clinical nurse specialist/advance nurse practitioner, respiratory physiotherapy)</li> <li>Intervention 2: asthma-related self-management or education intervention delivered in the outpatient specialist setting (including those initiated in an inpatient or emergency department setting).</li> </ul> <p><b>Exclude:</b></p> <ul style="list-style-type: none"> <li>interventions aimed at current inpatients only, without continuation in the outpatient setting</li> <li>studies focusing on all asthma patients, regardless of previous hospital attendance</li> <li>interventions delivered in primary care or general practice settings.</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| <b>Comparator</b>   | Usual care, no intervention, or other intervention.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| <b>Outcome</b>      | <p><b>“Critical” outcomes:</b></p> <ul style="list-style-type: none"> <li>subsequent severe asthma exacerbation requiring hospitalisation (emergency department visit or inpatient admission) within a timeframe of up to 90 days from the index presentation (number of events and or proportion of patients experiencing events)</li> <li>patient satisfaction/acceptability of intervention, measured using a validated tool (for example Theoretical Framework of Acceptability (TFA))</li> <li>improvement in patient’s asthma-related knowledge or confidence within a timeframe of up to 90 days, measured pre and post-intervention using a validated tool (for example Knowledge Attitude Self-Efficacy Asthma Questionnaire (KASE-AQ)).</li> </ul> <p><b>“Important” outcomes:</b></p> <ul style="list-style-type: none"> <li>subsequent asthma exacerbation (any severity, defined as an exacerbation requiring a change in treatment) within a timeframe of up to 90 days (number of events and or proportion of patients experiencing events)</li> <li>treatment adherence within a timeframe of up to 90 days, measured using for example self-report, collateral report, medical records, and or objective measurements such as canister weighing, electronic tracking, or biomarkers</li> <li>asthma control (for example Asthma Control Test (ACT), Asthma Control Questionnaire (ACQ) post intervention, within a timeframe of up to 90 days)</li> <li>asthma-related quality of life (for example Asthma Quality of Life Questionnaire (AQLQ), EuroQoL 5-Dimension 5-Level (EQ-5D-5L)) post intervention, within a timeframe of up to 90 days.</li> </ul> <p>Any relevant measures of costs and benefits which may be applicable to the Irish setting, see section 2.3</p> |
| <b>Study design</b> | <p><b>Include:</b></p> <ul style="list-style-type: none"> <li>randomised controlled trials, non-randomised controlled trials</li> <li>cohort studies</li> <li>economic evaluation studies.</li> </ul> <p><b>Exclude:</b></p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |

|                      |                                                                                                                                                    |
|----------------------|----------------------------------------------------------------------------------------------------------------------------------------------------|
|                      | <ul style="list-style-type: none"> <li>▪ cross-sectional studies with no follow-up, case-control studies, case series, costing studies.</li> </ul> |
| <b>Search period</b> | All time for evaluating clinical effectiveness, 10 years for cost-effectiveness.                                                                   |

## 2.3 Health economic studies

### 2.3.1 Types of studies

The systematic reviews will aim to identify health economic studies including economic evaluations (cost-effectiveness analyses, cost-utility analyses, cost-minimisation analyses and cost-benefit analyses) related to the review questions. If no relevant economic evaluations are identified, the review will consider costing studies and comparative resource use studies.

### 2.3.2 Types of outcomes

The following is a non-exhaustive list of economic outcome measures considered applicable to this review:

#### Economic evaluations

- Cost-utility and or cost-effectiveness analysis:
  - incremental cost-effectiveness ratio (ICER)
  - cost per unit of effect (such as cost per life year gained) or effects per unit cost (for example, life years gained per Euro spent)
  - quality-adjusted life years (QALYs), disability-adjusted life years, or health/life years equivalent
  - incremental net monetary benefit.
- Cost-benefit and or cost-minimisation analysis:
  - net monetary benefit
  - incremental costs.

#### Other economic outcome measures

- Costs and resource use:
  - direct (for example, cost of staffing and equipment) and indirect (for example, prescription costs) costs, offsets and savings
  - length of hospital stay
  - implementation costs (for example, training and education)

- service utilisation cost.

## **2.4 Search strategy**

Electronic searches will be conducted in MEDLINE, Embase, CINAHL, Cochrane Library, Clinical Trials and APA PsycINFO. The search terms for each review are provided in Appendix 1 and include database-specific thesauri and free-text terms.

The anti-IL-5 review search terms were informed by a similar 2022 systematic review of clinical effectiveness of anti-IL-5 drugs for acute asthma exacerbation, which was conducted for a Dutch national clinical guideline<sup>(62)</sup> and included searches run from the beginning of time until August 2022. The search strategy will be quality-appraised using the Peer Review of Electronic Search Strategies (PRESS) tool<sup>(63)</sup> and approved for use by a librarian. An updated search for the anti-IL-5 review will be run from September 2022.

## **2.5 Selection of eligible publications**

All citations identified from the database searches (see Appendix 1) will be exported to EndNote (Version 20) for reference management, where duplicates will be identified and removed. Using Covidence ([www.covidence.org](http://www.covidence.org)), two reviewers will independently review the titles and abstracts of the remaining citations to identify those for full-text review. The full texts will be obtained and independently evaluated by two reviewers applying the defined inclusion and exclusion criteria. Where disagreements around eligibility occur, discussions will be held to reach consensus and, where necessary, a third reviewer will be involved. Citations excluded during the full-text review stage will be documented alongside the reason for their exclusion and included in a study flow diagram. Google Translate or DeepL Pro will be used to obtain translations of non-English language documents where appropriate.

## **2.6 Data extraction and management**

Data will be extracted from studies by one reviewer and checked for accuracy and omissions by a second. Where disagreements occur, discussions will be held to reach consensus and, where necessary, a third reviewer will be involved. Data extraction will include the characteristics of the study (country, study design, description of the study intervention, description of the comparison group where applicable), critical and important clinical outcomes, and cost-related outcomes. A draft data extraction template is available in Appendix 2. This will be piloted and amended as required.

## **2.7 Quality appraisal**

Two reviewers will independently assess the quality of included studies using validated critical appraisal instruments, including Cochrane Risk of Bias (RoB) 2 for randomised controlled trials (RCTs),<sup>(64)</sup> Cochrane Risk Of Bias In Non-randomised Studies of Interventions (ROBINS-I) for non-randomised controlled trials (nRCTs),<sup>(65)</sup> the Newcastle Ottawa Scale (NOS) for cohort studies,<sup>(66)</sup> and the Consensus Health Economic Criteria (CHEC)-list<sup>(67)</sup> and International Society for Pharmacoeconomics and Outcomes Research (ISPOR) questionnaire<sup>(68)</sup> for economic studies.

Significant discrepancies for any domain will be discussed to reach consensus and, where necessary, reviewed by a third member of the research team.

## **2.8 Data synthesis**

Due to the anticipated low number of identified studies for anti-IL-5 therapy, and heterogeneity between studies in terms of outcomes and follow-up for studies on specialist management and educational interventions post-exacerbation, narrative syntheses will likely be conducted for all review questions. However, if deemed appropriate, a meta-analysis will be performed. Depending on the number and variety of studies located, we aim to use the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to assess and summarise certainty of evidence across studies for each outcome. In accordance with national HIQA guidelines,<sup>(60)</sup> the costs from identified economic evaluations will be adjusted and presented in 2025 euro in parentheses alongside the original figures. Cost calculations will be undertaken by one reviewer and checked by a second reviewer.

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## Appendices

### Appendix 1: Search strategy

#### Anti-IL-5 for acute exacerbations (Embase 1974 to 2024)

| No. | Query                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
|-----|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| #27 | #25 NOT #26                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| #26 | #3 AND #23 AND [01-09-2022]/sd AND ('conference abstract'/it OR 'conference paper'/it OR 'conference review'/it OR 'editorial'/it)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| #25 | #3 AND #23 AND [01-09-2022]/sd                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| #24 | #3 AND #23                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| #23 | #4 OR #5 OR #22                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| #22 | #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| #21 | (unit NEXT/1 cost*):ti,ab,de,tn                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| #20 | (cost NEXT/1 variable\$):ti,ab,de,tn                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| #19 | (cost NEXT/1 estimate*):ti,ab,de,tn                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| #18 | 'cost minimization analysis'/de                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| #17 | fiscal:ti,ab OR financial:ti,ab OR finance:ti,ab OR funding:ti,ab                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| #16 | 'hospital cost'/de                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| #15 | 'health economics'/de                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| #14 | 'health care financing'/de                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| #13 | 'health care cost'/de                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| #12 | 'financial management'/de                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| #11 | 'economic aspect'/de                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| #10 | 'cost control'/de                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| #9  | 'cost of illness'/de                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| #8  | 'cost effectiveness analysis'/de                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| #7  | 'socioeconomics'/de                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| #6  | 'cost benefit analysis'/de                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| #5  | 'randomized controlled trial'/exp OR random*:ti,ab OR (((pragmatic OR practical) NEAR/1 'clinical trial*'):ti,ab) OR (((('non inferiority' OR noninferiority OR superiority OR equivalence) NEAR/3 trial*'):ti,ab) OR rct:ti,ab,kw                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| #4  | 'meta analysis'/exp OR 'meta analysis (topic)'/exp OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR metanaly*:ti,ab OR 'systematic review'/de OR 'cochrane database of systematic reviews'/jt OR prisma:ti,ab OR prospero:ti,ab OR (((systemati* OR scoping OR umbrella OR 'structured literature') NEAR/3 (review* OR overview*)):ti,ab) OR ((systemic* NEAR/1 review*):ti,ab) OR (((systemati* OR literature OR database* OR 'data base*') NEAR/10 search*):ti,ab) OR (((structured OR comprehensive* OR systemic*) NEAR/3 search*):ti,ab) OR (((literature NEAR/3 review*):ti,ab) AND (search*:ti,ab OR database*:ti,ab OR 'data base*':ti,ab)) OR (('data extraction':ti,ab OR 'data source*':ti,ab) AND 'study selection':ti,ab) OR ('search strategy':ti,ab AND 'selection criteria':ti,ab) OR ('data source*':ti,ab AND 'data synthesis':ti,ab) OR medline:ab OR pubmed:ab OR embase:ab OR cochrane:ab OR (((critical OR rapid) NEAR/2 (review* OR overview* OR syntheses*)):ti) OR (((critical* OR rapid*) NEAR/3 (review* OR overview* OR |

|    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
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|    | synthes*)):ab) AND (search*:ab OR database*:ab OR 'data base*':ab)) OR metasyntes*:ti,ab OR 'meta syntes*':ti,ab                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| #3 | #1 AND #2                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|    | <p>'leukotriene receptor blocking agent'/exp OR 'benralizumab'/exp OR 'magnesium sulfate'/exp OR 'montelukast'/exp OR 'salbutamol'/exp OR 'mepolizumab'/exp OR 'reslizumab'/exp OR 'interleukin 5 antibody'/exp OR ((leu?otriene NEAR/3 (antagonist* OR block* OR inhibitor*)):ti,ab,kw) OR 'epsom salt':ti,ab,kw OR 'magnesium sulfate':ti,ab,kw OR 'mg longoral':ti,ab,kw OR 'sulfamag':ti,ab,kw OR 'sulmetin':ti,ab,kw OR 'magnesium sulphate':ti,ab,kw OR 'aero clenil':ti,ab,kw OR 'aeroclenil':ti,ab,kw OR 'ah 3365':ti,ab,kw OR 'ah3365':ti,ab,kw OR 'albuterol':ti,ab,kw OR 'almotex':ti,ab,kw OR 'asmacaire':ti,ab,kw OR 'asmadil':ti,ab,kw OR 'asmalin':ti,ab,kw OR 'asmasal':ti,ab,kw OR 'asmamol':ti,ab,kw OR 'asmaven':ti,ab,kw OR 'asmavent':ti,ab,kw OR 'asmidon':ti,ab,kw OR 'asmol':ti,ab,kw OR 'broncho spray':ti,ab,kw OR 'broncho-spray':ti,ab,kw OR 'bronter':ti,ab,kw OR 'brytolin':ti,ab,kw OR 'butahale':ti,ab,kw OR 'buto-asma':ti,ab,kw OR 'butomix':ti,ab,kw OR 'butotal':ti,ab,kw OR 'butovent':ti,ab,kw OR 'buventol':ti,ab,kw OR 'cibutamol':ti,ab,kw OR 'cletal':ti,ab,kw OR 'cybutol':ti,ab,kw OR 'dilatomol':ti,ab,kw OR 'ecovent':ti,ab,kw OR 'emplusal':ti,ab,kw OR 'exafil':ti,ab,kw OR 'farcolin':ti,ab,kw OR 'frespire':ti,ab,kw OR 'glisend':ti,ab,kw OR 'grafalin':ti,ab,kw OR 'krosalburol':ti,ab,kw OR 'libretin':ti,ab,kw OR 'loftan':ti,ab,kw OR 'mozal':ti,ab,kw OR 'novosalmol':ti,ab,kw OR 'parasma':ti,ab,kw OR 'proventil':ti,ab,kw OR 'prox-s':ti,ab,kw OR 'pulmol s':ti,ab,kw OR 'repetabs':ti,ab,kw OR 'respolin':ti,ab,kw OR 'salamol':ti,ab,kw OR 'salbuair':ti,ab,kw OR 'salbulin':ti,ab,kw OR 'salbumol fort':ti,ab,kw OR 'salbupart':ti,ab,kw OR 'salbutamol':ti,ab,kw OR 'salbuvent':ti,ab,kw OR 'salden':ti,ab,kw OR 'salgem':ti,ab,kw OR 'salmol':ti,ab,kw OR 'saltos':ti,ab,kw OR 'solbutamol':ti,ab,kw OR 'spacehaler':ti,ab,kw OR 'sultanol':ti,ab,kw OR 'venetlin':ti,ab,kw OR 'ventilan':ti,ab,kw OR 'ventodisk':ti,ab,kw OR 'ventodisks':ti,ab,kw OR 'ventol':ti,ab,kw OR 'volmac':ti,ab,kw OR 'benralizumab':ti,ab,kw OR 'fasenra':ti,ab,kw OR 'medi 563':ti,ab,kw OR 'medi563':ti,ab,kw OR 'bosatria':ti,ab,kw OR 'mepolizumab':ti,ab,kw OR 'nucala':ti,ab,kw OR 'sb 240563':ti,ab,kw OR 'sb-240563':ti,ab,kw OR 'sb240563':ti,ab,kw OR 'cinquaero':ti,ab,kw OR 'cinqair':ti,ab,kw OR 'reslizumab':ti,ab,kw OR 'sch 55700':ti,ab,kw OR 'sch55700':ti,ab,kw OR 'actamone':ti,ab,kw OR 'airathon':ti,ab,kw OR 'airing':ti,ab,kw OR 'alvokast':ti,ab,kw OR 'apilone':ti,ab,kw OR 'ascafi':ti,ab,kw OR 'ascolin':ti,ab,kw OR 'asmenol':ti,ab,kw OR 'asprevent':ti,ab,kw OR 'astecon':ti,ab,kw OR 'asthator':ti,ab,kw OR 'asthasan':ti,ab,kw OR 'asthmont':ti,ab,kw OR 'astmirex':ti,ab,kw OR 'astmodil':ti,ab,kw OR 'atentus':ti,ab,kw OR 'atlabiclo':ti,ab,kw OR 'belokast':ti,ab,kw OR 'brolyt':ti,ab,kw OR 'castispir':ti,ab,kw OR 'chesmon':ti,ab,kw OR 'deprive':ti,ab,kw OR 'elukan':ti,ab,kw OR 'elunkast':ti,ab,kw OR 'eonic':ti,ab,kw OR 'filkast':ti,ab,kw OR 'fulmont':ti,ab,kw OR 'imvlo':ti,ab,kw OR 'ispyrra':ti,ab,kw OR 'jepafex':ti,ab,kw OR 'kipres':ti,ab,kw OR 'I 706631':ti,ab,kw OR 'I706631':ti,ab,kw OR 'lanair':ti,ab,kw OR 'leukast':ti,ab,kw OR 'lukair':ti,ab,kw OR 'lukanof':ti,ab,kw OR 'lukas aiwa':ti,ab,kw OR 'lukasm':ti,ab,kw OR 'lukastang':ti,ab,kw OR 'lukavent':ti,ab,kw OR 'melarth':ti,ab,kw OR 'metigrenul':ti,ab,kw OR 'milukante':ti,ab,kw OR 'mintalos':ti,ab,kw OR 'miralust':ti,ab,kw OR 'mk 0476':ti,ab,kw OR 'mk 476':ti,ab,kw OR 'mk0476':ti,ab,kw OR 'mk476':ti,ab,kw OR 'modrian':ti,ab,kw OR 'modulair':ti,ab,kw OR 'mofenstra':ti,ab,kw OR 'mokast':ti,ab,kw OR 'molucar':ti,ab,kw OR 'monalux':ti,ab,kw OR 'monart':ti,ab,kw OR 'monast':ti,ab,kw OR 'moncas':ti,ab,kw OR 'mondeo':ti,ab,kw OR 'monkasta':ti,ab,kw OR 'monlast':ti,ab,kw OR 'monlucare':ti,ab,kw OR 'monspes':ti,ab,kw OR 'monstonol':ti,ab,kw OR 'montair':ti,ab,kw OR 'montast':ti,ab,kw OR 'montecell':ti,ab,kw OR 'montecon':ti,ab,kw OR 'montefar':ti,ab,kw OR 'montegen':ti,ab,kw OR 'montelair':ti,ab,kw OR 'montelak':ti,ab,kw OR 'montelar':ti,ab,kw OR 'montelext':ti,ab,kw OR 'montelubronch':ti,ab,kw OR 'montelucaste':ti,ab,kw OR 'montelukast*':ti,ab,kw OR 'montelux':ti,ab,kw OR 'montemyl':ti,ab,kw OR 'montep':ti,ab,kw OR 'monterast':ti,ab,kw OR 'monteresp':ti,ab,kw OR</p> |
| #2 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |

|    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|----|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|    | 'montespir':ti,ab,kw OR 'montewin':ti,ab,kw OR 'montexal':ti,ab,kw OR 'monthan':ti,ab,kw OR 'montol':ti,ab,kw OR 'montus':ti,ab,kw OR 'moolpas':ti,ab,kw OR 'nal 6336':ti,ab,kw OR 'nal6336':ti,ab,kw OR 'orilukast':ti,ab,kw OR 'otelus':ti,ab,kw OR 'pentafeno':ti,ab,kw OR 'perasm':ti,ab,kw OR 'pluralais':ti,ab,kw OR 'pneumo-kast':ti,ab,kw OR 'promonta':ti,ab,kw OR 'rasec':ti,ab,kw OR 'relukas':ti,ab,kw OR 'respilukas':ti,ab,kw OR 'romilast':ti,ab,kw OR 'saslong':ti,ab,kw OR 'singodem':ti,ab,kw OR 'singulair':ti,ab,kw OR 'singulair allergy':ti,ab,kw OR 'singulair ar':ti,ab,kw OR 'singulair chew':ti,ab,kw OR 'singulair mini':ti,ab,kw OR 'singulergy':ti,ab,kw OR 'solok':ti,ab,kw OR 'spirokast':ti,ab,kw OR 'spiromon':ti,ab,kw OR 'surfair':ti,ab,kw OR 'symlukast':ti,ab,kw OR 'telelux':ti,ab,kw OR 'telukast':ti,ab,kw OR 'teluki':ti,ab,kw OR 'tevalukast':ti,ab,kw OR 'thordel':ti,ab,kw OR 'valnuen':ti,ab,kw OR 'velukast':ti,ab,kw OR 'xaira':ti,ab,kw OR 'yekast':ti,ab,kw OR 'zakomoxit':ti,ab,kw OR 'interleukin 5 antibody':ti,ab,kw |
| #1 | 'asthma attack'/exp OR 'asthma attack' OR 'asthma exacerbation'/exp OR 'asthma exacerbation' OR 'asthmatic state'/exp OR 'asthmatic state' OR 'acute severe asthma':ti,ab,kw OR 'severe acute asthma':ti,ab,kw OR 'status asthmaticus':ti,ab,kw OR ((asthma* NEAR/3 (cris?s OR shock OR state OR attack* OR exacerbation*)):ti,ab,kw) OR (('asthma'/exp OR 'asthma' OR asthma:ti,ab,kw) AND ('respiratory failure'/exp OR 'respiratory failure' OR 'fatal attack*':ti,ab,kw OR 'near fatal':ti,ab,kw OR 'respiratory failure':ti,ab,kw)) OR 'acute asthma':ti,ab,kw                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |

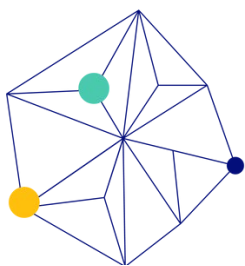
**Specialist assessment / self-management education intervention post hospitalisation with an acute exacerbation (Embase 1974 to 2024)**

| No. | Query                                                                                                                                                                                                                                                 |
|-----|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| #40 | #29 OR #39                                                                                                                                                                                                                                            |
| #39 | #18 AND #37 AND [2015-2025]/py                                                                                                                                                                                                                        |
| #38 | #18 AND #37                                                                                                                                                                                                                                           |
| #37 | #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36                                                                                                                                                                                                         |
| #36 | ((adjusted OR 'quality adjusted') NEAR/1 year*):ab,ti                                                                                                                                                                                                 |
| #35 | (expenditure* NEAR/2 (health OR direct OR indirect)):ab,ti                                                                                                                                                                                            |
| #34 | ('out of pocket' NEAR/1 (payment* OR expenditure* OR cost* OR spending OR expense*)):ab,ti                                                                                                                                                            |
| #33 | 'quality adjusted life year'/exp OR 'cost of illness'/exp                                                                                                                                                                                             |
| #32 | 'quality-adjusted life years':ab,ti OR 'quality adjusted life years':ab,ti OR qaly*:ab,ti                                                                                                                                                             |
| #31 | (burden* NEAR/1 (illness OR disease* OR condition* OR economic*)):ab,ti                                                                                                                                                                               |
| #30 | 'cost'/exp OR 'cost benefit analysis'/exp OR 'health care cost'/exp OR 'cost':ab,ti                                                                                                                                                                   |
| #29 | #18 AND #28                                                                                                                                                                                                                                           |
| #28 | #23 OR #26 OR #27                                                                                                                                                                                                                                     |
| #27 | 'systematic review'/exp OR 'systematic review' OR 'meta analysis'/exp OR 'meta analysis' OR ((systematic* NEAR/2 (review* OR overview*)):ti,ab) OR 'meta analys*':ti,ab OR 'meta analyz*':ti,ab OR ((literature NEAR/3 (review* OR overview*)):ti,ab) |
| #26 | #24 OR #25                                                                                                                                                                                                                                            |
| #25 | ((cohort OR longitudinal OR prospective OR 'follow up' OR retrospective) NEAR/1 (study OR analys* OR design OR method*)):ab,ti                                                                                                                        |
| #24 | 'cohort analysis'/exp OR 'cohort analysis' OR 'longitudinal study'/exp OR 'longitudinal study' OR 'prospective study'/exp OR 'prospective study' OR 'follow up'/exp OR 'follow up' OR 'retrospective study'/exp OR 'retrospective study'              |
| #23 | #21 NOT #22                                                                                                                                                                                                                                           |
| #22 | 'animal'/exp NOT 'human'/exp                                                                                                                                                                                                                          |

|     |                                                                                                                                    |
|-----|------------------------------------------------------------------------------------------------------------------------------------|
| #21 | #19 OR #20                                                                                                                         |
| #20 | randomized:ab OR placebo:ab OR randomly:ab OR trial:ab OR groups:ab                                                                |
| #19 | 'randomized controlled trial'/exp OR 'clinical trial'/it                                                                           |
| #18 | #7 AND #17                                                                                                                         |
| #17 | #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16                                                                          |
| #16 | (specialist* NEAR/3 (service* OR assess* OR management OR consultant OR physio* OR clinic* OR hub* OR nurs* OR respiratory)):ab,ti |
| #15 | outpatient*:ab,ti                                                                                                                  |
| #14 | 'outpatient department'/exp                                                                                                        |
| #13 | 'personal care':ab,ti OR 'self efficacy':ab,ti                                                                                     |
| #12 | (patient* NEAR/3 (knowledge OR education* OR learning)):ab,ti                                                                      |
| #11 | 'self manag*':ab,ti OR 'self care':ab,ti                                                                                           |
| #10 | 'patient participation'/exp                                                                                                        |
| #9  | 'patient education'/exp                                                                                                            |
| #8  | 'self care'/exp                                                                                                                    |
| #7  | #1 OR #2 OR #3 OR #6                                                                                                               |
| #6  | #4 AND #5                                                                                                                          |
| #5  | 'airway obstruction'/exp OR 'fatal attack*':ab,ti OR 'near fatal':ab,ti OR 'respiratory failure':ab,ti                             |
| #4  | 'asthma'/exp OR asthma                                                                                                             |
| #3  | (asthma* NEAR/3 (crisis OR shock OR state OR attack* OR exacerbat*)):ab,ti                                                         |
| #2  | 'severe asthma':ab,ti OR 'acute asthma':ab,ti OR 'status asthmaticus':ab,ti                                                        |
| #1  | 'asthmatic state'/exp                                                                                                              |

## Appendix 2: Data extraction template

|                          |              |            |                     |               |              |                        |              |            |
|--------------------------|--------------|------------|---------------------|---------------|--------------|------------------------|--------------|------------|
| Study characteristics    |              |            |                     |               |              |                        |              |            |
| Authors                  | Title        |            | Year of Publication | Country       | Study design | Number of participants | Intervention | Comparator |
|                          |              |            |                     |               |              |                        |              |            |
| Clinical effectiveness   |              |            |                     |               |              |                        |              |            |
| Clinical outcome measure |              |            | Time to follow up   |               | Results      |                        |              |            |
|                          |              |            |                     |               |              |                        |              |            |
| Cost effectiveness       |              |            |                     |               |              |                        |              |            |
| Study perspective        | Time horizon | Model type | Discount rate       | Cost outcomes |              | Clinical Outcomes      | Results      |            |
|                          |              |            |                     |               |              |                        |              |            |



# CICER

Tacaíocht don Treoirline Chliniciúil  
Clinical Guideline Support

Published by the Health Information  
and Quality Authority (HIQA).

Health Information and Quality Authority

George's Court

George's Lane

Smithfield

Dublin 7

D07 E98Y

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