CICER
Tacaíocht don Treoirlíne Chliniciúil
Clinical Guideline Support

THE MANAGEMENT OF ACUTE ASTHMA ATTACKS IN ADULTS

A systematic review of international clinical guidelines

December 2025

Health Information and Quality Authority
An tÚdarás Um Fhaisnéis agus Cáilíocht Sláinte

Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
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NATIONAL CLINICAL EFFECTIVENESS COMMITTEE

HRB An Bord Taighde Sláinte Health Research Board

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 and National Clinical Audits. 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. The CICER team 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 adaption to Ireland; and supports the development of evidence-based recommendations informed within the National Clinical Guidelines.

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List of abbreviations used in this report

AGREE-GRS	Appraisal of Guidelines for Research and Evaluation Global Rating Scale
AHRQ	Agency for Healthcare, Research and Quality
AWMF	Association of Scientific Medical Societies
BÄK	German Medical Association
BTS	British Thoracic Society
CICER	Centre in Ireland for Clinical Guideline Support and Evidence Reviews
CO_2	carbon dioxide
CPG	clinical practice guideline
$ECCO_2R$	extracorporeal carbon dioxide removal
ECMO	extracorporeal membrane oxygenation
ED	emergency department
EtD	Evidence to Decision framework
FENAER	Spanish Federation of Allergy and Airways Diseases Patients' Associations
FeNO	fractional exhaled nitric oxide
FEV1	forced expiratory volume in one second
FiO_2	fraction of inspired oxygen
g	gram
GDG	guideline development group
GEMA	Guía Espanola para el Manejo del Asma
GFRUP	Groupe Francophone de Reanimation et d'Urgences Pédiatriques
GINA	Global Initiative for Asthma
GRADE	Grading of Recommendations, Assessment, Development, and Evaluations
GRADE-ADOLOPMENT	Grading of Recommendations Assessment, Development and Evaluation Evidence to Decision framework process for adoption, adaptation, and de novo development of trustworthy recommendations
HIQA	Health Information and Quality Authority

HRB	Health Research Board
HSE	Health Service Executive
ICU	intensive care unit
INPECS	Institute for Clinical and Healthcare Excellence
IQWIG	Institute for Quality and Efficiency in Health Care
IV	intravenous
KBV	National Association of Statutory Health Insurance Physicians
kg	kilogram
l/min	litre per minute
LTRA	leukotriene-receptor antagonist
mg	milligram
mcg	microgram
min	minute
N/A	not applicable
NACA	National Asthma Council of Australia
NCEC	National Clinical Effectiveness Committee
NCG	National Clinical Guideline
NHMRC	National Health and Medical Research Council
NICE	National Institute for Health and Care Excellence
NIV	non-invasive ventilation
NVALT	Dutch Association of Pulmonologists
NVL	National Care Guidelines (Germany)
PEF	peak expiratory flow
PICO	Population, Interest, Context and Outcome framework
(p)MDI	(pressurised) metred dose inhaler
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RCT	randomised control trial

RRS	Russian Respiratory Society
SaO_2	oxygen saturation (arterial blood)
SEPAR	Sociedad Española de Neumología y Cirugía Torácica
SFMU	Societe Francaise de Medecine d'Urgence
SIGN	Scottish Intercollegiate Guideline Network
SINA	Saudi Initiative for Asthma
SpO_2	oxygen saturation
SRLF	Societe de Reanimation de Langue Francaise
SRS	Swiss Respiratory Society
UK	United Kingdom

1. Background

1.1 Description of the condition in adults

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.[1] Asthma can range in severity from mild to severe with typical symptoms including wheezing, coughing, shortness of breath, and chest tightness.[2] Asthma is a complex disorder whose risk factors include air pollution, smoking, atopy (a genetic tendency to develop an exaggerated immune response), stress, and obesity.[3, 4]

Asthma can develop at any age, and risk factors and comorbidities appear to vary by age of onset.[5, 6] In childhood, more boys than girls have asthma while in adulthood, women have higher rates of asthma than men.[7, 8] There is evidence from high-income countries that socioeconomic deprivation is associated with worse asthma control and increased exacerbation rates.[9-12]

Approximately 5-10% of the adult population in Ireland has been diagnosed with asthma.[13, 14] In 2022, asthma was the registered cause of death in 81 fatalities in Ireland,[15] though some limitations have been noted around the reliability of attributing deaths to asthma in the United Kingdom (UK) that might also apply to asthma-related death data in Ireland. Asthma is associated with an increased risk of accompanying health conditions, including rhinitis, sinusitis, gastroesophageal reflux, and obstructive sleep apnoea.[16, 17] Asthma can have a significant impact on individuals' quality of life, especially when it is in the severe range.[18] Asthma may interfere with daily activities and can lead to negative psychological effects like depression and anxiety.[19] It can also lead to missed work or school and to financial costs for the individual and the health system.[20, 21]

Routine management of asthma usually involves monitoring for signs and symptoms, avoiding triggers, and taking medications.[22] 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,[23] while steroid inhalers (such as fluticasone, beclomethasone, and budesonide) work by reducing inflammation in the airway.[24] More severe chronic asthma

may require management with oral medicines, such as leukotriene-receptor antagonists (LTRAs) or steroid tablets, or with injectable biologic therapies.[25]

Occasionally, individuals with asthma may experience sudden worsening of their symptoms, also known as an asthma exacerbation or an asthma attack. Asthma attacks are characterised by rapid breathing, difficulty speaking, accelerated heart rate, and low oxygen saturation.[26] They can be triggered by viral respiratory infections, like the common cold, or by exposure to allergens.[27, 28] Asthma attacks can sometimes become severe and or life-threatening, requiring emergency medical intervention. Emergency treatment for an acute asthma attack may include supplemental oxygen, bronchodilators, and corticosteroids, and in extreme cases, mechanical ventilation.[29] Fatal asthma attacks are more likely among those with a history of near-fatal asthma and those who have had a hospitalisation or emergency care visit for asthma in the past year.[30] A confidential inquiry in the UK in 2014, into all deaths across all ages from asthma, found that two-thirds of deaths from asthma involved at least one potentially avoidable factor, most often clinicians not recognising patients' high-risk status and clinicians lacking specific asthma expertise.[31]

1.2 Clinical guidelines on asthma in adults

In 2015, a National Clinical Guideline (NCG No. 14) on *Management of an Acute Asthma Attack in Adults (aged 16 years and older)* was published in Ireland.[32] The guideline was developed by a sub-group of the Health Service Executive (HSE) National Clinical Programme for Asthma. The aim of the guideline was to assist healthcare professionals in all care settings in assessing and making decisions on the management of an acute asthma attack in adults and to assist policy makers and those planning acute services for adult asthma patients. Children aged less than 16 years and those with "difficult/severe but stable" asthma were outside of the scope of the guideline. Many of the recommendations in the 2015 guideline were adapted from the British Guideline on the Management of Asthma (2014)[33] and the Global Strategy for Asthma Management and Prevention (2015).[34] A guideline development group (GDG) has been established to update the existing NCG no. 14. The scope of the updated NCG will remain unchanged, and will focus on the management of acute asthma attacks in adults and adolescents aged 16 years and older.

1.3 Purpose of this systematic review

The purpose of this review is to identify and appraise current clinical guidelines on the management of acute asthma attacks in adults. This review will identify clinical guidelines that could be used to support the update of the current NCG (NCG No. 14) on *Management of an Acute Asthma Attack in Adults (aged 16 years and older)*.[32] Specifically, this review will present:

- current international recommendations relevant to primary topics identified by the GDG
- the strength of the recommendations
- their currency and quality
- summary of underpinning evidence.

The findings of this review can be used to inform the Grading of Recommendations Assessment, Development and Evaluation Evidence to Decision framework process for adoption, adaptation, and de novo development of trustworthy recommendations (GRADE-ADOLOPMENT).[35]

2. Methods

This systematic review of international clinical guidelines on the management of an acute asthma attack in adults was carried out in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria.[36] Full details of this systematic review of international clinical guidelines are available in the protocol.[37]

2.1 Review question

This review considered the following questions:

- What relevant clinical guidelines on the management of an acute asthma attack in adults (aged 16 years and above) are currently in use internationally?
- What recommendations of interest to the GDG do these guidelines include and what is the evidence underlying each recommendation?

The review questions were formulated in line with a modified version of the PICO (Population, Intervention, Comparison, Outcome) framework, as presented in Table 1. Both primary and secondary topics of interest were identified through consultation with the GDG in advance of this review.

Table 1 Population, Interest, Context, Search period for review of asthma guidelines

Population	Adults (defined as those aged 16 years or older) experiencing an acute asthma attack (defined as sudden worsening of asthma symptoms and lung function) presenting to primary care or hospital settings
Interest	Clinical guidelines that describe the management of an acute asthma attack in adults, relating to one or more of the following primary topics of interest to the GDG: ▪ Peak flow cut-offs as an indicator to inform hospital admission and or ED discharge ▪ Respiratory rate as an indicator to inform hospital referral and/or admission and/or ICU admission ▪ Use of chest X-ray in an acute asthma attack ▪ Use of high-flow oxygen in an acute asthma attack ▪ Use of oxygen-driven versus air-driven nebulisers in an acute asthma attack in primary care ▪ Addition of an anticholinergic to β_2 agonist bronchodilators in an acute asthma attack ▪ Use of IV β_2 agonists in an acute asthma attack

	▪ Use of heliox in an acute asthma attack ▪ Use of IV magnesium in an acute asthma attack ▪ Use of ECMO for near-fatal asthma attack refractory to conventional ventilator treatment ▪ Use of IV aminophylline in an acute asthma attack ▪ Use of LRTAs, orally or IV, in an acute asthma attack ▪ Use of antibiotics in an acute asthma attack ▪ Use of NIV in an acute asthma attack Secondary topics of interest to the GDG include: ▪ FEV1 for detecting and or assessing an acute asthma attack and to inform hospital referral and/or admission ▪ FeNO for detecting and or assessing an acute asthma attack ▪ Respiratory rate for assessing severity of an asthma attack ▪ Use of nebulised magnesium sulphate in an acute asthma attack ▪ Use of IV fluid regimes in an acute asthma attack ▪ Use of nebulised furosemide in an acute asthma attack
Context	▪ Clinical guidelines (international or national), defined as systematically developed statements, based on a thorough evaluation of the evidence, to assist practitioner and patient decisions about appropriate healthcare for specific clinical circumstances. ▪ Regional or hospital-specific guidelines will not be included.
Search period	▪ 2018-present

Key: ECMO - extracorporeal membrane oxygenation; ED - emergency department; FeNO - fractional exhaled nitric oxide; FEV1- forced expiratory volume in one second; GDG - Guideline Development Group; ICU – intensive care unit; IV – intravenous; LTRA – leukotriene-receptor antagonists; NIV – non-invasive ventilation.

1.2 Search strategy

Electronic searches were conducted in MEDLINE Complete (Ebscohost), Embase (Ovid), CINAHL Complete (Ebscohost) and PsycINFO (Ebscohost) on 2 August 2024 to identify potentially eligible clinical guidelines. The search terms are provided in the protocol and include database specific thesauri and free-text terms. As well as locating peer-reviewed publications of guidelines, the scientific database search allowed us to identify guidelines that were named or discussed in peer-reviewed publications but published elsewhere. Grey literature sources, including guideline repositories, guideline developer websites, websites of national ministries of health and specific clinical specialty websites listed in the protocol, were searched between 12 August to 23 August 2024. Searches were conducted for key terms within each organisation's website and the first 50 hits within each site were reviewed for potentially eligible guidelines.

1.3 Eligibility criteria

The inclusion and exclusion criteria for this review are provided in Table 2. Clinical guidelines are defined as "systematically developed statements, based on a thorough evaluation of the evidence, to assist practitioner and patient decisions about appropriate healthcare for specific clinical circumstances, across the entire clinical spectrum".[38]

Table 2 Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria

Guidelines for asthma that:
▪ focus on adults (defined as those aged ≥16 years)
▪ clearly state the guideline development process and the evidence base that underpins each guideline recommendation
▪ provide recommendations relating to acute asthma attacks, defined as sudden worsening of asthma symptoms and lung function, related to one or more of the following:
  ▪ indicators of presence and or severity of an acute asthma attack
  ▪ criteria for referral, admission and or discharge for an acute asthma attack
  ▪ medications to treat an acute asthma attack, including β2 agonists, anticholinergics, magnesium, aminophylline, LTRA, and furosemide for an acute asthma attack
  ▪ use of oxygen and heliox for an acute asthma attack
  ▪ use of ventilation, including NIV and ECMO for an acute asthma attack
  ▪ include a rating of the certainty or quality of evidence that underpins the recommendations using an approach such as GRADE[39]
▪ are novel guidelines or have been adapted from another guideline where an update of the evidence was conducted.
	Guidelines for asthma that:
	▪ describe the management of asthma as part of a guideline on another health condition
	▪ are regional, local or hospital level
	▪ refer only to children/adolescents <16 years
	▪ have been superseded by a more recent version
	▪ are adopted directly from another guideline if no updated searches were conducted during adoption
	▪ were published before 2018 to ensure identified guidelines are applicable to current practice.

Key: ECMO – extracorporeal membrane oxygenation; GRADE - Grading of Recommendations, Assessment, Development, and Evaluation; LTRA – leukotriene-receptor antagonists; NIV – non-invasive ventilation.

1.4 Selection of eligible publications

All citations identified from the collective search strategy were exported to EndNote® (Version 20)[40] for reference management, where duplicates were identified and removed.

Using Covidence®,[41] two reviewers (CL, MG) independently reviewed the titles and abstracts of the remaining citations to identify literature eligible for full-text review. The full-texts were obtained and independently evaluated by two reviewers (from CL, AB, and MG) applying the defined inclusion and exclusion criteria. Google Translate and Deepl Pro were used to obtain translations of non-English language documents, where required and where possible. If an English language translation could not be obtained, or where translation was judged to be sufficiently incomplete that the data could not confidently be extracted with due accuracy, these guidelines were excluded. Where disagreements around eligibility occurred, discussions were held to reach consensus and where necessary, a third reviewer (from CL, AB, and MG) was involved. Citations excluded during the full-text review stage were documented alongside the reason for their exclusion and included in a study flow diagram.

1.5 Data extraction and management

Data were extracted from guidelines and peer-reviewed articles by two reviewers (from CL, AB, MG, and RM) and compared for accuracy and omissions. Where disagreements occurred, discussions were held to reach consensus and where necessary, a third reviewer was involved. Data extraction was conducted in Microsoft Excel®,[42] using a purposefully designed data extraction form, which was piloted and refined prior to commencement of extraction. Data extraction included the characteristics of the guideline, all relevant recommendations and their underlying evidence, including Evidence to Decision (EtD) frameworks[43] where provided.

1.6 Quality appraisal

Two reviewers (from CL, AB, MG, and BT) independently assessed the quality of included guidelines using the Appraisal of Guidelines for Research & Evaluation Global Rating Scale (AGREE-GRS).[44] Scores were calculated and reported in accordance with the AGREE-GRS manual,[44] including the average score for each of the four pre-defined core items and the overall quality assessment score. Significant discrepancies for any domain were discussed to reach consensus, and where necessary reviewed by a third member of the research team.

1.7 Currency of guidelines

Currency of the included guidelines was assessed by reviewing the publication date of the guideline and the dates covered by the most recent evidence search, to ascertain whether the most current evidence had been included.[35] As outlined in the protocol in advance of this review, it had been agreed that should a significant number of relevant guidelines be returned following full-text review, currency and or quality would be used as thresholds for inclusion in the narrative summary.

1.8 Data synthesis

A narrative synthesis of the characteristics of the included clinical guidelines, and appraisal of quality and assessment of currency of the clinical guidelines was produced. Recommendations relating to primary topics of interest as identified by the GDG, and their underlying evidence, were also summarised and compared where appropriate to the recommendations within NCG No. 14. A narrative synthesis of recommendations related to secondary topics of interest to the GDG is also provided.

1.9 Deviation from the protocol

Upon request by the GDG during the report finalisation process, several additions were made to the draft report:

1) Chest X-ray and antibiotics for acute asthma were included as additional primary topics for data extraction

2) Non-invasive ventilation (NIV) was promoted to a primary topic of interest, rather than a secondary topic of interest as in the original protocol.

3. Results

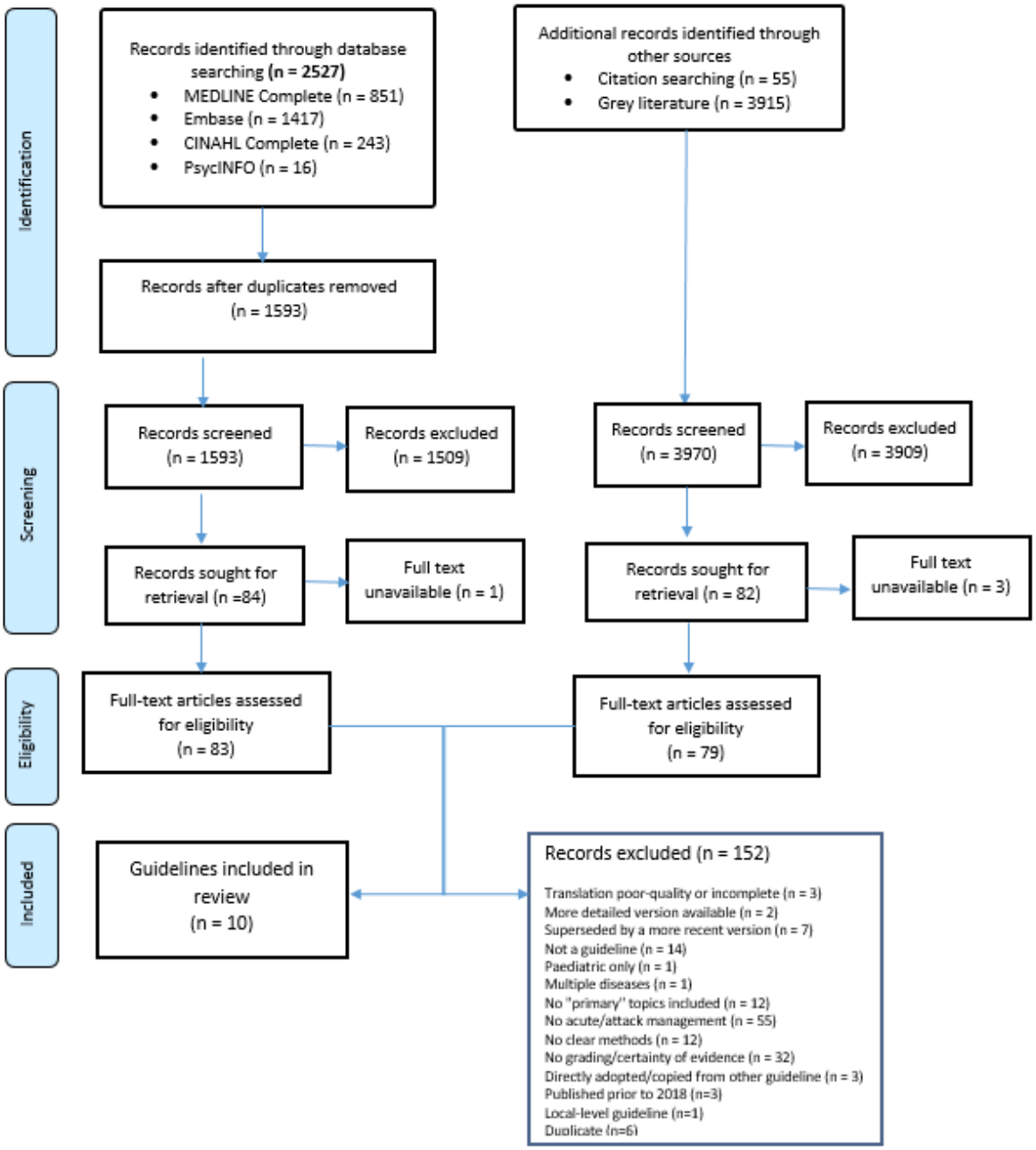
3.1 Search results

The search of electronic databases identified 2,527 citations. After removal of duplicates, the titles and available summaries of 1,593 citations were independently screened by two reviewers, after which 1,509 records were excluded. Eighty-four full-texts were sought for retrieval, of which one full-text could not be obtained. A total of 83 full-texts were independently assessed by two reviewers applying the predefined inclusion and exclusion criteria (Table 2), resulting in the exclusion of a further 78 records. This resulted in five clinical guidelines identified for inclusion in this review,[45-49] of which four were published in English language,[45-47, 49] and one required English translation.[48]

A total of 55 additional guidelines were mentioned in the title or abstract of peer-reviewed articles and were located online for full-text review leading to five additional eligible guidelines identified for inclusion (three in English,[50-52] and two requiring English translation[53, 54]).

The grey literature search was conducted independently by two reviewers, and yielded 3,915 hits across 60 organisations' websites. Fifty-three potential guidelines were identified, of which 27 had not been identified during the scientific search. However, none of these additional guidelines were eligible for inclusion. A PRISMA flow chart summarising the search process and subsequent results is provided in Figure 1.

Figure 1 PRISMA Flow Chart



3.2 Guideline characteristics

Ten guidelines were included in this review of international clinical guidelines.[45-54] An overview of the general characteristics of these guidelines is outlined in Table 3 and described in sections 3.2.1 and 3.2.2. Two guidelines were developed to specifically address the management of acute asthma exacerbation only,[45, 54] while eight guidelines addressed the management of acute asthma as a subsection of a guideline addressing the management of asthma generally.[46-53]

3.2.1 3.2.1 Origin and developers

One guideline was developed and published jointly by the British Thoracic Society (BTS) and the Scottish Intercollegiate Guideline Network (SIGN).[50] Five guidelines were developed and published by European associations.[45, 46, 52-54] These included the Guía Espanola para el Manejo del Asma (GEMA) guideline (version 5.3), produced by the Sociedad Española de Neumología y Cirugía Torácica (SEPAR) for Spain,[47] and clinical practice guidelines (CPGs) produced by the Swiss Respiratory Society (SRS) for Switzerland[46] and the Dutch Association of Pulmonologists (NVALT) for the Netherlands, in association with the Dutch Federation of Medical Specialists.[54] A guideline for Germany produced by the National Care Guidelines (NVL) program was developed by the German Medical Association (BÄK), National Association of Statutory Health Insurance Physicians (KBV), and the Association of Scientific Medical Societies (AWMF).[53] A guideline for France was produced by the Société Française de Médecine d'Urgence (SFMU), the Société de Réanimation de Langue Française (SRLF) and Groupe Francophone de Reanimation et d'Urgences Pédiatriques (GFRUP).[45] A further three national level guidelines were identified, developed for Russia by the Russian Respiratory Society (RRS),[48] for Saudi Arabia by the Saudi Initiative for Asthma (SINA)[49] and for Australia by the National Asthma Council (NACA).[51] The final publication, the Global Strategy for Asthma Management and Prevention (2024), was developed with international involvement, by the Global Initiative for Asthma (GINA).[52] Two of the guidelines focused on the acute care setting including the emergency department (ED), while the others included additional clinical settings, such as primary care and specialist care (Table 3).[45, 54]

Table 3 Characteristics of included guidelines

Year Shorthand name Country	Guideline title	Associated society or body	Primary topic of guideline
2024 GINA[52] International	GINA Global Strategy for Asthma Management and Prevention (2024)	Global Initiative for Asthma (GINA)	Asthma management and prevention for all ages, at home, primary care, and acute care.
2024 NVALT[54] The Netherlands	Asthma Attack (2024) *Translation required from Dutch to English*	Dutch Association of Pulmonologists (Nederlandse Vereniging van Artsen voor Longziekten en Tuberculose [NVALT]), Dutch Federation of Medical Specialists	Management of acute asthma exacerbation in adults aged over 18 years in an ED setting.
2024 NVL[53] Germany	National Care Guideline for Asthma, Version 5.0 *Translation required from German to English*	German Medical Association (BÄK), National Association of Statutory Health Insurance Physicians (KBV), Association of Scientific Medical Societies (AWMF). National Care Guidelines (NVL) program	Management of asthma in children and adults across multiple care settings, including primary care, specialised care, and inpatient setting.
2024 SINA[49] Saudi Arabia	Guidelines for the Diagnosis and Management of Asthma in Adults and Children, Version 6	The Saudi initiative for asthma (sponsored by the Saudi Thoracic Society)	Management of asthma in adults, adolescents, children aged 5-12 years, and children aged <5 years, through self-management, and in primary care, acute care/ED and hospital settings.
2023 GEMA[47] Spain	GEMA Spanish Guideline on the Management of Asthma, Version 5.3	Sociedad Española de Neumología y Cirugía Torácica (SEPAR)	Management of asthma in both adults and children in primary care and specialised care (including outpatient clinic, ED, hospital inpatient).

Year Shorthand name Country	Guideline title	Associated society or body	Primary topic of guideline
2022 NACA[51] Australia	Australian Asthma Handbook, Version 2.2	National Asthma Council of Australia	Management of adults and children with asthma. While this CPG was developed for primary care professionals, the section outlining management of acute asthma exacerbation includes management in other clinical settings, such as the ED.
2022 RRS[48] Russia	Federal Clinical Guideline on Bronchial Asthma (2022) *Translation required from Russian to English*	Russian Respiratory Society	Management of asthma in children, adolescents, adults and pregnant women, across various healthcare settings, including primary care, specialised outpatient clinics, EDs, and hospitals.
2019 BTS/SIGN[50] United Kingdom	SIGN 158: British Guideline on the Management of Asthma (2019)	Scottish Intercollegiate Guidelines Network (SIGN), British Thoracic Society (BTS)	Management of asthma in adults, adolescents, children in clinical settings.
2019 SFMU/SRLF[45] France	Management of Severe Asthma Exacerbation (2019)	Societe Francaise de Medecine d'Urgence, the Societe de Reanimation de Langue Francaise and the French Group for Pediatric Intensive Care and Emergencies	Management of severe asthma exacerbation in adults, children, and pregnant women in an acute care setting.
2018 SRS[46] Switzerland	Diagnosis and Management of Asthma (2018)	Swiss Respiratory Society	Diagnosis and management of asthma in adults, adolescents and children aged 6-11 years of age, including self-management, primary care, ED and or acute care settings.

Key: BTS – British Thoracic Society; CPG - clinical practice guideline; ED –emergency department; GEMA - Guía Espanola para el Manejo del Asma; GINA – Global Initiative for Asthma; NACA – National Asthma Council Australia; NVALT – Dutch Association of Pulmonologists; NVL – National Care Guidelines (Germany); RRS – Russian Respiratory Society; SIGN – Scottish Intercollegiate Guidelines Network; SINA – Saudi Initiative for Asthma; SRS – Swiss Respiratory Society; SFMU/SRLF - Societe Francaise de Medecine d'Urgence, the Societe de Reanimation de Langue Francaise.

3.2.2 Methods to obtain evidence and recommendations

Methods to obtain evidence used to formulate the recommendations varied across guidelines, and were often poorly reported. Eight of the 10 guidelines outlined that a systematic search for relevant literature was conducted,[45, 47, 48, 50-54], of which five provided insufficient detail to indicate whether anything more than a broad search was conducted and three clearly outlined details of topic-specific searches conducted.[50, 53, 54] Two guidelines failed to sufficiently describe how the evidence base was obtained.[46, 49]

All guidelines reported that recommendations and or overall guideline development were informed by the available evidence base and consensus agreement. Three of the guidelines reported using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) methodology to guide the certainty of the evidence and the strength of the recommendation.[45, 53, 54] Three guidelines classified both the certainty of the evidence and the strength of recommendations based on alternative pre-defined scales,[47, 48, 50] while four guidelines only classified the level of evidence to support the recommendation.[46, 49, 52, 54] An overview of the methods to obtain evidence and formulate recommendations reported in the included guidelines is outlined in Table 4.

Overall, details of the EtD processes adopted by GDGs in the development of the guidelines were not well-reported. All GDGs considered the quality of the available scientific literature and peer-reviewed studies in the development of evidence-based guidelines. Four guidelines reported that clinical relevance of the evidence and clinical best practice were also considered,[50, 51, 53, 54] and only one guideline specifically reported considering the applicability of study results to the relevant target population as outlined in the guideline. [53] Four guidelines clearly outlined that benefits and risks or harms of interventions were considered as part of the EtD process,[47, 51, 53, 54] while only two guidelines explicitly reported considering costs when formulating recommendations.[47, 54] Patient preferences and acceptability were reported as considerations in the development process for three guidelines.[47, 53, 54] Three of the included guidelines stated that feasibility was a consideration in the EtD process.[51, 53, 54] Only one GDG reported having considered ethical implications when developing recommendations as part of guideline development.[53]

Table 4 Guideline development process

Shorthand name Year	Development process	Details of evidence base Search dates	Certainty of evidence and strength of recommendations	EtD process
GINA[52] 2024	Results of literature review reviewed by a scientific committee. The respiratory community was invited to submit any other peer-reviewed article for consideration. External review of final draft document by patient advocates and experts internationally.	Twice yearly review of the literature. Two PubMed searches per year, each covering the previous 18 months. Filters established by the Science committee: only items with abstracts, clinical trials (RCTs and observational) or meta-analyses or systematic review. Broad search terms: asthma, all ages. Specific search dates not reported.	**Level of evidence:** Grading system is based on that developed by the National Heart Lung and Blood Institute, where sources of evidence for each are: **A:** RCTs, systematic review, observational evidence, i.e. rich body of data. **B:** RCTs and systematic review, but limited body of data. **C:** Non-randomised trials or observational studies. **D:** Panel consensus judgement.	Quality and relevance of original research and scientific review publications discussed. GRADE assessments of systematic review considered.
NVALT[54] 2024	The evidence was gathered from systematic reviews and clinical studies, decisions were based on a consensus-driven process,	Systematic search strategy including databases searched, dates of inclusion are outlined.	GRADE methodology: Naming and prioritising clinically (patient) relevant outcome measures, a systematic review per outcome measure, and an assessment of the strength of evidence per outcome measure based on the eight GRADE domains. **GRADE definitions:**	Evidence tables were included. The evidence was gathered from systematic reviews and clinical studies, decisions were made based on a consensus-

Shorthand name Year	Development process	Details of evidence base Search dates	Certainty of evidence and strength of recommendations	EtD process
	supported by GRADE methodology.	Detailed search strategies located in an accompanying document. Search dates varied by topic; searches for some topics included literature up until December 2021, with other topics including literature until August 2022.	**High:** High confidence that true treatment effect is close the estimated treatment effect; highly unlikely that new large-scale studies would change conclusion **Reasonable:** Reasonable certainty that true effect of treatment is close to estimated treatment effect; possible that new large-scale studies would change conclusion **Low:** Low confidence that true treatment effect is close to estimated treatment effect; real chance that new large-scale studies would change conclusion **Very low:** Very low confidence that true treatment effect is close to the estimated treatment effect; conclusion is very uncertain.	driven process, supported by GRADE methodology. The following domains were considered: Pros and cons of the intervention and the quality of the evidence; values and preferences of patients (and possibly their caregivers); costs; acceptability and feasibility of implementation.
NVL[53] 2024	Cross-topic systematic search conducted to inform guideline development. As part of the update of the NVL Asthma (to version 5), the contents of all chapters were reviewed, updated	Cross-topic structured search was conducted using broad search terms for 4 research institutions (NICE, IQWIG, Cochrane and AHRQ) from November 2018 (end of search period for 4th edition of the NVL), until September (IQWIG, NICE, AHRQ) or October (Cochrane only) 2022.	GRADE methodology used. It was noted whether the recommendation was based on a critical evaluation of the results of a systematic literature search or whether it was made on the basis of consensus. Additionally, it is noted whether the recommendation is: ▪ new-newly formulated	Yes (tables included). In addition to the underlying evidence (assessment of the benefits and harms of interventions), the awarding of recommendation grades also took into account ethical obligations, clinical relevance of the effectiveness measures of the studies, applicability of the study results to the target

Shorthand name Year	Development process	Details of evidence base Search dates	Certainty of evidence and strength of recommendations	EtD process
	where necessary and formally confirmed by the guideline group.		▪ modified-whether it is a review and adaptation of a previously existing recommendation, or ▪ confirmed-whether it is adopted without changes from the previous edition or version after review by the GDG. Detailed information on methodology (e.g. composition of the guideline group, patient participation, selection and evaluation of evidence, consensus process, handling of conflicts of interest) is linked in accompanying document.[55]	patient group, patient preferences and feasibility in everyday medical practice.
SINA[49] 2024	Each section internally reviewed at least twice by SINA panel members. A panel of international experts reviewed the guidelines, and their recommendations were "thoughtfully considered".	Details of search databases, search strings and search dates not reported. Noted that this CPG was previously updated in 2021, and that this update was produced based on the available evidence, with a particular emphasis on local literature and the current setting in Saudi Arabia.	**Level of evidence** Evidence graded A,B,C,D, where: **A:** RCTs with a rich body of data. **B:** RCTs with a limited body of data. **C:** Non-randomised trials and observational studies. **D:** SINA panel consensus judgement. Used in cases where provision of guidance was deemed valuable, but clinical literature on the subject was insufficient to justify placement in one of the other categories.	Reported that guidelines are based on the best available evidence, with emphasis on local literature and current setting in Saudi Arabia. Where inadequate or lack of evidence, consensus among the SINA Panel was followed. The SINA panel conducted frequent roundtable discussions and virtual discussions. International experts

Shorthand name Year	Development process	Details of evidence base Search dates	Certainty of evidence and strength of recommendations	EtD process
				contributed to draft guidelines.
GEMA[47] 2023	Systematic search of the literature. Evidence was rated on a pre-defined rating scale, and recommendation provided. Experts in the methodology of clinical practice guidelines from the INPECS critically reviewed the methodology and writing of the updated guidelines, including both the text and the recommendations. Final recommendations revised and agreed on (Delphi method) by a group of experts in asthma from the	Annual update consisted of 4 experts identifying, reviewing and incorporating new and relevant studies published in 2022, since the previous GEMA update (version 5.2). A systematic search of the literature was undertaken, and reference lists of main international guidelines searched. These experts selected the 40 most appropriate citations for the update, focusing on journals with high-impact factors (details of journals not specified). Details of search terms not provided.	**Level of Evidence:** Rated from A to D, where: **A:** Systematic review of RCTs with or without meta-analysis; and RCTs with low risk of bias. Evidence is based on a substantial number of well-designed studies with consistent results. **B:** Systematic review of RCTs with or without meta-analysis; and RCTs with moderate risk of bias. Evidence obtained from a limited number of studies and/or inconsistent results. **C:** Evidence obtained from non-randomised, observational or uncontrolled studies. **D:** Clinical experience or scientific literature that cannot be included in category C. **Rating of Recommendation:** Two levels of recommendation: **R1:** Robust recommendations, associated with more benefits than risks according to the opinion of the group of authors **R2:** Weak recommendations, that is, those in which some uncertainty exists as to whether its application might entail more benefits than risks.	Evidence was classified by level, then recommendations formulated based on the evidence obtained. The quality of the information was weighed based on this classification, along with the balance between risks and benefits of interventions, the costs (according to the available specialised literature), and the patients values and preferences (through the participation of FENAER members). The categorisation of the recommendations established by consensus, of the authors and then by the reviewers (Delphi method).

Shorthand name Year	Development process	Details of evidence base Search dates	Certainty of evidence and strength of recommendations	EtD process
	participating societies. Recommendations not achieving a certain consensus level were removed from the final document.			
NACA[51] 2022	Guideline was developed following structured literature reviews, with recommendations graded on the level of available evidence. Where searches were inconclusive, consensus recommendations could also be made, formulated by multi-disciplinary working group. Final recommendations were formulated by working group	Details of search databases, search strings and search dates not reported. While specific search dates were not provided, the guideline notes that the development work for this update undertaken between August 2021 and April 2022. Reported that evidence-based recommendations are based on the evidence synthesised from structured literature reviews.	**Evidence-based recommendations** Graded A-D, where: **A:** Based on a systematic literature review and formulated by multidisciplinary working group using NHMRC grading method. Body of evidence can be trusted to guide practice. **B:** Based on a systematic literature review and formulated by multidisciplinary working group using NHMRC grading method. Body of evidence can be trusted to guide practice in most situations. **C:** Based on a systematic literature review and formulated by multidisciplinary working group using NHMRC grading method. Body of evidence provides some support for recommendation but care should be taken in its application. **D:** Based on a systematic literature review and formulated by multidisciplinary working group using NHMRC grading method. Body of evidence is weak and recommendation must be applied with caution.	When formulating evidence-based recommendations on interventions, working groups followed a structured consensus process to consider a range of factors such as effect sizes, harms and benefits, reliability of the evidence, relevance of the evidence to Australian clinical practice, and feasibility of implementing the intervention. For recommendations on clinical questions and topics not selected for structured literature search, working groups formulated recommendations through a consensus process.

Shorthand name Year	Development process	Details of evidence base Search dates	Certainty of evidence and strength of recommendations	EtD process
	involving structured consensus process.		*Additionally recommendations could be classified as:* Consensus recommendation (following inconclusive literature search): Formulated by a multidisciplinary working group based on available evidence, clinical experience and expert opinion after structured literature review yielded insufficient evidence for an evidence-based recommendation. Adapted from existing guidance: Based on a reliable clinical practice guideline or position statement. Consensus recommendation: Formulated by a multidisciplinary working group based on clinical experience and expert opinion (informed by evidence, where available).	
RRS[48] 2022	Reported that CPG was developed following systematic reviews and expert consensus. The final recommendations were approved by the Scientific and Practical Council of the Ministry of	Details of search strings, search dates, and search databases not reported. States that guidelines are systematically updated at least once every 3 years, and not more than every 6 months.	**Level of evidence for prevention, treatment and rehabilitation interventions** Numbered 1-5, where: **1:** Systematic review of RCTs using meta-analyses **2:** Single RCTs and systematic reviews of studies of any design, except RCTs using meta-analyses **3:** Non-randomised comparative studies, including cohort studies **4:** Non-comparative studies, description of a clinical case or case series, case-control studies	

Shorthand name Year	Development process	Details of evidence base Search dates	Certainty of evidence and strength of recommendations	EtD process
	Health of the Russian Federation.		**5:** Only the rationale for the mechanism of action of the intervention (pre-clinical studies) or expert opinion is available. **Strength of recommendation for prevention, diagnosis, treatment, and rehabilitation methods** Rated A,B,C, where: **A:** Strong recommendation (where all performance criteria/outcomes are important, all studies are of high or satisfactory methodological quality, conclusions on the outcomes of interest are consistent). **B:** Conditional recommendation (not all performance criteria/outcomes considered are important, not all studies are of high or satisfactory methodological quality, and or conclusions on outcomes of interest are not consistent). **C:** Weak recommendation (lack of evidence of adequate quality; all performance criteria/outcomes considered are unimportant, all studies are of poor methodological quality and conclusions on outcomes of interest are not consistent).	
BTS/SIGN[50] 2019	Developed by multidisciplinary groups of practising clinicians using a standard methodology based on a systematic	A systematic review of the literature was carried out using an explicit search strategy. Broad searches carried out in May/June 2018 (to	**Levels of evidence** **1++:** High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias. **1+:** Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias.	The considered judgement and recommendations in the guideline were developed by the self-management Evidence Review Group in accordance with SIGN methodology.

Shorthand name Year	Development process	Details of evidence base Search dates	Certainty of evidence and strength of recommendations	EtD process
	review of the evidence, public consultation, independent expert review	include literature from 2012-2018) to identify studies looking at ECMO or other potentially lifesaving therapies for people with life-threatening or near-fatal asthma. No study design filter was applied. Specific details of search available on SIGN website.[56]	**1:** Meta-analyses, systematic reviews, or RCTs with a high risk of bias. **2++:** High-quality systematic reviews of case-control or cohort studies; high-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal. **2+:** Well-conducted case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal; **2:** Case-control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal **3:** Non-analytic studies, e.g. case reports, case series **4:** Expert opinion **Grades of recommendation** **A:** At least one meta-analysis, systematic review, or RCT rated as 1++ directly applicable to the target population; or body of evidence mostly of "1+" studies, directly applicable and overall consistent **B:** Body of evidence of studies rated 2++, directly applicable and overall consistent; or Extrapolated evidence from "1++" or "1+" studies **C:** Body of evidence of studies rated 2+, directly applicable and overall consistent; or Extrapolated evidence from "2++" studies	This included systematic literature reviews, consultation, and peer review, which ensured that recommendations are evidence-based and reflect current best practices.

Shorthand name Year	Development process	Details of evidence base Search dates	Certainty of evidence and strength of recommendations	EtD process
			D: Evidence level 3 or 4; or Extrapolated evidence from "2+" studies	
SFMU/SRLF[45] 2019	Bibliographic search was conducted to obtain literature of interest. Guidelines formulated according to GRADE methodology.	Reported that bibliographic search was conducted using the MEDLINE database via PubMed and the Cochrane database. Publications had to be in English or French. Details of search dates or search strings not reported.	The literature was analysed and the guidelines formulated using GRADE methodology. The analysis focused on recent data according to an order of appraisal ranging from meta-analyses to randomised trials to observational studies	To approve a recommendation regarding a criterion, at least 50% of the experts had to be in agreement (with GRADE recommendation) and less than 20% in disagreement. For an agreement to be strong, at least 70% of the experts had to agree. In the absence of strong agreement, the recommendations were reformulated and rated again, with a view to reaching a consensus. Only expert opinions that elicited strong agreement were kept.
SRS[46] 2018	Stated that CPG was developed based on evidence from clinical studies, 2016 GINA report, and expert consensus.	Details of search databases, search strings and search dates not reported.	**Level of evidence:** Rated A, B, C, D, where: **A:** RCTs, rich body of data. (i.e. consistent pattern of findings in the population of interest, substantial no. of studies, substantial no. of participants)	Detail of EtD process not provided, however it is stated that the CPG was developed based on evidence from clinical studies, GINA report (2016) and expert consensus.

Shorthand name Year	Development process	Details of evidence base Search dates	Certainty of evidence and strength of recommendations	EtD process
		CPG states that the Swiss Respiratory Society felt the need to provide a new guideline based on both the available literature and the recommendations of the 2016 GINA report.	**B:** RCTs, limited body of data (i.e. limited no. of RCTs, and post-hoc, subgroup or meta-analysis of RCTs. Or, if RCTs, they could be small, population could differ from target population, or results could be inconsistent). **C:** Non-randomised trials, or observational studies. **D:** Panel consensus judgement (i.e. used if provision of guidance was deemed valuable, but clinical literature was deemed insufficient to justify placement in category A,B, or C. Panel consensus is based on clinical experience or knowledge that does not meet the other criteria above).	

Key: AHRQ – Agency for Healthcare, Research and Quality; BTS– British Thoracic Society; CPG – clinical practice guideline; ECMO – extra-corporeal membrane oxygenation; EtD – evidence to decision; FENAER - Spanish Federation of Allergy and Airways Diseases Patients' Associations; GDG – guideline development group; GEMA - Guía Espanola para el Manejo del Asma; GINA – Global Initiative for Asthma; GRADE – Grading of Recommendations, Assessment, Development, and Evaluations; INPECS – Institute for Clinical and Healthcare Excellence; IQWIG – Institute for Quality and Efficiency in Health Care; NACA – National Asthma Council Australia; NICE – National Institute for Health and Care Excellence; NHMRC – National Health and Medical Research Council; NVALT – Dutch Association of Pulmonologists; NVL – National Care Guidelines; RCT – randomised controlled trial; RRS – Russian Respiratory Society; SIGN – Scottish Intercollegiate Guidelines Network; SINA – Saudi Initiative for Asthma; SRS – Swiss Respiratory Society; SFMU/SRLF - Societe Francaise de Medecine d'Urgence, the Societe de Reanimation de Langue Francaise.

3.3 Currency of guidelines

Of the 10 guidelines included in this review, four were published in 2024,[49, 52-54] one in 2023,[47] two each were published in 2022[46, 48] and 2019,[45, 50] and one was published in 2018.[46] Reporting of methodological approach varied widely across the included guidelines, with few guidelines reporting sufficient detail to enable a replicable systematic search of the literature. Only three guidelines clearly reported conducting topic-specific systematic searches of the literature.[50, 53, 54] NVL (2024)[53] and NVALT (2024)[54] report that topic-specific searches were conducted across dates in 2021 and 2022. BTS/SIGN (2019) also reported topic-specific searches, with the search specifically relating to a primary topic of interest for this review (extracorporeal membrane oxygenation (ECMO)) conducted in 2018.[50]

Details of search dates are included in Table 4. Two guidelines, GINA (2024)[52] and GEMA (2023),[47] were identified as having conducted the most recent broad systematic searches of the literature related to asthma. GINA (2024) stated that a broad systematic search is conducted twice yearly, over the preceding 18 month period, but does not specify precise search dates.[52] GEMA (2023) reported that a systematic search was conducted for literature published in 2022, as part of an annual guideline update.[47]

3.4 Quality appraisal

An overview of the methodological quality of the included guidelines, as assessed by the AGREE-GRS tool,[44] is provided in Table 5 and summarised below. Quality was assessed under four core items, and mean scores between one (lowest rating) and seven (highest rating) for each guideline are provided. In addition, each guideline was ascribed an overall quality assessment score. The included guidelines varied in terms of quality, with some guidelines found to be of consistently high quality across all domains.

3.4.1 Process of development

Two guidelines, NVL (2024)[53] and NVALT (2024),[54] were deemed to have the highest possible rating (7) with regard to process development, with GEMA (2023)[47] and BTS/SIGN (2019)[50] also scoring highly in this core item. Though most guidelines report that the evidence base underpinning the guideline was obtained through a systematic literature search, reviewers noted that NVL (2024),[53] NVALT (2024)[54] and BTS/SIGN (2019)[50] provide

greater detail as to how their evidence base was systematically developed. Furthermore, reviewers noted that these three guidelines comprehensively review each of (i) alternative treatment options, (ii) health benefits and harms, (iii) risks and (iv) costs concerning the primary topics of interest, domains that are not always extensively addressed in other guidelines.

3.4.2 Presentation style

NVL (2024),[53] NVALT (2024),[54] BTS/SIGN (2019)[50] and GEMA (2023)[47] were deemed to have the highest scores with regard to presentation style and navigability. Reviewers noted that, while some guidelines clearly outlined recommendations and associated evidence underpinning each recommendation, often guidelines did not clearly present recommendations, and the associated rationale was not always clearly outlined. Where guidelines do include care schematic pathways, this aided accessibility.

3.4.3 Completeness of reporting

Reviewers considered whether guidelines were complete enough to inform decision-making, and whether the development process was transparent and reproducible. Reviewers noted that guidelines do not always consistently describe the certainty of recommendations or level of evidence underpinning each clinical topic addressed (Table 1). Reporting of methodological approach adopted in the guideline development process often lacks granularity and hence reproducibility. BTS/SIGN (2019),[50] NVL (2024)[53] and NVALT (2024)[54] were highly rated (6.5 out of 7) in this domain.

3.4.4 Clinical validity

When judging the clinical validity of guidelines, reviewers (AB and MG) considered whether recommendations were clinically sound, and whether they were appropriate for the intended patients. Overall, recommendations made across guidelines are evidence-based and consistent, with broad patient applicability. Many guidelines scored highly, with BTS/SIGN (2019)[50] and NVL (2024)[53] deemed to have the highest rating in this domain (rating 6.5), followed by GINA (2024),[52] GEMA (2023),[47] NVALT (2024),[54] NACA (2022)[51] and SFMU/SRLF (2019)[45] (each rating 6). However, it was noted that guidelines vary in their level of detail provided, and in some cases, guidelines lack comprehensive rationale accompanying

certain recommendations. Reviewers noted that it was often difficult to discern clinical recommendations from good practice points, or from supporting information provided.

3.4.5 Overall quality assessment score

Reviewers assigned an overall quality assessment score to the included guidelines, with NVL (2024)[53] and NVALT (2024)[54] deemed to have the highest overall scores (6.5), followed by BTS/SIGN (2019)[50] (rating 6), and GEMA (2024),[47] rating 5.5. Guidelines that were deemed to be of medium quality included GINA (2024),[52] rating 4.5, and SFMU/SRLF (2019)[45] and NACA (2022),[51] which both had a rating of 4. Guidelines deemed to be of lower quality included SRS (2018),[46] RRS (2022),[48] and SINA (2024).[49]

Table 5 Quality of included guidelines using AGREE-GRS

Shorthand name	Process of development	Presentation style	Completeness of reporting	Clinical validity	Overall quality assessment score
GINA (2024)[52]	5	4.5	4	6	4.5
NVALT (2024)[54]	7	6.5	6.5	6	6.5
NVL (2024)[53]	7	6.5	6.5	6.5	6.5
SINA (2024)[49]	2.5	2.5	2	5	3
GEMA (2023)[47]	6	5.5	5.5	6	5.5
NACA (2022)[51]	4	3	4	6	4
RRS (2022)[48]	4	3.5	2.5	3	3
BTS/SIGN (2019)[50]	6	6	6.5	6.5	6
SFMU/SRLF (2019)[45]	4	4.5	3.5	6	4
SRS (2018)[46]	3	3	3	3.5	3

Key: AGREE-GRS- Appraisal of Guidelines for Research and Evaluation Global Rating Scale; BTS/SIGN – British Thoracic Society/Scottish Intercollegiate Guidelines Network; GEMA - Guía Espanola para el Manejo del Asma; GINA – Global Initiative for Asthma; NACA – National Asthma Council Australia; NVALT – Dutch Association of Pulmonologists; NVL – National Care Guidelines (Germany); RRS – Russian Respiratory Society; SINA – Saudi Initiative for Asthma; SRS – Swiss Respiratory Society; SFMU/SRLF - Societe Francaise de Medecine d'Urgence, the Societe de Reanimation de Langue Francaise.
Note: Within each domain the possible score ranged from 0 to 7.

3.5 Comparison of 2015 Irish recommendations and international recommendations

Table 6 provides an overview of how the findings of this review of international guidelines compare with the current Irish NCG No. 14, *Management of an Acute Asthma Attack in Adults (aged 16 years and older),*[32] published in 2015. Outlined are current recommendations from the NCG relating to primary topics of interest as specified by the GDG in the PIC for the current review (Table 1) in addition to a summary of developments identified through this review concerning each primary topic. Reviewers considered as developments of interest (i) whether the included guidelines lacked consensus either with each other, or with the current recommendation outlined in NCG No. 14,[32] (ii) the strength of the recommendation or certainty of evidence underpinning these, as identified in the guidelines included in this

review, and (iii) whether emerging evidence was identified. The most recent search dates identified relating to each primary topic of interest are also outlined, to indicate the most recent evidence synthesis conducted by GDGs. As previously noted, while searches were often reported as being systematically conducted, specifics of the searches were not always provided. As such, Table 6 outlines both the most recent broad searches conducted, and topic-specific searches where these were specified.

Table 6 Table of new developments relating to primary topics of interest in this review

Primary topic of interest	NCG No. 14 (2015)[32] Recommendation	New developments in international CPGs	Details of most recent search dates from eligible CPGs
Peak flow cut-offs as an indicator to inform hospital admission and ED discharge	**Recommendation No. 5** Admit patients to hospital whose peak flow is less than 75% best or predicted after initial treatment. **Recommendation No. 6** Patients whose peak flow is greater than 75% best or predicted one hour after initial treatment may be discharged from ED unless they meet any of the following criteria, when admission may be appropriate….. **Recommendation No. 21** Refer any patient: ▪ Requiring ventilator support ▪ With acute severe or life threatening asthma, failing to respond to therapy, evidenced by [*listed indicators, including*] deteriorating PEF	Nine guidelines discuss PEF cut-offs as indicators to inform either hospital admission or ED discharge, seven of which provided specific values. Broadly, guidelines consider hospital admission where PEF<50% predicted or best, and consider discharge from ED where PEF is 60-80%, while also taking into account other clinical aspects. Recommendations were rarely graded, and evidence often not cited. Where evidence was cited, there was little consistency across guidelines. Two guidelines note difficulties with using PEF values to inform decisions relating to care setting, one of which cites strength of this advice as very low GRADE.	**Broad search date:** Ongoing broad searches carried out by GINA (2024) every 6 months, covering literature from previous 18 months (no date specified). GEMA (2023). Annual update, including literature published in 2022. **Topic-specific search:** NVALT (2024) Targeted systematic literature search performed 28 March 2022, with no date limit specified.*
Respiratory rate as an indicator to inform hospital referral and/or admission and/or ICU admission	Not addressed	Seven guidelines refer to respiratory rate as an indicator to inform level of care, five of which note a specific rate (25 breaths per minute or 30 breaths per minute) to inform transfer from primary care to acute care. Rates to inform transfer to ICU were not indicated. Evidence in support of the recommendations were rarely reported. Recommendations were rarely graded.	**Broad search:** Ongoing broad searches carried out by GINA (2024) every 6 months, covering literature from previous 18 months (no date specified). GEMA (2023). Annual update, including literature published in 2022. **Topic-specific search:** Not conducted

Primary topic of interest	NCG No. 14 (2015)[32] Recommendation	New developments in international CPGs	Details of most recent search dates from eligible CPGs
Chest X-ray	**Not a formal recommendation but elaboration under Recommendation No. 7** Good clinical practice suggests that a chest X-ray is not routinely recommended in patients with an asthma attack in the absence of: suspected pneumomediastinum or pneumothorax suspected consolidation life threatening asthma failure to respond to treatment satisfactorily requirement for ventilation	Nine guidelines refer to the use of chest X-ray and one guideline refers to imaging. Five state that chest X-ray is not routinely recommended. Nine guidelines state that it may be considered if a complicating or alternative cardiopulmonary process (most often pneumothorax, pneumomediastinum/ mediastinal emphysema, consolidation, or pneumonia) is suspected, five when patients are not responding to treatment, four when the asthma attack is life-threatening, and two when the patient requires ventilation.	**Broad search:** Ongoing broad searches carried out by GINA (2024) every 6 months, covering literature from previous 18 months (no date specified). GEMA (2023). Annual update, including literature published in 2022. **Topic-specific search:** Not conducted
High-flow oxygen	Not addressed	Five guidelines specifically address the use of high-flow oxygen for acute asthma exacerbations. Few provide strength of recommendation or level of evidence associated with recommendation. Overall, guidelines recommend against use in acute exacerbations, and/or specify that the use of controlled flow oxygen is preferred. Regarding the use of high flow nasal cannula, NVALT (2024) having undertaken the most recent topic-specific review, found that the emerging evidence to support high-flow oxygen over conventional oxygen delivery is uncertain.	**Broad search:** Ongoing broad searches carried out by GEMA (2023), Annual update, including identified literature published in 2022. **Topic-specific search:** NVALT (2024) Targeted systematic literature search performed to include literature until December 2021.
NIV	**Not a formal recommendation** Good practice point: NIV for acute asthma should only be considered in an ICU or equivalent clinical setting.	Eight guidelines refer to the use of NIV. Three guidelines do not provide recommendations, citing lack of evidence. One guideline provides a recommendation against use of NIV for acute asthma. Four guidelines indicate that NIV may be used in certain circumstances such as respiratory failure; in the presence of severe dyspnea, hypercapnia, clinical signs of increased work of	**Broad search: Ongoing broad searches carried out by** GINA (2024) every 6 months, covering literature from previous 18 months (no date specified). GEMA (2023). Annual update, including literature published in 2022. **Topic-specific search:** NVALT (2024) Targeted systematic literature search performed to include literature until December 2021.

Primary topic of interest	NCG No. 14 (2015)[32] Recommendation	New developments in international CPGs	Details of most recent search dates from eligible CPGs
		respiratory muscles; severe exacerbations resistant to treatment; and in ICU setting.	
Oxygen-driven vs. air-driven nebulisation	**Recommendation No. 9** In hospital, ambulance and primary care, nebulised β_2 agonist bronchodilators should be driven by oxygen. **Recommendation No. 14** *(Re. β_2 agonist bronchodilators)* In acute asthma with life threatening features the nebulised route (oxygen-driven) is recommended.	Four guidelines refer to the use of oxygen-driven vs. air-driven nebulisation. One guideline reports that air-driven nebulisation may be used (based on consensus recommendation), two favour oxygen-driven nebulisation (level of evidence graded highly), and one reports that a systematic search yielded no evidence in non-hypoxaemic patients. Sparse literature identified. No emerging evidence was identified, but if air-driven delivery is becoming more commonly used in clinical practice, there is potential for a developing evidence base.	**Broad search:** Ongoing broad searches carried out by GINA (2024) every 6 months, covering literature from previous 18 months (no date specified). **Topic-specific search:** Not conducted.
Heliox	**Recommendation No. 20** Heliox is not recommended for use in acute asthma outside a clinical trial setting.	Six guidelines address heliox, with none advocating for its introduction to routine use or as part of a care pathway. Where reported, level of certainty in evidence is high, or strong agreement in recommendation. No emerging evidence is cited.	**Broad search:** Ongoing broad searches carried out by GINA (2024) every 6 months, covering literature from previous 18 months (no date specified). GEMA (2023). Annual update, including literature published in 2022. **Topic-specific search:** Not conducted
ECMO	Not addressed	Three guidelines refer to ECMO. Two from 2019 conditionally recommend it for refractory acute asthma. Sparse literature identified. Where evidence is graded, quality is low.	**Broad search:** NVL (2024) Broad search identified literature from November 2018 to search dates (September/October 2022). **Topic-specific search:** BTS/SIGN (2019) ECMO-specific search carried out in May/June 2018 to include literature published from 2012-2018.
IV β_2 agonists	**Recommendation No. 15** Reserve intravenous β2 agonists for those patients in whom inhaled therapy cannot be used reliably.	Nine guidelines refer to IV β_2 agonists. All recommendations broadly recommend against routine use, six conditionally recommend in situations where inhaled route is not possible, or where other treatments have failed. Where graded, level of evidence was deemed to be high. No emerging evidence is cited.	**Broad search:** Ongoing broad searches carried out by GINA (2024) every 6 months, covering literature from previous 18 months (no date specified). GEMA (2023). Annual update, including literature published in 2022. **Topic-specific search:** NVALT (2024) Targeted systematic literature search performed 31 August 2022, with no date limit specified.
IV magnesium sulphate	**Recommendation No. 18** Consider giving a single dose of IV magnesium sulphate for patients with: acute severe asthma who have not had a good initial response to	Ten guidelines refer to IV magnesium. All but one allow for the use of IV magnesium sulphate in patients experiencing severe asthma attack or failure to respond to treatment. NVALT (2024) recommended only giving IV magnesium sulphate as	**Broad search:** Ongoing broad searches carried out by GINA (2024) every 6 months, covering literature from previous 18 months (no date specified).

Primary topic of interest	NCG No. 14 (2015)[32] Recommendation	New developments in international CPGs	Details of most recent search dates from eligible CPGs
	inhaled bronchodilator therapy; Life threatening or near fatal asthma. IV Magnesium sulphate (1.2 - 2g IV infusion over 20 minutes) should only be used following consultation with senior medical staff.	an attempt to avoid mechanical ventilation or to shorten the duration of mechanical ventilation (no to low GRADE evidence).	GEMA (2023). Annual update, including literature published in 2022. **Topic-specific search:** NVALT (2024) Targeted systematic literature search performed 28 March 2022, with no date limit specified
IV aminophylline	Not addressed	Six guidelines refer to the use of IV aminophylline, three of which specifically recommend against use, two of which state it may be considered in life-threatening acute attack where other add-on treatments have failed, and one further guideline noting benefit above standard care is unlikely. Limited evidence and risk of adverse effects noted. Strength of recommendation or certainty in level of evidence rarely provided. No emerging evidence is cited.	**Broad search:** Ongoing broad searches carried out by GINA (2024) every 6 months, covering literature from previous 18 months (no date specified). **Topic-specific search:** NVALT (2024) Targeted systematic literature search performed 21 December 2021, with no date limit specified.
Ipratropium bromide	**Recommendation No. 17** Add nebulised ipratropium bromide (0.5 mg 4-6 hourly) to β_2 agonist treatment for patients with acute severe or life-threatening asthma or those with a poor initial response to β_2 agonist therapy.	Nine guidelines refer to the use of anticholinergics as an addition to short-acting β_2 agonists, all of which are in agreement with NCG guideline recommendation, and where reported, cite a high certainty in the recommendation. No emerging evidence is cited.	**Broad search:** Ongoing broad searches carried out by GINA (2024) every 6 months, covering literature from previous 18 months (no date specified). GEMA (2023). Annual update, including literature published in 2022. **Topic-specific search:** Not conducted
LTRAs (oral or IV)	Not addressed	Six guidelines refer to LTRAs. None recommend the use of LTRAs (oral or IV) as an add-on treatment in acute asthma exacerbation. Three guidelines state that further study is required to determine their clinical effectiveness in management of acute exacerbation. Strength of recommendation or certainty in evidence rarely provided. No emerging evidence is cited.	**Broad search:** Ongoing broad searches carried out by GINA (2024) every 6 months, covering literature from previous 18 months (no date specified). GEMA (2023). Annual update, including identified literature published in 2022. **Topic-specific search:** NVALT (2024) Targeted systematic literature search performed 31 August 2022, with no date limit specified.
Antibiotics	**Recommendation No. 17** Routine prescription of antibiotics is not indicated for patients with acute asthma.	Nine guidelines refer to the use of antibiotics. All nine guidelines state that they should not be used routinely in acute asthma unless indicated for signs of infection, with five guidelines specifying that the infection should be bacterial in nature.	**Broad search:** Ongoing broad searches carried out by GINA (2024) every 6 months, covering literature from previous 18 months (no date specified). GEMA (2023). Annual update, including literature published in 2022. **Topic-specific search:** Not conducted

Key: CPG – clinical practice guideline; ECMO – extracorporeal membrane oxygenation; ED – emergency department; g – gram; GEMA -Guía Espanola para el Manejo del Asma; GINA – Global Initiative for Asthma; ICU – intensive care unit; IV – intravenous; LTRA – leukotriene-receptor antagonist; mg- milligram; NCG – National Clinical Guideline; NIV – non-invasive ventilation; NVALT – Dutch Association of Pulmonologists; NVL – National Care Guidelines (Germany); PEF – peak expiratory flow.
* This search specifically related to the question "What is the place of lung function measurement with a peak flow meter, spirometer, or FeNOmeter in the diagnosis of adults with an asthma attack in the first two hours after presentation to the hospital", as such it not specifically answering the research question posed in this review.

3.6 Recommendations relating to primary topics of interest

Fourteen primary topics of interest for guideline recommendations were highlighted by the GDG, and included in the PIC for this review (see Table 1). The primary topics have been divided into four subgroups, relating to assessment of lung function and imaging, the use of oxygen-related interventions, the use of pharmacological interventions by intravenous (IV) route, and the use of other pharmacological interventions. A matrix for the primary topics included by the guidelines is provided in Table 7. A detailed overview of the recommendations are provided in Table 8, 9, 10 and 11.

Table 7 Matrix for the primary topics of interest addressed in the guidelines

	GINA (2024)[52]	NVALT (2024)[54]	NVL (2024)[53]	SINA (2024)[49]	GEMA (2023)[47]	NACA (2022)[51]	RRS (2022)[48]	BTS/SIGN (2019)[50]	SFMU/SRLF (2019)[45]	SRS (2018)[46]
Assessment of lung function and imaging										
PEF for admission and or discharge	✓	✓	✓	✓	✓	✓	✓	✓	✓	
Respiratory rate for ED discharge	✓		✓	✓	✓	✓		✓		✓
Chest X-ray	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Use of oxygen-related interventions										
High flow oxygen	✓	✓		✓	✓	✓				
Oxygen-driven vs. air-driven nebulisation				✓		✓		✓	✓	
Heliox	✓				✓	✓	✓	✓	✓	
ECMO			✓					✓	✓	
Use of NIV	✓	✓			✓	✓	✓	✓	✓	✓
Use of pharmacological interventions – IV route										
IV Magnesium	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
IV β_2 agonists	✓	✓	✓	✓	✓	✓		✓	✓	✓
IV aminophylline	✓	✓			✓	✓	✓	✓		
Use of pharmacological intervention – other										
Addition of anticholinergic to β_2 agonist	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
LTRAs	✓	✓			✓	✓	✓	✓		
Antibiotics	✓		✓	✓	✓	✓	✓	✓	✓	✓

Key: BTS/SIGN – British Thoracic Society/Scottish Intercollegiate Guidelines Network; ECMO – extra-corporeal membrane oxygenation; ED – emergency department; GEMA - Guía Espanola para el Manejo del Asma; GINA – Global Initiative for Asthma; IV - intravenous; LTRA – leukotriene-receptor antagonist; NACA – National Asthma Council Australia; NIV – Non-invasive ventilation; NVALT – Dutch Association of Pulmonologists; NVL – National Care Guidelines (Germany); PEF – peak expiratory flow; RRS – Russian Respiratory Society; SINA – Saudi Initiative for Asthma; SRS – Swiss Respiratory Society; SFMU/SRLF - Societe Francaise de Medecine d'Urgence, the Societe de Reanimation de Langue Francaise; vs – versus.

3.6.1 Lung function assessment and imaging

Peak flow cut-offs as an indicator to inform hospital admission and or ED discharge

Nine of the 10 included guidelines make reference to the use of peak expiratory flow (PEF) cut-off values to inform either hospital admission or ED discharge.[45-54] These values were often presented in care schematic pathways or figures, and strength of recommendations or associated level of evidence were rarely reported. Sources of evidence cited varied across the included guidelines, as did the cut-off values specified. Notable citations for each guideline are outlined in Table 8.

Peak flow cut-offs as an indicator to inform hospital admission

Seven guidelines discuss an initial PEF cut-off value to inform hospital admission for acute care.[45, 47-50, 52, 53] Overall, there was inconsistency observed across guidelines in the specific PEF cut-off values or ranges used to inform level of care required, though guidelines broadly indicate transfer to ED where PEF is less than or equal to 50% predicted, and admission to the intensive care unit (ICU) where PEF is less than or equal to 33% of predicted. GINA (2024) recommends that, where PEF is less than or equal to 50% of expected or previous best, it is necessary to refer the patient from primary care for treatment in an acute care or ED setting.[52] GINA (2024) also strongly recommends the measurement of lung function and, where possible and without unduly delaying treatment, PEF (or forced expiratory volume in one second (FEV1)) should be recorded before treatment is initiated.[52] The guideline also recommends that, in an acute care or ED setting, if pre-treatment PEF is less than 25% or post-treatment PEF is less than 40%, the patient should be admitted.[52] BTS/SIGN (2019) report similar PEF cut-off values, recommending that a PEF of 33–50% of previous best or predicted indicates acute severe exacerbation and should be treated in an acute care setting, while a PEF of less than 33% best or predicted is life-threatening and warrants admission to the ICU (Grade of recommendation D; Level of evidence 2+, 2++).[50] BTS/SIGN (2019) also note that predicted PEF values should be used to recognise acute asthma only if the recent best PEF (within two years) is unknown (Level of evidence 4).[50]

NVL (2024) reports that, if PEF is less than or equal to 50% predicted or best (indicating severe exacerbation) upon arrival to the doctor’s office or emergency room, hospital admission

should be considered, and if PEF is less than 33% predicted or best (indicating life-threatening exacerbation), emergency medical attendance is required.[53] NVL (2024) also reports that if PEF remains less than 40% after initial treatment, then ICU admission is necessary.[53] GEMA (2023) notes that admission to hospital is necessary if PEF is less than 50-60% after treatment, or PEF or FEV1 is 50-70% on arrival.[47] While no specific PEF value was provided to indicate ICU admission, GEMA (2023) states that admission may be necessary if progressive functional deterioration is occurring despite treatment.[47] SINA (2024) report that where PEF is 30-50% predicted, exacerbation should be treated in the ED, and where PEF is less than 30% of predicted, referral to ICU is necessary.[49] RRS (2022) does not indicate a PEF cut-off for referral to acute care or ED setting, however it does state that where PEF is 60-80% or better, treatment for the exacerbation may be continued at home rather than requiring admission to ED.[48]

SFMU/SRLF (2019) did not provide a PEF cut-off value for admission to acute care, noting that PEF on admission was seldom studied.[46] Similarly, no PEF value to denote transfer to ICU care was provided, and instead the guideline recommends that admission to intensive care of adult patients with severe asthma exacerbation should be discussed early, and on an individual basis, owing to the lack of specific criteria on the subject.[46]

Peak flow cut-offs as an indicator to inform ED discharge

Five guidelines refer to a PEF value as an indicator to inform ED discharge, with most guidelines recommending consideration of discharge if PEF meets cut-offs between 60% and 80%,[45, 47, 50, 52, 53] taken in combination with other clinical considerations and conditions. BTS/SIGN (2019) recommends that, provided other pre-specified criteria are met, which would warrant further treatment, patients whose peak flow is greater than 75% (best or predicted) one hour after initial treatment may be discharged from ED (Grade of recommendation C).[50] GEMA (2023) notes that patients with PEF of greater than 70% (predicted or personal best value) and with minimal symptoms can be discharged from the hospital (Strength of recommendation R2). If additional treatment was required, and after one to three hours a patient has shown a good response to treatment, is stable and asymptomatic, with a PEF of greater than 60%, discharge can be considered.[47] GINA (2024) reports similar, recommending that discharge may be considered if PEF is 60-80% of predicted

or personal best, but if PEF is less than 60%, treatment should be continued.[52] GINA (2024) also recommends that, in an acute care or ED setting after considering the patient's risk factors, and the availability of follow-up care, if post-treatment lung function is greater than 60%, discharge is recommended and if post-treatment lung function is 40-60%, discharge may be possible.[52] SMFU/SRLF (2019) report that, after an hour of continuous treatment with short-acting β_2 adrenergic agonists, patients with improved symptoms, including PEF that is 60-80% of the patient's theoretical maximum value, can be considered for discharge.[45] NVL (2024) reports that patient may be discharged from ED if PEF stabilises after either (i) one to three hours of treatment or (ii) one hour since last treatment.[53]

Peak flow cut-offs as an indicator in the management of acute asthma attack

Two guidelines do not provide PEF cut-off values to indicate either discharge from ED or admission to hospital, but instead discuss the use of PEF values in the management of acute asthma exacerbations.[51, 54] NACA (2022),[51] notes that PEF rates obtained using a peak flow meter underestimates the severity of airflow limitation in patients with acute asthma, compared with FEV1 obtained by spirometry,[57] and that PEF is not a sensitive measure of small clinical improvements as perceived by the patient.[58] NVALT (2024) similarly notes that it is unclear whether PEF measured within two hours of presentation predicts (i) the risk of admission to critical care in adults presenting at the ED with acute asthma (very low GRADE), or (ii) the risk of admission or to critical care or relapse within seven days in adults presenting at the ED with acute asthma,[54] citing Goodacre et al. (2014)[59] as underlying evidence.

Respiratory rate as an indicator to inform hospital referral and or admission and or ICU admission

Seven guidelines refer to respiratory rate as an indicator to inform level of care.[46, 47, 49-53] Few guidelines clearly provide sources or the certainty of evidence underpinning recommendations. GEMA (2023)[47] cite Pinera-Salmerón et al. (2020)[60] as supporting evidence for their recommendation, while NACA (2022)[51] cite two studies by Wilson et al. (2003)[61] and Aldington et al. (2007).[62] Two guidelines, BTS/SIGN (2019)[50] and NVL (2024),[53] recommend transfer to hospital from primary care if a patient's respiratory rate is greater than 25 breaths per minute (BTS/SIGN (2019): Grade of recommendation B).[50] However, three guidelines, (GINA (2024),[52] SRS (2018),[46] and SINA (2024)[49]), two of which

were deemed lower quality, recommend transfer where respiratory rate is greater than 30 breaths per minute. No guideline notes a specific respiratory rate to inform referral to ICU admission, though several note that poor respiratory effort and respiratory arrest are indicators of a life-threatening exacerbation, in which case ICU admission would be required.[47, 49-51, 53]

Chest X-ray in acute asthma attack

Nine guidelines refer to the use of chest X-ray in the treatment of an acute asthma attack[45-52, 54] and one guideline refers to imaging broadly that likely includes chest X-ray.[53] Five guidelines state that chest X-ray is not routinely recommended.[46, 49, 50, 52, 53] Nine guidelines state that chest X-ray may be considered if a complicating or alternative cardiopulmonary process (most often pneumothorax, pneumomediastinum/ mediastinal emphysema, pneumonitis, consolidation, or pneumonia) is suspected.[46-52] Five guidelines allow for the use of chest X-ray when patients are not responding to treatment,[45-47, 50, 52, 53] four when the asthma attack is life-threatening,[47-50] and two when the patient requires ventilation.[48, 50] The most common citation was a 1991 paper by White and colleagues[63] cited by three of the guidelines.[47, 48, 52] Six guidelines[46, 47, 49, 52-54] did not indicate the strength or level of evidence in referring to chest X-ray in the guidelines. For the other guidelines, the strength or level of evidence tended to be low or consensus.[45, 48, 50, 51]

Table 8 Overview of recommendations relating to measures of assessment included by guidelines

Shorthand name	Recommendations on peak flow cut-offs as an indicator to inform hospital admission and or ED discharge	Recommendations on respiratory rate as an indicator to inform hospital referral and or admission and or ICU admission	Recommendations on chest X-ray
GINA (2024)[52]	**Recommendation** *Initial presentation at either primary care or ED/acute setting:* PEF >50% predicted or best is considered mild/moderate in both primary care and ED setting. No transfer from primary care required. PEF ≤50% predicted or best is considered severe exacerbation in both primary care and ED settings. Transfer to acute care from primary care is required. *Noted for primary care setting:* The frequency of symptoms may be a more sensitive measure of the onset of an exacerbation than PEF. *In ED/acute care setting:* Measurement of lung function is strongly recommended. If possible and without unduly delaying treatment, PEF (or FEV1) should be recorded before treatment is initiated. If PEF is >60% of predicted or personal best, consider discharge from ED. If PEF is <60% of predicted or personal best, continue treatment. If pre-treatment PEF is <25% or post-treatment PEF is <40%, hospitalise. *After considering patient's risk factors and availability of follow-up care:* If post-treatment lung function is 40-60%, discharge possible, if post-treatment lung function is >60%, discharge recommended.[64] If final PEF <50% predicted, likelihood of readmission is increased. **Strength of recommendation and Level of evidence** Not provided **Key references** Chan-Yeung et al (1996),[65] Grunfeld et al. (1996)[64]	**Recommendation** *In primary care:* Transfer to acute care/ED if respiratory rate is >30/min. *In ED:* If respiratory rate increased, classify as mild/moderate exacerbation. If respiratory rate is >30/min, classified as severe. If respiratory rate continues to deteriorate, exacerbation is classed as severe and reassessed for ICU. If respiratory rate is >22/min, this is a factor associated with increased likelihood of need for admission from ED. **Strength of recommendation and Level of evidence** Not provided **Key references** Not provided	**Recommendation** Chest X-ray is not routinely recommended: In adults, chest X-ray should be considered if a complicating or alternative cardiopulmonary process is suspected (especially in older patients), or for patients who are not responding to treatment where a pneumothorax may be difficut to diagnose clinically **Strength of recommendation and Level of evidence** Not provided **Key references** White et al., (1991)[63]
NVALT (2024)[54]	**Recommendation** It is unclear whether PEF rate measured within 2 hours of presentation predicts the risk of admission to critical care in adults presenting at the ED with acute asthma.	**Recommendation** Not provided **Strength of recommendation and Level of evidence**	**Recommendation** *No formal recommendation regarding X-ray, guideline states:* Management in emergency department

Shorthand name	Recommendations on peak flow cut-offs as an indicator to inform hospital admission and or ED discharge	Recommendations on respiratory rate as an indicator to inform hospital referral and or admission and or ICU admission	Recommendations on chest X-ray
	Strength of recommendation and level of evidence: Strength of recommendation: Very low GRADE Level of evidence: Not provided **Recommendation:** It is unclear whether PEF rate measured within 2 hours of presentation predicts the risk of admission or to critical care or relapse within 7 days in adults presenting at the ED with acute asthma. **Strength of recommendation and Level of evidence** Strength of recommendation: Very low GRADE Level of evidence: Not provided **Key references** Goodacre et al. (2014)[59]	N/A **Key references** N/A	/hospital): Consider using viral diagnostics in the form of a throat swab and taking a chest X-ray. **Strength of recommendation and Level of evidence** Not provided **Key references** Not provided
NVL (2024)[53]	**Recommendation** If PEF is >50% of personal best value, considered mild/moderate exacerbation, thus no transfer from primary care required. If initial presentation is to ED, continue treatment in ED. If PEF is ≤50% predicted or best, considered severe exacerbation, thus consider hospital admission. If PEF is <33% predicted or best, considered life-threatening exacerbation, requiring emergency medical attendance. If PEF remains <40% after initial treatment, ICU admission required. Discharge if PEF stabilises after 1-3 hours of treatment/60 mins since last treatment. **Strength of recommendation and Level of evidence** Strongly recommended (as per care schematic). Level of evidence: Not reported **Key references** Not provided	**Recommendation** *In primary care and ED:* If respiratory rate is >25/min, exacerbation is classified as severe, consider hospital admission. If shallow breathing or no breathing sounds, the exacerbation is classified as life-threatening and requires immediate medical attendance. *In ICU* ICU admission indications do not include respiratory rate. **Strength of recommendation and Level of evidence** Strength of recommendation: Not specifically addressed, but the above recommendation forms part of "strongly recommended care schematic" or pathway. Level of evidence: Not reported. **Key references** Not provided	**Recommendation** *No formal recommendation regarding X-ray, guideline states:* Further diagnostics in the hospital include: […] if necessary, imaging *[X-ray is not listed specifically].* This mainly serves to exclude differential diagnoses but also to identify pneumonia as the cause of the asthma exacerbation. **Strength of recommendation and Level of evidence** N/A **Key references** N/A

Shorthand name	Recommendations on peak flow cut-offs as an indicator to inform hospital admission and or ED discharge	Recommendations on respiratory rate as an indicator to inform hospital referral and or admission and or ICU admission	Recommendations on chest X-ray
SINA (2024)[49]	**Recommendation** *Moderate exacerbation: classified as 50-75% of predicted*: Could treat in primary care based off treatment plan (based on care schematic) *Severe exacerbation (classified as 30-50% predicted):* Treatment in ED necessary (based on care schematic) *Life-threatening exacerbation (classified as <30% of predicted):* Treatment in ICU is necessary **Strength of recommendation and Level of evidence** Not provided **Key references** Not provided	**Recommendation** If respiratory rate is >30/min or in respiratory failure, classified as life-threatening, and then ICU referral mandatory. If respiratory rate is >30/min, could also be classified as severe exacerbation, depending on other indicators, and then treatment in ED necessary. If respiratory rate is 20-30/min, classified as moderate exacerbation, and could be treated in primary care setting. **Strength of recommendation and Level of evidence** Not provided **Key references** Not provided	**Recommendation** Do not request routine chest X-rays […] unless indicated. *For mild-moderate*: Chest X-rays is not usually required for moderate asthma exacerbations unless pneumonia is suspected. *For severe*: Chest X-ray is required if complications are clinically suspected, such as pneumothorax or pneumonia *For life-threatening:* Chest X-rays is mandatory in life-threatening asthma to rule out complications, such as pneumothorax or pneumomediastinum. **Strength of recommendation and Level of evidence** Not provided **Key references** Not provided
GEMA (2023)[47]	**Recommendation** Patients with FEV1 or PEF >70% (predicted or best personal value) and with minimal symptoms can be discharged from the hospital. **Strength of Recommendation and Level of Evidence** Strength of recommendation: R2 Level of evidence: Not provided Noted in care schematic: Moderate (PEF <70%) and severe (PEF <50%) exacerbations should be treated in ED/acute care, and mild (PEF ≥70%) may be suitable to treat in primary care/at home. Assessment of response to treatment: If poor response to treatment after 1-3 hours, and FEV1 or PEF <60% unstable and symptomatic, hospitalisation required. If good response to treatment after 1-3 hours, asymptomatic and FEV1 or PEF either >80% stable, or >60% stable, then suitable for discharge from care setting. • Admission to hospital necessary if ▪ -PEF is <50-60% after treatment with oxygen	**Recommendation** States respiratory arrest as a criterion for ICU admission, however doesn't reference respiratory rate as an indicator to inform hospital referral/admission **Strength of recommendation and Level of evidence** Not provided **Key references** Pinera-Salmerón et al. (2020)[60]	**Recommendation** *No formal recommendation regarding X-ray, guideline states*: Other complementary studies at the beginning of an asthma attack, such as chest X-rays […] are indicated in case of fever or suspicion of infection (pneumonia), pain or intense dyspnea that may suggest the presence of pneumothorax or pneumomediastinum, or when therapeutic response measured by objective parameters, is not appropriate and in case of a life threatening asthma exacerbation. **Strength of recommendation and Level of evidence** Not provided **Key references** White et al. (1991)[63], Rodrigo et al (2004)[66]

Shorthand name	Recommendations on peak flow cut-offs as an indicator to inform hospital admission and or ED discharge	Recommendations on respiratory rate as an indicator to inform hospital referral and or admission and or ICU admission	Recommendations on chest X-ray
	▪ -PEF or FEV1 is 50-70% on arrival. • Discharge: There is no functional parameter that defines when a patient should be discharged, although PEF <75% and variability higher than 25% are associated with a higher rate of readmission. • No specific value indicated for ICU admission, but notes may be necessary where progressive functional deterioration despite treatment. **Strength of recommendation and Level of evidence** Not provided **Key references** Not cited		
NACA (2022)[51]	**Recommendation** No recommendation made. Noted that PEF rate obtained using a peak flow meter underestimates the severity of airflow limitation in patients with acute asthma, compared with FEV1 obtained by spirometry,[57] and that PEF is not a sensitive measure of small clinical improvements as perceived by the patient.[58] **Strength of recommendation and Level of evidence** Not provided **Key references** Choi et al. (2002),[57] Karras et al. (2000)[58]	**Recommendation** *In the case of life-threatening asthma exacerbation (classified as poor respiratory effort):* Arrange immediate transfer to higher-level care. *In the case of secondary assessment (i.e., following primary assessment and initial treatment)*: Consider admitting patient to hospital if … respiratory distress/increased work of breathing unresolved **Strength of recommendation and Level of evidence** Strength of recommendation: Consensus Level of evidence: Not provided **Key references** Wilson et al. (2003),[61] Aldington et al. (2007)[62]	**Recommendation** Arrange chest X-ray if pneumonia, atelectasis, pneumothorax or pneumomediastinum is suspected. **Strength of recommendation and Level of evidence** Consensus **Key references** Not reported
RRS (2022)[48]	**Recommendation** *Home/Primary care:* After taking action to treat, if PEF ≥60-80% can continue treatment at home rather than admitting to ED. *ED/acute care:* After initial treatment, if PEF >60-80% or better for the patient, with significant improvement in symptoms, continue treatment.	**Recommendation** No specific cut-off values reported. Noted: Ventilation is required in the case of respiratory arrest. **Strength of recommendation and Level of evidence** Not provided	**Recommendation** OGC [chest] X-ray in direct projection is recommended for patients with exacerbation of [asthma] to exclude mediastinal emphysema or pneumothorax, in case of suspected pneumonia, clinical signs of life-threatening exacerbation, and the need for mechanical ventilation **Strength of recommendation and Level of evidence**

Shorthand name	Recommendations on peak flow cut-offs as an indicator to inform hospital admission and or ED discharge	Recommendations on respiratory rate as an indicator to inform hospital referral and or admission and or ICU admission	Recommendations on chest X-ray
	If PEF <60% or personal best, exacerbation is classified as severe, so continue treatment with regular monitoring. **Strength of recommendation and Level of evidence** Not provided **Key references** Not provided	**Key references** Not provided	Strength of recommendation:C Level of evidence: 4 **Key references** White et al. (1991)[63]
BTS/SIGN (2019)[50]	**Recommendation** Refer to hospital any patients with features of acute severe or life-threatening asthma. Noted that acute severe includes PEF 33–50% best or predicted; Life-threatening asthma means PEF <33% best or predicted. **Strength of recommendation and Level of evidence** Grade of Recommendation: D Level of Evidence for use of PEF for assessment: 2+. **Recommendation** Admit patients with any feature of a life-threatening or near-fatal asthma attack. (Note: No specific PEF value defined for "near-fatal asthma"). Admit patients with any feature of a severe asthma attack persisting after initial treatment. **Strength of recommendation and Level of evidence** Grade of recommendation: B Level of evidence for use of PEF for admission: 2++, 2+. **Recommendation** Patients whose peak flow >75% best or predicted 1 hour after initial treatment may be discharged from ED (unless they meet other pre-specified listed criteria when admission may be appropriate). **Strength of recommendation and Level of evidence** Grade of recommendation: C Level of evidence: Not provided	**Recommendation** Refer to hospital any patients with features of acute severe or life- threatening asthma. **Strength of recommendation and Level of evidence** Grade of Recommendation D **Recommendation** Admit patients with any feature of a life-threatening or near-fatal asthma attack. Note: Acute severe attack includes respiratory rate ≥25/min; Life-threatening asthma includes "Poor respiratory effort". **Strength of recommendation and Level of evidence** Grade of Recommendation B **Key references** Not clearly specified	**Recommendation** *No formal recommendation regarding X-ray, guideline states*: Chest X-ray is not routinely recommended in the absence of: – suspected pneumomediastinum or pneumothorax – suspected consolidation – life-threatening asthma – failure to respond to treatment satisfactorily – requirement for ventilation. **Strength of recommendation and Level of evidence** Grade of Recommendation: not provided Level of evidence from use of chest X-ray: 4 **Key references** Not provided

Shorthand name	Recommendations on peak flow cut-offs as an indicator to inform hospital admission and or ED discharge	Recommendations on respiratory rate as an indicator to inform hospital referral and or admission and or ICU admission	Recommendations on chest X-ray
	Noted that predicted PEF values should be used to recognise acute asthma only if the recent best PEF (within 2 years) is unknown (Level of evidence: 4). **Key references** Shim et al (1980),[67] Emerman et al (1995),[68] Campbell et al. (1997),[69] Innes et al. (1998),[70] BTS (1995),[71] SIGN (1999),[72] National Heart, Lung and Blood Institute (1992),[73] Neville et al. (1991),[74] Brenner et al. (1998),[75] Boulet et al. (1999)[76]		
SFMU/SRLF (2019)[45]	**Recommendation** The experts suggest that the decision to send patients with severe asthma exacerbation home should be based on an assessment taking into account patient's characteristics, the frequency of exacerbations, the severity of the initial clinical presentation, the response to treatment, including the progression of PEF, and the patient's ability to be managed at home (referral to the primary care physician). **Strength of recommendation and Level of evidence:** Strength of recommendation: Expert opinion Level of evidence: Not provided Noted: After an hour of continuous treatment with short-acting β_2 agonists, a return home can be envisaged for patients with improved symptoms, including PEF that is 60%–80% of the patient's theoretical maximum value.[77] PEF measured at admission was seldom studied, but was not associated with a poor prognosis.[78, 79] No cut-off provided for PEF. **Recommendation** The experts suggest that admission to intensive care of adult and paediatric patients with severe asthma exacerbation should be discussed early, on a case by case basis, because there are no specific criteria on this subject. **Strength of recommendation and Level of evidence** Strength of recommendation: Expert opinion Level of evidence: Not provided	**Recommendation** Not discussed **Strength of recommendation and Level of evidence** N/A **Key references** N/A	**Recommendation** Chest radiography […] should probably be done if there is a diagnostic doubt or non-response to treatment. **Strength of recommendation and Level of evidence** Strength of recommendation: Grade 2+ Level of evidence: Not provided **Key references** Tsai et al. (1993)[80]

Shorthand name	Recommendations on peak flow cut-offs as an indicator to inform hospital admission and or ED discharge	Recommendations on respiratory rate as an indicator to inform hospital referral and or admission and or ICU admission	Recommendations on chest X-ray
	Key references GINA (2018),[77] Weber et al. (2002),[79] Turner et al. (1998)[78]		
SRS (2018)[46]	**Recommendation** Not discussed **Strength of recommendation and Level of evidence** N/A **Key references** N/A	**Recommendation** *In Primary care:* If respiratory rate > 30/min, this is a sign of life-threatening exacerbation, and patient should be transferred to acute care immediately. **Strength of recommendation and Level of evidence** Not provided **Key references** Not provided	**Recommendation** *ED/acute care*: Chest X-ray is not routinely performed, and should be considered if a complicating or alternative process is suspected or for patients not responding to treatment. **Strength of recommendation and Level of evidence** Not provided **Key references** Not provided

Key: BTS/SIGN – British Thoracic Society/Scottish Intercollegiate Guidelines Network; ED – emergency department; FEV1 – forced expiratory volume in one second; GEMA - Guía Espanola para el Manejo del Asma; GINA – Global Initiative for Asthma; GRADE - Grading of Recommendations, Assessment, Development, and Evaluations; ICU – intensive care unit; N/A – not applicable; NACA – National Asthma Council Australia; NVALT – Dutch Association of Pulmonologists; NVL – National Care Guidelines (Germany); PEF – peak expiratory flow; RRS – Russian Respiratory Society; SINA – Saudi Initiative for Asthma; SRS – Swiss Respiratory Society; SFMU/SRLF - Societe Francaise de Medecine d'Urgence, the Societe de Reanimation de Langue Francaise.

3.6.2 Oxygen-related interventions

Use of high-flow oxygen in acute asthma attack

Five of the 10 guidelines included in this review provide recommendations or advice specifically relating to the use of high-flow oxygen in acute asthma exacerbation.[47, 49, 51, 52, 54] While a further three guidelines do not explicitly reference the use of high-flow oxygen, they do provide recommendations or advice supporting the use of controlled flow oxygen in the management of acute asthma attack. The recommendation strength and the certainty of the supporting evidence varies across guidelines. Three key references are cited by a number of guidelines. A randomised trial conducted (RCT) by Rodrigo et al. (2003)[81] that studied the effects of short-term (28%) versus 100% oxygen on partial pressure of carbon dioxide and PEF in acute asthma; a RCT conducted by Perrin et al. (2011),[82] which studied the use of high-flow versus titrated oxygen in patients with acute asthma exacerbations; and a pre-and post-interventional comparison study by Chien et al. (2000)[83] of ED-treated exacerbations focused on uncontrolled oxygen administration and respiratory failure in acute asthma (Table 9).

Four guidelines broadly advise that the use of controlled flow oxygen is recommended, or is preferable to, the use of high-flow, or high-concentration oxygen delivery.[47, 49, 51, 52] GINA (2024) does not issue a specific recommendation,[52] but notes that, in severe exacerbations, controlled low flow oxygen therapy using pulse oximetry to achieve target oxygen saturation levels is associated with better physiological outcomes than with high concentration (100%) oxygen therapy (Evidence Level B).[81-83] GEMA (2023) states that the use of oxygen with controlled fraction of inspired oxygen (FiO_2)to obtain saturations around 93-95% is preferable to the use of high-flow oxygen therapy with which saturations around 100% can be achieved,[49] citing Rodrigo et al. (2003)[81] and Perrin et al. (2011).[82] NACA (2022) recommends that oxygen therapy be initiated for adults with oxygen saturation less than 92% (consensus recommendation),[51] noting that titrated oxygen therapy using pulse oximetry to maintain oxygen saturation at 93-95% while avoiding hyperoxaemia achieves better physiological outcomes than 100% oxygen at high flow rate (8 litres/min), citing Perrin et al. (2011).[45] SINA (2024) state that adjusted low-flow oxygen is recommended to maintain saturation greater than or equal to 92%, as patients who received 28% oxygen did better than those who received 100% oxygen,[84] citing a BTS/SIGN guideline for emergency oxygen use

in adult patients [85] and Chien et al. (2000).[83] Notably, SINA (2024) also states that life-threatening exacerbation requires high-flow oxygen therapy to achieve target oxygen saturation greater than or equal to 92%,[49] but does not cite any evidence to support this recommendation.

Two guidelines provide guidance on the delivery of high-flow oxygen by nasal cannulae.[51, 54] NVALT (2024) recommends against the use of non-invasive respiratory support in patients with a lung attack of asthma with respiratory failure, where NIV is understood to include high-flow nasal cannula (GRADE very low).[54] NVALT (2024) also notes that, the evidence for the use of high-flow nasal cannula over conventional oxygen therapy is very uncertain in patients with an acute asthma exacerbation, specifically concerning treatment failure and duration of hospitalisation,[54] citing three studies published in 2019,[86] 2020[87] and 2021.[88] NACA (2022)[51] observes that humidification of oxygen via high flow nasal cannulae may improve comfort and tolerance[89] and that delivery of high-flow oxygen via nasal cannulae is increasingly common practice in Australian emergency rooms, but that high-concentration and high-flow oxygen therapy causes a clinically significant increase in blood carbon dioxide (CO_2) concentration in adults with acute asthma.[82, 90] They note that there is sparse evidence to support its use in acute asthma treatment,[89] with no published studies having evaluated its use in adults with acute asthma at the time of guideline development.

While three of the 10 eligible guidelines do not specifically discuss the use of high-flow oxygen,[46, 48, 50] they do recommend the use of controlled flow oxygen for acute asthma attack. BTS/SIGN (2019) recommends controlled supplementary oxygen to all hypoxaemic patients with acute severe asthma,[50] (grade of recommendation C) citing the BTS guideline for emergency oxygen use in adult patients (2008) (level of evidence 1+, 2, 4).[85] SRS (2018) recommends when treating acute asthma exacerbations in ED, titrated low flow oxygen therapy be administered by nasal cannulae or mask to achieve target oxygen saturation levels.[46] RRS (2022) recommends that patients with oxygen saturation levels of 90% receive inhaled administration of oxygen through nasal cannulae at a flow rate of 4-5 litre per minute (l/min), indicating that low-flow oxygen administration is recommended,[48] citing evidence from Perrin et al. (2011),[82] Chien et al. (2000),[83] and Rodrigo et al. (2003)[81] in support of their recommendation.

Use of oxygen-driven versus air-driven nebulisers in primary care for acute asthma attack

Four guidelines address the issue of whether an oxygen-driven nebuliser is preferable to an air-driven nebuliser,[45, 49-51] with only one specifically referring to the primary care context.[50] In a best practice statement, BTS/SIGN (2019) guidelines state that nebulisers for giving β_2 agonist bronchodilators should preferably be driven by oxygen in settings including primary care because of the risk of oxygen desaturation while using air-driven compressors,[50] citing a systematic review by Cates et al. (2013; Level of evidence 1++).[91] However, that review focused on comparing spacers to nebulisers in acute care settings and found no evidence around the outcome of oxygen saturation in adults.[91] BTS/SIGN (2019) notes that the absence of supplemental oxygen should not prevent nebulised therapy from being administered when appropriate,[50] also citing Douglas et al. (1985)(level of evidence: 4).[92] In a guideline focusing on acute care, SFMU/SRLF (2019) states that there is no proof of the advantage of using oxygen compared with air as the aerosol carrier gas in non-hypoxemic patients, noting that a systematic search conducted yielded no citations.[45] Based on consensus and without reference to setting, NACA (2022) recommends that nebulisers used in the management of acute asthma may be driven by air or oxygen.[51] The guideline recommends that, for patients in the initial management of severe exacerbations, nebulisers delivering salbutamol and ipratropium bromide should be driven by air unless oxygen therapy is required.[51] NACA (2022) also specifies that, for patients with life-threatening asthma, β_2 agonist bronchodilators should be delivered via continuous nebulisation driven by oxygen, switching to air-driven intermittent nebulisation once breathing improves.[51] They caution avoiding over-oxygenation (oxygen saturation >95%) in adults as it can increase the risk of hypercapnia.[51] Without specifying a clinical setting, SINA (2024) states that oxygen-driven nebulizers are needed to avoid the risk of oxygen desaturation while using air-driven compressors,[49] citing "Level A" evidence comprised of two systematic reviews about corticosteroids that appear not to be relevant and a small ICU-based study by Douglas et al. (1985)[92] that did not compare oxygen-driven to air-driven nebulisers.

Use of heliox in acute asthma attack

Six guidelines address the use of heliox as an intervention in those experiencing acute asthma attack.[45, 47, 48, 50-52] All six guidelines reference a Cochrane systematic review and meta-analysis conducted by Rodrigo et al. (2014),[93] which analysed data pertaining to the use of

heliox-driven β_2 agonists nebulization for children and adults with acute asthma. GINA (2024),[52] GEMA (2023)[47] and RRS (2022)[48] indicate that heliox should not be considered for routine use in the management of acute asthma exacerbations (RRS, 2022; Strength of recommendation A; Level of evidence 1), but rather for those experiencing severe exacerbations that do not respond to standard treatment, with GEMA (2023)[47] noting that Rodrigo et al. (2014)[93] found a lack of consistent clinical efficacy data to support its use. BTS/SIGN (2019) specifically states that heliox is not recommended for use outside of a clinical trial setting (Grade of recommendation B; Level of evidence 1++, 1+),[50] and SFMU/SRLF (2019) states that helium probably should not be used as carrier gas [mixed with oxygen] in nebulisers in those with severe acute exacerbation (Strong agreement; Level of evidence 2-).[45] While SFMU/SRLF (2019) cite a number of individual studies[94-101] and the meta-analysis conducted by Rodrigo et al. (2014)[93] to support this recommendation, the guideline notes that the studies were very heterogeneous and included small populations, and as such, no definitive conclusion regarding heliox could be drawn from the available literature at time of review.[45] NACA (2022) does not provide a recommendation on the use of heliox in acute asthma exacerbation but does note that is not routinely available nor commonly used in Australian EDs.[51] NACA (2022)[51] also notes that heliox has negligible adverse effects[102] and may not have any benefit for patients with severe asthma requiring mechanical ventilation,[103] but reports that, when giving nebulised bronchodilators in acute asthma, using heliox to drive the nebuliser may be more effective than oxygen for improving lung function and reducing hospital admission rates.[93]

Use of ECMO for near-fatal asthma attack refractory to conventional ventilator treatment

Three guidelines refer to the use of ECMO as an intervention in those experiencing acute asthma attack,[45, 50, 53] each citing different evidence sources. Two of the guidelines were from 2019 and one from 2024. BTS/SIGN (2019) recommends that ECMO may be considered in adults with near-fatal asthma refractory to conventional ventilator treatment (Grade of recommendation D; Level of evidence 3),[50] citing a single study by Yeo et al. (2017),[104] which analysed data from the Extracorporeal Life Support Organisation registry in South Korea. SFMU/SRLF (2019) recommends (based on expert opinion) that the use of extracorporeal life support (including either venovenous ECMO or extracorporeal CO_2 removal ($ECCO_2R$)) should be discussed with an expert centre, in the case of respiratory acidosis and or severe

hypoxemia refractory to optimal medical treatment and to well-conducted mechanical ventilation.[45] SFMU/SRLF (2019) also highlights the absence of compelling data in patients with severe asthma exacerbation,[45] noting that existing data pertains to small retrospective cohorts,[105-107] and that $ECCO_2R$ can be considered as a more accessible and less invasive technique than ECMO, as hypercapnia is prominent in refractory severe asthma exacerbation.[105] NVL (2024) does not make a specific recommendation as to the use of ECMO,[53] however it does cite another guideline published in 2017 that provides guidance for the use of invasive ventilation and use of extracorporeal procedures for acute respiratory insufficiency, and which recommends ECMO as an intervention for individuals with acute respiratory failure where rescue is required.[108] It is noteworthy that none of the guidelines provide a recent systematic review of the literature on the use of ECMO in acute asthma and therefore further literature review may be required.

Use of NIV

Eight guidelines refer to the use of NIV for acute asthma exacerbation.[45-48, 50-52, 54] Three guidelines do not provide recommendations for or against the use of NIV, citing lack of evidence.[45, 46, 52] Four guidelines indicate that NIV may be used in certain circumstances such as the patient starting to tire or show signs of respiratory failure;[51] in the presence of severe dyspnea, hypercapnia, clinical signs of increased work of respiratory muscles;[48] for severe exacerbations resistant to treatment (contingent on close monitoring so as not to delay the use of invasive mechanical ventilation if needed),[47] and in the ICU setting.[50] NVALT (2024) recommends against the use of NIV for acute asthma exacerbation[54] due to paucity of evidence. Two guidelines advised against the use of sedation if NIV is used. [51, 52] While NVL (2024)[53] does not make a specific recommendation, it signposts to another guideline published in 2023 that indicates that NIV may be attempted in acute asthma using a similar approach outlined in acute exacerbation of COPD recommendations.[109]

A Cochrane systematic review published in 2012 was cited by five guidelines. [45, 50-52, 54] Of the five guidelines that provide a recommendation related to NIV, two do not provide strength of recommendation,[52, 54] two are consensus statements,[50, 51] and in RSS's (2022)[48] the strength of recommendation is weak.

Table 9 Overview of recommendations relating to the use of oxygen-related interventions included by guidelines

Shorthand name	High-flow oxygen	Oxygen-driven versus air-driven nebulisers in primary care	Heliox	ECMO for near-fatal asthma attack refractory to conventional ventilator treatment	Use of NIV
GINA (2024)[52]	**Recommendation** No explicit recommendation provided Noted*:* *Primary care:* Controlled flow oxygen supplementation[110] titrated against pulse oximetry is recommended (if available) to maintain oxygen saturation at 93-95% for adults and children aged ≥12. A*cute care/ED:* Oxygen should be administered by nasal cannulae or mask, to achieve oxygen saturation of 93-95% in adults and children > 12 years. *Hospitalised patients:* Controlled or titrated oxygen therapy is associated with lower mortality and better outcomes than high concentration (100%) oxygen therapy (Evidence level A).[81-83] *In severe exacerbations:* Controlled low flow oxygen therapy using pulse oximetry to maintain saturation at 93-95% is associated with better physiological outcomes than with high concentration (100%) oxygen therapy (Evidence Level B).[81-83] **Strength of recommendation and level of evidence** Strength of recommendation: Not provided.	**Recommendation** Not discussed **Strength of recommendation and level of evidence** N/A **Key references** N/A	**Recommendation** *Acute care/ED:* Heliox may be considered for patients who do not respond to standard therapy, however availability, cost and technical issues should be considered. It was noted that a systematic review of studies comparing helium-oxygen with air-oxygen suggested there is no role for this intervention in routine care.[93] **Strength of recommendation and level of evidence** Strength of recommendation: Not provided. Level of evidence (for reference): B **Key references** Rodrigo et al. (2014)[93]	**Recommendation** Not discussed **Strength of recommendation and level of evidence** N/A **Key references** N/A	**Recommendation** Given the small size of the studies, no recommendation is offered [on use of NIV]. If NIV is tried, the patient should be monitored closely. It should not be attempted in agitated patients, and patient should not be sedated to receive NIV. **Strength of recommendation and level of evidence** Strength of recommendation: Not provided Level of evidence (for second and third statements only): D **Key references** Lim et al. (2012)[111]

Shorthand name	High-flow oxygen	Oxygen-driven versus air-driven nebulisers in primary care	Heliox	ECMO for near-fatal asthma attack refractory to conventional ventilator treatment	Use of NIV
	Level of evidence: A;[81-83] B[81-83] **Key references** Fitzgerald et al. (1996),[110] Chien et al. (2000), Rodrigo et al. (2003),[81] Perrin et al. (2011),[82]				
NVALT (2024)[54]	**Recommendation** Do not use NIV in patients with a lung attack of asthma with respiratory failure. (Noted that NIV is understood to include high-flow nasal cannula.) Noted that, concerning treatment failure and duration of hospitalisation, the evidence for the use of high-flow nasal cannula over conventional oxygen therapy is very uncertain in patients with an acute asthma exacerbation. **Strength of recommendation and level of evidence** Strength of recommendation: Very low GRADE Level of evidence: Not reported **Key references~** Raesi et al. (2019),[86] Geng et al. (2020),[87] Ruangsomboon et al. (2021)[88]	**Recommendation** Not discussed **Strength of recommendation and level of evidence** N/A **Key references** N/A	**Recommendation** Not discussed **Strength of recommendation and level of evidence** N/A **Key references** N/A	**Recommendation** Not discussed **Strength of recommendation and level of evidence** N/A **Key references** N/A	**Recommendation** Do not use NIV (non-invasive respiratory support) in patients with a lung attack of asthma with respiratory failure. (Note that non-invasive respiratory support is understood to include: BiPAP, CPAP and High flow nasal cannuala. NIVis understood to refer to BiPAP) **Strength of recommendation and level of evidence** Not reported **Key references (BiPAP)** Lim et al. (2012),[111] Filho et al. (2009),[112] Soroksky et al. (2003),[113] Gupta et al. (2010)[114]
NVL (2024)[53]	**Recommendation** Not discussed **Strength of recommendation and level of evidence** N/A **Key references** N/A	**Recommendation** Not discussed **Strength of recommendation and level of evidence** N/A **Key references** N/A	**Recommendation** Not discussed **Strength of recommendation and level of evidence** N/A **Key references** N/A	**Recommendation** None directly provided; Reference is made to another guideline which recommends ECMO as an intervention for individuals with acute respiratory failure where rescue is required.[108]	**Recommendation** None directly provided; Reference is made to another guideline "E11 In acute hypercapnic exacerbation of bronchial asthma, NIV can be attempted according to the acute exacerbation-COPD recommendations" [109]

Shorthand name	High-flow oxygen	Oxygen-driven versus air-driven nebulisers in primary care	Heliox	ECMO for near-fatal asthma attack refractory to conventional ventilator treatment	Use of NIV
				Strength of recommendation and level of evidence Not specified **Key references** Association of the Scientific Medical Societies in Germany (2017)[108]	**Strength of recommendation and level of evidence** N/A **Key references** Association of the Scientific Medical Societies in Germany (2023)[109] Stefan et al. (2016),[115] Miller et al. (2017)[116]
SINA (2024)[49]	**Recommendation** *For severe acute exacerbation:* Adjusted low-flow oxygen is recommended to maintain saturation ≥92%, as patients who received 28% oxygen did better than those who received 100% oxygen.[83, 85] *Noted in care schematic:* Severe asthma exacerbation requires oxygen therapy to keep SaO_2 to ≥92%. Life-threatening exacerbation requires high-flow oxygen therapy to achieve oxygen saturation ≥92%. **Strength of recommendation and level of evidence** Not provided **Key references** Chien et al. (2000),[83] O'Driscoll et al. (2008)[85]	**Recommendation** *Severe asthma exacerbation (treated in ED):* Oxygen-driven nebulizers are needed to avoid the risk of oxygen desaturation while using air-driven compressors.[92] *Life-threatening asthma exacerbation:* Oxygen-driven nebulizers are mandatory due to the risk of oxygen desaturation while using air-driven compressors.[92] **Strength of recommendation and level of evidence** Strength of recommendation: Not provided Level of evidence (Douglas et al., 1985):[92] A **Key references** Douglas et al. (1985)[92]	**Recommendation** Not discussed **Strength of recommendation and level of evidence** N/A **Key references** N/A	**Recommendation** Not discussed **Strength of recommendation and level of evidence** N/A **Key references** N/A	**Recommendation** Not discussed **Strength of recommendation and level of evidence** N/A **Key references** N/A
GEMA (2023)[47]	**Recommendation** *Moderate and severe exacerbations*: Oxygen should be administered immediately with a	**Recommendation** Not discussed **Strength of recommendation and level of evidence**	**Recommendation** Heliox may be considered in patients who do not respond to the usual treatment,[117, 118]	**Recommendation** Not discussed **Strength of recommendation and level of evidence**	**Recommendation** No formal recommendation, guideline states "The use of non-invasive mechanical

Shorthand name	High-flow oxygen	Oxygen-driven versus air-driven nebulisers in primary care	Heliox	ECMO for near-fatal asthma attack refractory to conventional ventilator treatment	Use of NIV
	flow providing a saturation >90% (or >95 in the case of pregnant women, or in patients with concomitant heart disease).[81] *Severe exacerbations with greater airflow obstruction and risk of hypercapnia*: The use of oxygen with controlled FiO_2 to obtain saturations around 93-95% is preferable than the use of high-flow oxygen therapy with which saturations around 100% can be achieved.[81, 82] **Strength of recommendation and level of evidence** Not reported **Key references** Rodrigo et al. (2003),[81] Perrin et al. (2011),[82]	N/A **Key references** N/A	particularly to nebulizing short acting β_2 agonists;[93] however also, noted that heliox, in 80/20 or 70/30 proportions, has no place in the routine management of exacerbations due to the lack of consistent data regarding its efficacy. **Strength of recommendation and level of evidence** Not provided **Key references** Rodrigo et al. (2006),[117] Colebourn et al. (2007),[118] Rodrigo et al. (2014)[93]	N/A **Key references** N/A	ventilation may be an option in severe exacerbations resistant to treatment [….] Close monitoring is necessary so as not to delay the use of invasive mechanical ventilation in patients with an imminent life-threatening compromise" **Strength of recommendation and level of evidence** Not reported **Key references** Pallin and Naughton (2014)[119]
NACA (2022)[51]	**Recommendation** Recommendation is to start oxygen therapy for adults with oxygen saturation <92%. **Strength of recommendation and level of evidence** Consensus recommendation Noted: In adults with acute asthma, titrated oxygen therapy using pulse oximetry to maintain oxygen saturation at 93–95% while avoiding hyperoxaemia achieves better physiological outcomes than 100% oxygen at high flow rate (8 l/min).[82] High-concentration and	**Recommendation** Nebulisers can be driven by air, piped oxygen, or an oxygen cylinder fitted with a high-flow regulator capable of delivering >6 l/min. In care schematic: Noted that in the management of severe exacerbations, deliver nebulisation of salbutamol and ipratropium by air unless oxygen therapy is required. Noted: For patients with life-threatening asthma, deliver salbutamol via continuous nebulisation driven by oxygen	**Recommendation** No specific recommendation given. Noted that heliox is not commonly used in Australian EDs and is not routinely available. **Strength of recommendation and level of evidence** Not provided **Key references** Rehder et al. (2017),[102] Rodrigo et al. (2014),[93] Leatherman et al. (2018)[103]	**Recommendation** Not discussed **Strength of recommendation and level of evidence** N/A **Key references** N/A	**Recommendation** In adults […], non-invasive positive pressure ventilation can be considered if the patient is starting to tire or shows signs of respiratory failure. Do not sedate patient If no improvement, intubate and start mechanical ventilation. **Strength of recommendation and level of evidence** Consensus recommendation **Key references** Lim et al. (2012),[111] Gupta et al. (2010),[114] Soma et al.

Shorthand name	High-flow oxygen	Oxygen-driven versus air-driven nebulisers in primary care	Heliox	ECMO for near-fatal asthma attack refractory to conventional ventilator treatment	Use of NIV
	high-flow oxygen therapy cause a clinically significant increase in blood CO_2 concentration in adults with acute asthma.[82, 90] Humidification of oxygen via high flow nasal cannulae may improve comfort and tolerance.[89] Delivery of high-flow oxygen via nasal cannulae is increasingly common practice in Australian EDs. There is very little evidence to support its use in acute asthma treatment,[89] but it does not appear to be associated with significant risks. No published studies have evaluated its use in adults with acute asthma. If using oxygen to drive a nebuliser, do not exceed 8–10 l/min and avoid over-oxygenation (increases risk of hypercapnia). **Key references** Beasley et al. (2015),[89] Perrin et al. (2011),[82] Rau et al. (1996)[90]	until breathing improves, then consider changing to a pressurised metered-dose inhaler plus spacer or intermittent nebuliser.[120-122] To deliver intermittent nebulised bronchodilators in a patient receiving oxygen therapy, use an air-driven compressor nebuliser and administer oxygen by nasal cannulae.[89] **Strength of recommendation and level of evidence** Consensus recommendation **Key references** Beasley et al. (2015),[89] Camargo et al. (2003),[120] Rodrigo and Rodrigo (2002),[121] Shrestha et al. (1996)[122]			(2008),[123] Brandão er al. (2009)[124]
RRS (2022)[48]	**Recommendation** Use of high-flow oxygen not specifically discussed. Noted that patients with asthma exacerbation and SpO_2 < 90% are recommended inhaled administration of oxygen (4-5 l/min through nasal cannulas).[81-83]	**Recommendation** Not discussed **Strength of recommendation and level of evidence** N/A **Key references** N/A	**Recommendation** Heliox therapy is recommended to be considered as an adjunct to drug therapy in patients with severe exacerbation of asthma who have not responded to standard treatment.[93, 125] **Strength of recommendation and level of evidence**	**Recommendation** Not discussed **Strength of recommendation and level of evidence** N/A **Key references** N/A	**Recommendation** NIV is recommended in patients with exacerbation of asthma in the presence of severe dyspnea, hypercapnia, clinical signs of increased work of respiratory muscles, but without signs of muscle fatigue and impaired level of

Shorthand name	High-flow oxygen	Oxygen-driven versus air-driven nebulisers in primary care	Heliox	ECMO for near-fatal asthma attack refractory to conventional ventilator treatment	Use of NIV
	Strength of recommendation and level of evidence Not provided **Key references** Chien et al. (2003),[83] Perrin et al. (2011),[82] Rodrigo et al. (2000)[81]		Strength of recommendation: A Level of evidence: 1 **Key references** Rodrigo et al. (2014),[93] Pozin et al. (2017)[125]		consciousness (stunned or coma). **Strength of recommendation and level of evidence** Recommendation:C Level of evidence:5 **Key references** GINA (2019),[126] Gupta et al. (2010),[114] Georgopoulous and Burchardi (1998),[127]Avdeev (2002)†
BTS/SIGN (2019)[50]	**Recommendation** Give controlled supplementary oxygen to all hypoxaemic patients with acute severe asthma titrated to maintain an oxygen saturation level of 94–98%. Do not delay oxygen administration in the absence of pulse oximetry but commence monitoring of oxygen saturation as soon as it becomes available.[85] **Strength of recommendation and level of evidence** Strength of recommendation: C. Level of evidence: 1+, 2+, 4. **Key references** O'Driscoll et al. (2008)[85]	**Recommendation** In hospital, ambulance and primary care, nebulisers for giving β_2 agonist bronchodilators should preferably be driven by oxygen. Best practice statement: In patients with acute asthma with acute-severe or life-threatening features the nebulised route (oxygen-driven) is recommended. Noted: While oxygen-driven nebulisers are preferred for nebulising β2 agonist bronchodilators because of the risk of oxygen desaturation while using air-driven compressors,[71, 91] the absence of supplemental oxygen should not prevent nebulised therapy from being	**Recommendation** Heliox is not recommended for use in patients with acute asthma outside a clinical trial setting. **Strength of recommendation and level of evidence** Strength of recommendation: B Level of evidence: 1++, 1+ **Key references** Kass et al. (1999),[94, 95] Henderson et al. (1999), Rodrigo et al. (2006),[117] Rodrigo et al. (2003)[128]	**Recommendation:** Where available, extracorporeal membrane oxygenation may be considered in adults with near-fatal asthma refractory to conventional ventilator treatment. **Strength of recommendation and level of evidence** Strength of recommendation: D Level of evidence: 3 **Key references:** Yeo et al. (2017)[104]	**Recommendation** Good-practice point: NIV should only be considered in an ICU or equivalent clinical setting. **Strength of recommendation and level of evidence** Strength of recommendation: no grade provided, recommended best practice based on the clinical experience of the guideline development group. Level of evidence: 4, 1++, 1+, 2- **Key references** Meduri er al. (1996),[129] Lim et al. (2012),[111] Galindo-Filho et al. (2013),[130] Pallin et al. (2015)[131]

Shorthand name	High-flow oxygen	Oxygen-driven versus air-driven nebulisers in primary care	Heliox	ECMO for near-fatal asthma attack refractory to conventional ventilator treatment	Use of NIV
		administered when appropriate.[92] **Strength of recommendation and level of evidence** Strength of recommendation: A; Level of evidence: 1++;[71, 91] 4[92] **Key references** BTS (1997),[71] Cates et al. (2013),[91] Douglas et al. (1985)[92]			
SFMU/SRLF (2019)[45]	**Recommendation** Not discussed **Strength of recommendation and level of evidence** N/A **Key references** N/A	**Recommendation** In adults, there is no proof of the advantage of using oxygen, compared with air, as the aerosol carrier gas in non-hypoxemic patients. **Strength of recommendation and level of evidence** Not provided **Key references** Not provided; noted that systematic search yielded no citations.	**Recommendation** Helium should probably not be used as carrier gas (mixed with oxygen) in nebulizers in adult and paediatric patients with severe acute exacerbation.[93-101] **Strength of recommendation and level of evidence** Strength of recommendation: Strong agreement Level of evidence: 2- **Key references** Henderson et al. (1999),[94] Kass et al. (1999),[95] L'her et al. (2000),[96] Dorfman et al. (2000),[97] Rose et al. (2002),[98] Kress et al. (2002),[99] Lee et al. (2005),[100] Xie et al. (2003),[101] Rodrigo et al. (2014)[93]	**Recommendation** In the absence of compelling data in adult and paediatric patients with severe asthma exacerbation, the experts suggest discussing with an expert centre the use of extracorporeal life support—venovenous ECMO or $ECCO_2R$—in the case of respiratory acidosis and/or severe hypoxemia refractory to optimal medical treatment and to well-conducted mechanical ventilation. Also noted that, as hypercapnia is prominent in refractory severe asthma exacerbation, $ECCO_2R$ can be considered as a more accessible and less invasive technique than ECMO.[105] **Strength of recommendation and level of evidence** Strength of recommendation: Expert opinion	**Recommendation** The experts were unable to recommend the use of NIV in severe asthma exacerbation. **Strength of recommendation and level of evidence** Not reported **Key references** Ganaesh et al. (2015),[132]) Fernández et al. (2001),[133] Murase et al. (2010),[134]Stefan et al. (2016),[115] Soroksky et al. (2003),[113] Soma et al.,[123] Gupta et al. (2010),[114] Brandao et al. (2009),[124] Lim et al. (2012),[111] Rochwerg et al. (2017)[135]

Shorthand name	High-flow oxygen	Oxygen-driven versus air-driven nebulisers in primary care	Heliox	ECMO for near-fatal asthma attack refractory to conventional ventilator treatment	Use of NIV
				Level of evidence: Not provided **Key references** Brenner et al. (2014),[105] Di Lascio et al. (2017),[106] Mikkelsen et al. (2009)[107]	
SRS (2018)[46]	**Recommendation** Use of high-flow oxygen not specifically discussed. Noted that in ED, it is recommended that titrated low flow oxygen therapy should be administered by nasal cannulae or mask to achieve oxygen saturation of 93–95%. **Strength of recommendation and level of evidence** Not provided **Key references** Not provided	**Recommendation** Not discussed **Strength of recommendation and level of evidence** N/A **Key references** N/A	**Recommendation** Not discussed **Strength of recommendation and level of evidence** N/A **Key references** N/A	**Recommendation** Not discussed **Strength of recommendation and level of evidence** N/A **Key references** N/A	**Recommendation** The evidence regarding the role of NIV is weak and no specific recommendation has been made in this regard. **Strength of recommendation and level of evidence** Not reported **Key references** Not reported

Key: BTS/SIGN – British Thoracic Society/Scottish Intercollegiate Guidelines Network; CO_2 – carbon dioxide; COPD – Chronic obstructive pulmonary disease; $ECCO_2R$ – extracorporeal carbon dioxide removal; ECMO – extracorporeal membrane oxygenation; ED – emergency department; FiO_2 – fraction of inspired oxygen; GEMA - Guía Espanola para el Manejo del Asma; GINA – Global Initiative for Asthma; GRADE – Grading of Recommendations, Assessment, Development and Evaluations; ICU – intensive care unit; l/min – litre per minute; N/A – not applicable; NACA - National Asthma Council Australia; NIV - non-invasive ventilation; NVALT – Dutch Association of Pulmonologists; NVL – National Care Guidelines (Germany); RRS – Russian Respiratory Society; SaO_2 – oxygen saturation (arterial blood). SINA – Saudi Initiative for Asthma; SpO_2 - oxygen saturation; SRS – Swiss Respiratory Society; SFMU/SRLF - Societe Francaise de Medecine d'Urgence, the Societe de Reanimation de Langue Francaise.
~Full citations could not be located within the guideline for Raesi et al. (2019),[86] Geng et al. (2020),[87] Ruangsomboon et al. (2021)[88], only surname of leading author and year of publication provided. †Reference could not be verified for Avdeev (2002).

3.6.3 Pharmacological interventions – IV route only

Use of IV β_2 agonists

As outlined in Table 10, nine of the 10 guidelines refer to the use of IV β_2 agonists during acute asthma attack,[45-47, 49-54] with seven guidelines[45-47, 50-53] citing a key systematic review by Travers et al. (2001,[136] 2012[137]) that focused on the addition of IV β_2 agonists to inhaled β_2 agonists for acute asthma. Where graded, the level of evidence was deemed to be high.[45, 46, 50, 52] Overall, the guidelines note that there is a lack of evidence to support the use of IV β2 agonists during acute asthma attack, with most advising against their routine use. SFMU/SRLF (2019)[45] and SINA (2024)[49] note that the inhaled route has fewer adverse effects than the IV route, and NVALT (2024) notes tachycardia and hypokalaemia as potential side effects of the IV route.[54] Six guidelines[47, 49-51, 53, 54] allow for the use of IV β_2 agonists in very select cases. These included patients in whom inhaled therapy cannot be used reliably, while monitoring serum lactate (BTS/SIGN 2019);[50] those under mechanical ventilation and monitored in an ICU with a very slow continuous infusion when there is no response to inhalation therapy (GEMA, 2023);[52] those who are not improving after initial treatment (NVL, 2024;[53] NACA, 2022[51]); if the response to the inhaled drug is poor or if the patient cannot tolerate the inhaled route (SINA, 2024);[49] and in an ED or ICU to avoid mechanical ventilation or to shorten the duration of mechanical ventilation, under potassium monitoring (NVALT, 2024).[54] NACA (2022) also note that, where IV β_2 agonists are deemed necessary, monitoring of blood electrolytes, heart rate and acid/base balance (blood lactate) is recommended, as salbutamol toxicity may occur with inhaled or IV salbutamol.[51]

Use of IV magnesium sulphate

All 10 included guidelines refer to the use of IV magnesium sulphate in acute asthma attack (Table 10). Key references cited by the guidelines include Cochrane systematic reviews by Rowe et al. (2000)[138] and Kew et al. (2014),[139] as well as a large RCT by Goodacre et al. (2013),[140] which excluded patients with more severe asthma. Based on a high level of evidence, three guidelines recommend against the routine use of IV magnesium sulphate in acute asthma attack (GINA, 2024;[52] GEMA, 2023;[47] SFMU/SRLF, 2019[45]). All but one of the guidelines allows for the use of IV magnesium sulphate (most often as a single 2g infusion over 20 minutes) in patients experiencing severe asthma attack (GINA, 2024;[52] BTS/SIGN,

2019;[50] GEMA, 2023;[47] RRS, 2022;[48] SRS, 2018;[46] SINA, 2024;[49] NACA, 2022[51]) and or failing to respond to treatment (BTS/SIGN, 2019;[50] NVL, 2024;[53] RRS, 2022;[48] SRS, 2018;[46] SINA, 2024;[49] NACA, 2022[51]).

NVALT (2024) recommends only giving magnesium sulphate IV in an ED or ICU as an attempt to avoid or to shorten the duration of mechanical ventilation: following a systematic search, they cite no to low GRADE evidence across a range of outcomes.[54]

Use of IV aminophylline

Six of the 10 guidelines note guidance relating to the use of IV aminophylline in acute asthma attack.[48-52, 54] Strength of recommendation or supporting evidence was rarely provided. GINA (2024),[52] NVALT (2024),[54] NACA (2022),[51]and RRS (2022)[48] cite an updated Cochrane systematic review by Nair et al. (2012)[141] as supporting evidence, concerning the addition of IV aminophylline to inhaled β_2 agonists in adults with acute asthma. BTS/SIGN (2019)[50] cites an earlier version of this Cochrane review (Parameswaren et al., 2000).[142] NACA (2022) cites a Cochrane systematic review by Travers et al. (2012),[143] which compared the use of IV β_2 agonists with IV aminophylline in acute asthma exacerbations.

GINA (2024)[52] and RRS (2022)[48] recommend that IV aminophylline not be used in the management of severe exacerbations (RRS, 2022; Strength of recommendation A; level of evidence 1).[48] BTS/SIGN (2019) recommends that the use of IV aminophylline in acute attack should only be considered after consultation with senior medical staff (expert opinion),[50] and its use is not likely to result in any additional bronchodilation over current standard of care (specifically, bronchodilators and steroids)(level of evidence 1++).[47] NACA (2022) recommends that IV aminophylline may be considered for patients with life-threatening acute asthma that have not responded to continuous nebulised salbutamol, after considering other add-on treatment options.[51] NVALT (2024) states that the use of phosphodiesterase inhibitors should be avoided in acute asthma attack.[54] Potential increased risk of adverse effects such as nausea,[51, 52] vomiting[50-52] and arrhythmias[50, 51] as a result of treatment with aminophylline are noted within a number of guidelines, with GINA (2024) also noting that the use of IV aminophylline is associated with severe and potentially fatal side effects, particularly in those already treated with sustained-release theophylline.[52] SINA (2024)[49] also cites a study published in 1987,[144] which noted that the risk of cardiac arrhythmia is theoretically

increased by hypokalaemia and QT interval prolongation related to the use of high-dose short acting β_2 agonist or IV aminophylline.

Table 10 Overview of recommendations included in guidelines on the use of IV interventions in acute asthma attack

Shorthand name	Use of IV β_2 agonist	Use of IV magnesium in an acute asthma attack	Use of IV aminophylline
GINA (2024)[52]	**Recommendation:** *Acute care/ED:* Current evidence does not support the routine use of IV β_2 agonists in most patients with severe asthma exacerbations. **Strength of recommendation and level of evidence** Strength of recommendation: Not provided Level of evidence: A[137] **Key references** Travers et al. (2012)[137]	**Recommendation:** *Acute care/ED* IV magnesium sulphate is not recommended for routine use in asthma exacerbations, and should only be considered in the case of severe exacerbations. When administered as a single 2g infusion over 20 mins, it reduces hospital admissions in some patients, including adults with FEV1 <25-30% predicted at presentation, and those who fail to respond to initial treatment. **Strength of recommendation and level of evidence** Strength of recommendation: Not provided Level of evidence: A[138, 145] **Key references** Rowe et al. (2000),[138] Fitzgerald et al. (2000)[145] Noted: RCTs that excluded patients with more severe asthma showed no benefit with the addition of IV or nebulised magnesium compared with placebo in the routine care of asthma exacerbations in adults and adolescents. **Strength of recommendation and level of evidence** Strength of recommendation: Not provided Level of evidence: B **Key references** Goodacre et al. (2013)[140]	**Recommendation:** *Acute care/ED:* IV aminophylline (and theophylline) should not be used in management of asthma exacerbations, owing to poor efficacy and safety profile, and greater effectiveness and relative safety of short acting β_2 agonist.[141] Noted: Nausea and vomiting are more common with aminophylline.[141] The use of IV aminophylline is associated with severe and potentially fatal side effects, particularly in those already treated with sustained-release theophylline. In adults with severe exacerbations, add-on treatment with aminophylline does not improve outcomes compared with short acting β_2 agonist alone.[141] **Strength of recommendation and level of evidence** None provided **Key references** Nair et al. (2012)[141]
NVALT (2024)[54]	**Recommendation** Only give salbutamol IV in an ED or ICU as an attempt to avoid mechanical ventilation or to shorten the duration of mechanical ventilation. If bronchodilators by nebulization are insufficient, consideration may be given to switching to IV administration and changing nebulization from continuous to as needed.	**Recommendation** Only give magnesium sulphate IV in an ED or ICU as an attempt to avoid mechanical ventilation or to shorten the duration of mechanical ventilation. **Strength of recommendation and level of evidence** Strength of recommendation: Not reported Level of evidence:	**Recommendation** Avoid routine use of phosphodiesterase inhibitors in the treatment of a lung attack of asthma. **Strength of recommendation and level of evidence** Not provided **Key references** Nair et al. (2012)[141]

Shorthand name	Use of IV β_2 agonist	Use of IV magnesium in an acute asthma attack	Use of IV aminophylline
	When starting salbutamol IV, it is important to take into account the side effects that may occur, tachycardia and hypokalaemia. It is preferable to use this treatment only in an ED or ICU and under potassium monitoring. No evidence was found regarding the effect of salbutamol in addition to usual care on any of the outcomes. **Strength of recommendation and level of evidence** Strength of recommendation: Not reported Level of evidence: No GRADE **Key references** Cheong et al. (1998)[146]	Low GRADE for ICU admission, length of stay in ICU, need for ventilation, adverse events Very low GRADE for admission rates No GRADE for mortality, duration of ventilation. **Key references** Bloch et al. (1995),[147] Boonyavorakul et al. (2000), Bradshaw et al. (2007),[148] Goodacre et al. (2014,[149] Green et al. (1992),[150] Porter et al. (2001),[151] Silverman et al. (2002),[152] Singh et al. (2008),[153] Skobeloff et al. (1989)[154]	
NVL (2024)[53]	**Recommendation** The guideline group considers the quality and significance of the identified evidence for the parenteral use of β_2 sympathomimetics to be very low. If not improving, If necessary, β_2 sympathomimetics should be administered parenterally. **Strength of recommendation and level of evidence** Not provided **Key references** Travers et al. (2012)[137]	**Recommendation** If no response to initial therapy in ED or ICU: If necessary, magnesium sulphate 2g over 20 min IV. **Strength of recommendation and level of evidence** Reliability of evidence relating to hospitalisation endpoint considered high **Key references** Kew et al. (2014)[139]	**Recommendation** None provided **Strength of recommendation and level of evidence** N/A **Key references** N/A
SINA (2024)[49]	**Recommendation** IV therapy should not be considered routinely and only used cautiously if the response to the inhaled drug is poor or if the patient cannot tolerate the inhaled route. As the inhaled route has a faster onset of action and fewer adverse effects, the use of IV short acting β_2 agonists in the initial treatment of patients with acute severe asthma is not generally recommended.[155] **Strength of recommendation and level of evidence** Not provided **Key references** Travers et al. (2002)[155]	**Recommendation** Consider other therapies, such as (ipratropium bromide and magnesium sulphate) in managing severe attacks. For severe: If there is an inadequate response to previous measures, it is recommended to administer a single dose of IV magnesium sulphate at a dose of 1–2g over 20 min. **Strength of recommendation and level of evidence** Strength of recommendation: Not reported Level of evidence: B **Key references** Rowe et al. (2000)*,[138] Kew et al. (2014)[139]	**Recommendation** None provided. Noted that the risk of cardiac arrhythmia is theoretically increased by hypokalaemia and QT interval prolongation related to the use of high-dose short acting β_2 agonists or IV aminophylline**.** **Strength of recommendation and level of evidence** Not provided **Key references** Crane et al. (1987)[144]

Shorthand name	Use of IV β_2 agonist	Use of IV magnesium in an acute asthma attack	Use of IV aminophylline
GEMA (2023)[47]	**Recommendation** There is no evidence to support the use of a route other than inhalation for the administration of bronchodilator medication,[137] (i.e. β_2 agonists) The IV route, with a very slow continuous infusion, should be used when there is no response to inhalation therapy in patients under mechanical ventilation and monitored in an ICU. In this situation, recommended dose is salbutamol IV 200 mcg infused over 30 min (followed by 0.1 to 0.2 mcg/kg/min). No beneficial effects have been demonstrated when adding IV therapy to inhaled therapy.[137] **Strength of recommendation and level of evidence** Not provided **Key references** Travers et al. (2012)[137]	**Recommendation:** Routine administration of magnesium sulphate is not indicated, however, in selected patients experiencing severe obstruction (i.e. FEV1 25-30% of predicted) or persistent hypoxemia, a single dose of 2g administered by infusion reduces the need for hospitalisation. **Strength of recommendation and level of evidence** Not provided **Key references:** Rowe et al. (2000),[138] Fitzgerald et al. (2000)[145]	**Recommendation** None provided **Strength of recommendation and level of evidence** N/A **Key references** N/A
NACA (2022)[51]	**Recommendation** Do not use IV short-acting β_2 agonists routinely for initial bronchodilator treatment. May be considered as a third-line bronchodilator in life-threatening acute asthma that has not responded to continuous nebulised salbutamol after considering other add-on treatment options. Noted that monitoring of blood electrolytes, heart rate and acid/base balance (blood lactate) is recommended, salbutamol toxicity may occur with inhaled or IV salbutamol. **Strength of recommendation and level of evidence** Strength of recommendation: Evidence-based recommendation Level of evidence: Not reported **Key references** Travers et al. (2012)[137]	**Recommendation:** For adults with severe or life-threatening acute asthma, or with poor response to repeated maximal doses of other bronchodilators, consider adding IV magnesium sulphate. **Strength of recommendation and level of evidence** Strength of recommendation: Consensus recommendation Level of evidence: Not reported **Key references** Green (2016),[156] Kew et al. (2014)[139]	**Recommendation:** In critical care units (e.g. ED, ICU, high-dependency unit), IV aminophylline can be considered for patients with life-threatening acute asthma that has not responded to continuous nebulised salbutamol, after considering other add-on treatment options. Noted that IV aminophylline should be considered as a third-line bronchodilator in such a scenario. **Strength of recommendation and level of evidence** Not provided **Key references** Travers et al. (2012),[143] Nair et al. (2012)[141]
RRS (2022)[48]	**Recommendation** None provided	**Recommendation**	**Recommendation**

Shorthand name	Use of IV β_2 agonist	Use of IV magnesium in an acute asthma attack	Use of IV aminophylline
	Strength of recommendation and level of evidence N/A **Key references** N/A	In patients with severe exacerbation of asthma who are refractory to short acting β_2 agonist administration, magnesium sulphate is recommended,[138, 145] with caution in patients with reduced renal function. **Strength of recommendation and level of evidence** Strength of recommendation: A Level of evidence: 2 **Key references** Rowe et al. (2000),[138] Fitzgerald et al. (2000)[145]	Administration of aminophylline in the treatment of severe exacerbations of asthma in adult patients is not recommended. **Strength of recommendation and level of evidence** Strength of recommendation: A Level of evidence: 1 **Key references** Nair et al. (2012)[141]
BTS/SIGN (2019)[50]	**Recommendation** Reserve IV β_2 agonists for those patients in whom inhaled therapy cannot be used reliably. Noted that inhaled β_2 agonists are as efficacious and preferable to IV β_2 agonists in adult acute asthma in the majority of cases.[136] If IV β_2 agonists are used, consider monitoring serum lactate.[157] **Strength of recommendation and level of evidence** Strength of recommendation: A Level of evidence: 1++,[136] 3[157] **Key references** Tracers et al. (2001),[136] Lewis et al. (2014)[157]	**Recommendation** Consider giving a single dose of IV magnesium sulphate to patients with acute severe asthma (PEF <50% best or predicted) who have not had a good initial response to inhaled bronchodilator therapy. Best practice statement: Magnesium sulphate (1.2–2 g IV infusion over 20 mins) should only be used following consultation with senior medical staff. **Strength of recommendation and level of evidence** Strength of recommendation: B Level of evidence: 1++, 1+ **Key references** Goodacre et al. (2013),[140] Rowe et al. (2000),[138] Kew et al. (2014)[139]	**Recommendation** IV aminophylline should be considered only after consultation with senior medical staff. **Strength of recommendation and level of evidence** Expert opinion **Key references** N/A **Recommendation** In an acute asthma attack, IV aminophylline is not likely to result in any additional bronchodilation compared with standard care with inhaled bronchodilators and steroids. Side effects such as arrhythmias and vomiting are increased if IV aminophylline is used.[142] **Strength of recommendation and level of evidence** Strength of recommendation: Not provided Level of evidence: 1++ **Key references** Parmeswaren et al. (2000)[142]
SFMU/SRLF (2019)[45]	**Recommendation** β_2 adrenergic agonists should not be administered IV first line in adult or paediatric patients with severe	**Recommendation** Magnesium sulphate should probably not be administered routinely to adult patients with severe asthma exacerbation.	**Recommendation** None provided **Strength of recommendation and level of evidence**

Shorthand name	Use of IV β_2 agonist	Use of IV magnesium in an acute asthma attack	Use of IV aminophylline
	asthma exacerbations even in mechanically ventilated patients.[136] The IV route offers no advantage over inhalation as it has been associated with more side effects.[136] **Strength of recommendation and level of evidence** Strength of recommendation: Strong Level of evidence: GRADE 1-[136] **Key references** Travers et al. (2001)[136]	**Strength of recommendation and level of evidence** Strength of recommendation: Strong Level of evidence: Grade 2− **Key references** Weber et al. (2002),[79] Goodacre et al. (2014),[149] Skobeloff et al. (1989)[154] Bloch et al. (1995),[147] Egelund et al. (2013),[158] Kew et al. (2014)[139]	N/A **Key references** N/A
SRS (2018)[46]	**Recommendation** Routine use of IV β_2 agonists in ED/acute care is not recommended. **Strength of recommendation and level of evidence** Strength of recommendation: Not provided Level of evidence: A **Key references** Travers et al. (2012)[137]	**Recommendation** In patients with FEV1 <25–30% predicted at presentation and those who fail to respond to initial treatment and have persistent hypoxia, IV magnesium sulphate (2 g infusion over 20 min) should be considered. **Strength of recommendation and level of evidence** Strength of recommendation: Not provided Level of evidence: A **Key references** Rowe et al. (2000)[138]	**Recommendation** None provided **Strength of recommendation and level of evidence** N/A **Key references** N/A

Key: BTS/SIGN – British Thoracic Society/Scottish Intercollegiate Guidelines Network; ED – emergency department; FEV1 – forced expiratory volume in one second; g – gram; GEMA - Guía Espanola para el Manejo del Asma; GINA – Global Initiative for Asthma; GRADE – Grading of Recommendations, Assessment, Development and Evaluations; kg – kilogram; ICU – intensive care unit; IV – intravenous; mcg – microgram; min – minute; N/A – not applicable; NACA – National Asthma Council Australia; NVALT – Dutch Association of Pulmonologists; NVL – National Care Guidelines (Germany); PEF – peak expiratory flow; RCT – randomised controlled trial; RRS – Russian Respiratory Society; SINA – Saudi Initiative for Asthma; SRS – Swiss Respiratory Society; SFMU/SRLF - Societe Francaise de Medecine d'Urgence, the Societe de Reanimation de Langue Francaise. *Cited incorrectly in SINA (2024)[49] as “Camargo et al. (2000)”

3.6.4 Pharmacological interventions – other

Addition of an anticholinergic to β_2 agonist bronchodilators

Nine of the 10 included guidelines report on the addition of an anticholinergic to β_2 agonist bronchodilators,[45, 47-54] all of which recommend the addition of an anticholinergic in the management of severe or life-threatening asthma exacerbation. Overall, strength of recommendations and level of evidence were deemed to be strong, where reported. Notable citations for each guideline are outlined in Table 11. Key references commonly cited across guidelines included two systematic reviews specifically addressing the use of combined β_2 agonists and anticholinergics in the treatment of acute asthma (Rodrigo et al. (2005)[159] and Kirkland et al. (2017)[160]). BTS/SIGN (2019),[50] SFMU/SRLF (2019),[45] and SINA (2024)[49] cite Rodrigo et al. (2005)[159] as supporting evidence, while Kirkland et al. (2017)[160] is cited by SFMU/SRLF (2019),[45] NACA (2022),[51] NVL (2024),[53] GINA (2024)[52] and SINA (2024).[49] An analysis of pooled studies published in 1998[161] is also cited by five guidelines.[45, 47, 49, 50, 52] Though GEMA (2023)[47] and NVL (2024)[53] note that an anticholinergic is not recommended for the management for mild exacerbations, GINA (2024),[52] BTS/SIGN (2019),[50] and NACA (2022)[51] state that an anticholinergic may be introduced as add-on therapy for mild exacerbations where a poor initial response to treatment was observed (NACA, 2022; Consensus recommendation).[51] Three guidelines explicitly referred to use of anticholinergics in a primary care setting.[48, 52, 53] One further guideline (NACA, 2022) specified that ipratropium bromide should be initiated immediately in the case of severe exacerbation without distinguishing the care setting, but also stated that immediate transfer to the acute care setting should be arranged if response to initial treatment is insufficient.[51] SINA (2024) recommends that anticholinergics be given alongside β_2 agonists in the management of severe (level of evidence B) and life-threatening exacerbations (level of evidence A).[49] While SRS (2019) does not make a specific recommendation on the use of anticholinergics as an additional therapy, it notes that ipratropium bromide and short acting β_2 agonists are associated with fewer hospitalisations and greater improvement in PEF and FEV1 compared with short acting β_2 agonists alone.[46]

Use of LTRAs for acute attack

Six of the 10 included guidelines discuss the potential use of LTRAs as an intervention in acute asthma attack.[47, 48, 50-52, 54] Sources of evidence cited by the guidelines to support their recommendations include a Cochrane systematic review of the use of LTRAs in acute asthma conducted by Watts et al. (2012),[162] which is cited by GINA (2024),[52] NACA (2022)[51] and BTS/SIGN (2019).[50] Other key references cited across guidelines relate to a number of RCTs of both oral[163-165] and IV[166] montelukast, and zafirlukast[167] in acute asthma. NVALT (2024) specifically does not recommend the use of montelukast as an add-on treatment for acute attack.[54] NACA (2022) states that oral montelukast is not recommended for the management of acute asthma exacerbation in an acute setting (evidence-based recommendation),[51] as evidence from RCTs does not support routine use in acute asthma.[162] GEMA (2023)[47] and BTS/SIGN (2019)[50] specify that, at the time of guideline development, no data exist to support either oral or IV use of LTRAs (level of evidence 1++). GINA (2024)[52] and RRS (2022)[48] state that there is little[48] or limited[52] data to support their use either in improving lung function,[52] or more specifically, PEF.[48] GINA (2024),[52] BTS/SIGN (2019)[50] and RRS (2022)[48] highlight that additional studies are necessary to assess the clinical effectiveness and safety of LTRAs.

Use of antibiotics for acute attack

Nine guidelines refer to the use of antibiotics:[45-53] all of these guidelines suggest that antbiotics should not be used routinely in acute asthma unless indicated for signs of infection. Five guidelines note that antibiotics may be used in case of a “respiratory”, “lung” or “chest” infection or pneumonia.[45-48, 52] Five guidelines specified that antibiotics should only be used if the infection is bacterial.[45, 48, 50, 51, 53] Six guidelines provided references to support their recommendation; a Cochrane systematic review by Normansell et al (2018)[168] was cited by three guidelines.[51-53] Graham et al. (1982)[169] was cited by two guidelines[45, 50] and Johnston et al. (2016) was cited by two guidelines.[45, 51] Four guidelines[45, 46, 48, 53] provided an indication of the strength of recommendations regarding antiobiotics which ranged from strong or high[45, 53] to weak.[48]

Table 11 Overview of recommendations included in guidelines relating to other pharmacological interventions for acute asthma attack

Shorthand name	Addition of an anticholinergic to β_2 agonist bronchodilators	Use of LTRAs (for acute management only)	Use of antibiotics
GINA (2024)[52]	**Recommendation** *Primary care:* If mild/moderate exacerbation is worsening after 1 hour, or if exacerbation is classed as severe or life-threatening, initiate anticholinergic (ipratropium bromide) and transfer to acute care. *For acute care/ED:* If moderate/severe exacerbation, initiate short acting β_2 agonist and anticholinergic (ipratropium bromide; short-acting), as this combination is associated with fewer hospitalisations[160] and greater improvement in PEF and FEV1 compared with short acting β_2 agonist alone.[159, 160] **Strength of recommendation and level of evidence** Strength of recommendation: Not provided Evidence level: A **Key references** Rodrigo et al. (2005),[159] Kirkland et al. (2017)[160]	**Recommendation:** *Acute care/ED:* There is limited evidence to support the use of oral or IV LTRAs in acute asthma. Small studies have demonstrated improvement in lung function, but the clinical role and safety of these agents requires more study. **Strength of recommendation and level of evidence** Not provided **Key references** Ramsay et al. (2011),[163] Watts et al. (2012)[162]	**Recommendation** Antibiotics (not recommended). Evidence does not support the routine use of antibiotics in the treatment of acute asthma exacerbations unless there is strong evidence of lung infection (e.g., fever and purulent sputum or radiographic evidence of pneumonia). **Strength of recommendation and level of evidence** Not provided **Key references** Normansell et al (2018)[168]
NVALT (2024)[54]	**Recommendation** No specific recommendation provided. Noted that, in case of a severe asthma attack, give nebulisation of salbutamol (2.5–5 mg) with ipratropium (0.5 mg). (Daily dosage: usually 4-6 times daily nebulization). Noted that this indication/dosage is off-label. **Strength of recommendation and level of evidence** Not provided **Key references** No relevant references provided	**Recommendation** Do not give montelukast as an add-on treatment for a lung attack of asthma. **Strength of recommendation and level of evidence** Not provided **Key references** Silverman et al. (2004),[167] Camargo et al. (2010),[166] Çýllý et al. (2003)[164]	**Recommendation** Not discussed **Strength of recommendation and level of evidence** N/A **Key references** N/A
NVL (2024)[53]	**Recommendation** *In primary care and ED*: Recommends combination therapy of short acting β_2 agonist and short-acting anticholinergics for severe/life-threatening asthma attacks only, not for mild/moderate. If severe or life-threatening asthma: If available, give ipratropium bromide 0.5 mg nebulised or 80 mcg from a MDI	**Recommendation** Not discussed **Strength of recommendation and level of evidence** N/A **Key references** N/A	**Recommendation** Without sufficient evidence of a bacterial infection, antibiotics should not be used to treat asthma attacks in adults **Strength of recommendation and level of evidence** Strong negative recommendation, recommendation level A

Shorthand name	Addition of an anticholinergic to β_2 agonist bronchodilators	Use of LTRAs (for acute management only)	Use of antibiotics
	with spacer. If no response to initial therapy, then ipratropium 250-500 mcg + short acting β_2 agonist nebulised in ED or ICU.[160] **Strength of recommendation and level of evidence** Strength of recommendation: Not provided Level of evidence: Moderate **Key references** Kirkland et al. (2017)[160]		**Key references** Normansell et al (2018)[168]
SINA (2024)[49]	**Recommendation** *As an add-on therapy in managing severe attacks*: Ipratropium bromide is recommended to be added to salbutamol at a dose of 0.5 mg every 20 mins for 3 doses by the nebulised route, then every 4–6 hours as needed. **Strength of recommendation and level of evidence** Strength of recommendation: Not provided Level of evidence: B Noted that, alternatively, ipratropium can be administered by MDI at a dose of 4–8 puffs every 20 min, then every 4–6 hours as needed.[161, 170-172] The efficacy of adding ipratropium to short acting β_2 agonists to treat severe acute asthma attacks has been examined in a number of trials and systematic reviews.[173] It has been shown that patients who received the combination therapy of short acting β_2 agonist and ipratropium were less likely to be admitted to the hospital than those treated with short acting β_2 agonist alone. This benefit pertained only to those presented with severe acute asthma attacks and not to those with mild or moderate exacerbations.[160] **Recommendation** *For life-threatening exacerbation:* Deliver continuous nebulised salbutamol at a dose of short acting β_2 agonist 10–15 mg with ipratropium bromide at a dose of 1.5 mg over 1 hour. **Strength of recommendation and level of evidence** Strength of recommendation: Not provided Level of evidence: A **Key references**	**Recommendation** Not discussed **Strength of recommendation and level of evidence** N/A **Key references** N/A	**Recommendation** Do not prescribe routine antibiotics […]unless indicated. **Strength of recommendation and level of evidence** Not provided **Key references** Not provided

Shorthand name	Addition of an anticholinergic to β_2 agonist bronchodilators	Use of LTRAs (for acute management only)	Use of antibiotics
	Lanes et al. (1998),[161] Chassany et al. (2000),[170] Rodrigo et al. (1999),[171] Stoodley et al. (1999),[172] Jackson et al. (2018),[173] Kirkland et al. (2017)[160]		
GEMA (2023)[47]	**Recommendation** The addition of ipratropium bromide is not necessary for mild attacks should not be routinely prescribed.[174, 175] The use of ipratropium bromide during the initial phase of moderate or severe exacerbations concomitantly with a short acting β_2 agonist is associated with a greater increase in pulmonary function (estimated by FEV1 or PEF) and a decrease in hospitalisations as compared to the use of short acting β_2 agonist alone.[159, 176] Recommended doses for treating exacerbations: (i) (p)MDI +spacer: 80-160 mcg (4-8 puffs of 20 mcg) every 10-15 mins. (ii) Nebulised, intermittent: 0.5 mg every 20 mins. **Strength of recommendation and level of evidence** Not provided **Key references** Soar et al. (2010),[174] Vanden Hoek et al. (2010)[175] Manser et al. (2001),[176] Rodrigo et al. (2005)[159]	**Recommendation** No data is available to support the use of LTRAs either orally or IV. **Strength of recommendation and level of evidence** Not provided **Key references** Not provided	**Recommendation** No formal recommendation about antibiotics, guideline states: *For mild exacerbation*: antibiotics should not be routinely prescribed. *For moderate and severe*: there is no evidence supporting the use of antibiotics, except in the presence of a clearly symptomatic respiratory infection **Strength of recommendation and level of evidence** Not provided **Key references** Not provided
NACA (2022)[51]	**Recommendation** Ipratropium bromide is recommended in combination with salbutamol in the initial treatment of patients with severe or life-threatening acute asthma via (p)MDI or spacer, or via nebulisation where necessary. Noted: If response to initial inhaled salbutamol is incomplete or poor, consider adding ipratropium bromide (if not used initially) or other add-on treatments. **Strength of recommendation and level of evidence** Strength of recommendation: Consensus recommendation Level of evidence: Not provided **Key references** Kirkland et al. (2017)[160]	**Recommendation** Montelukast is not recommended for the management of acute asthma in adults in acute care settings. **Strength of recommendation and level of evidence** Strength of recommendation: Evidence based recommendation Level of evidence: Not provided **Key references** Watts et al. (2012),[162] Zubairi et al. (2013),[165] Ramsay et al. (2011)[163]	**Recommendation** No formal recommendation about antibiotics, guideline states under 'more information': Antibiotics are not used routinely in the management of acute asthma but should be used if they would otherwise be indicated. **Strength of recommendation and level of evidence** Not reported **Key references** Normansell et al (2018),[168] Johnston et al (2016)[177]
RRS (2022)[48]	**Recommendation** *Pre-hospital management:*	**Recommendation**	**Recommendation**

Shorthand name	Addition of an anticholinergic to β_2 agonist bronchodilators	Use of LTRAs (for acute management only)	Use of antibiotics
	For patients experiencing mild to moderate asthma exacerbations, multiple administrations of inhaled short acting β_2 agonist or combinations of β_2 agonist and ipratropium bromide are **recommended.** *Hospital management:* Inhaled short acting β_2 agonist or a combination of short acting β_2 agonist and ipratropium bromide is recommended as first-line treatment for all patients with severe exacerbation of asthma.[120, 159] Noted: For acute exacerbation of asthma it is recommended to use ipratropium bromide with nebulizer at a dose of 500 mcg every 4-6 hours, more frequent use (every 2-4 hours) is possible. **Strength of recommendation and level of evidence** Strength of recommendation: A Level of evidence: 1 **Key references** Rodrigo et al. (2005),[159] Camargo et al. (2003)[120]	There is little data on the benefits of LTRA use in acute exacerbation of asthma. Small studies have shown improvement in PEF, but additional studies are needed to assess the clinical significance. **Strength of recommendation and level of evidence** Not provided **Key references** Silverman et al. (2004),[167] Ramsay et al. (2011)[163]	In patients with exacerbation of AD, the use of the following drugs and methods are not recommended: […] antibacterial drugs. Comment -Antibacterial drugs are indicated only in cases of bacterial infection - pneumonia, sinusitis. **Strength of recommendation and level of evidence** Level of persuasiveness: C Level of evidence: 5 **Key references** Not reported for antibacterial drugs specifically
BTS/SIGN (2019)[50]	**Recommendation** Add nebulised ipratropium bromide (0.5 mg 4–6 hourly) to β_2 agonist treatment for patients with acute severe or life-threatening asthma or those with a poor initial response to β_2 agonist therapy.[159, 161, 172] **Strength of recommendation and level of evidence** Grade of Recommendation: B Level of evidence: 1++ **Key references** Lanes et al. (1998),[161] Rodrigo et al. (2005),[159] Stoodley et al. (1999)[172]	**Recommendation** Current evidence on oral LTRAs does not support their use in patients with acute asthma. Further studies are required to assess whether IV treatment is effective and safe. **Strength of recommendation and level of evidence** Strength of recommendation: Not provided. Level of evidence: 1++ **Key references** Watts et al. (2012)[162]	**Recommendation** Routine prescription of antibiotics is not indicated for patients with acute asthma. The guideline also notes: when an infection precipitates an asthma attack it is likely to be viral. The role of bacterial infection has been overestimated. Decision making regarding the use of antibiotics in patients with acute asthma should be guided by objective measures including procalcitonin where available. (EL 1++, 1+) **Strength of recommendation and level of evidence** Grade of recommendation B Level of evidence: 1++, 1+ **Key references** Graham et al. (1982)[169], Long et al. (2014)[178], Tang et al. (2013)[179]

Shorthand name	Addition of an anticholinergic to β_2 agonist bronchodilators	Use of LTRAs (for acute management only)	Use of antibiotics
SFMU/SRLF (2019)[45]	**Recommendation** Inhaled anticholinergic drugs should be combined with β_2 agonists in adult and paediatric patients with severe asthma exacerbation. **Strength of recommendation and level of evidence** Strength of recommendation: Strong recommendation Level of evidence: Grade 1+ **Recommendation** The experts suggest administering a 0.5 mg dose of ipratropium bromide every 8 hours in adults and children > 6 years of age. **Strength of recommendation and level of evidence** Expert opinion Also noted: Compared with the administration of β_2 agonists alone, the anticholinergic/bronchodilator combination increased FEV1 and PEF. **Strength of recommendation and level of evidence** Not provided **Key references** Lanes et al. (1998),[161] Rodrigo et al. (1999),[171] Stoodley et al. 1999),[172] Kirkland et al. (2017),[160] Britton et al. (1988)[180]	**Recommendation** Not discussed **Strength of recommendation and level of evidence** N/A **Key references** N/A	**Recommendation** Antibiotic therapy should probably not be administered routinely during severe asthma exacerbation in adult […] patients. Antibiotic therapy should probably be reserved for cases of suspected bacterial pneumonia, based on usual clinical, radiological, and laboratory signs **Strength of recommendation and level of evidence** Level of evidence: Grade 2−, strong agreement **Key references** Marchello et al. (2016)[181], Talbot at al. (2005) [182], Gielen et al. (2010)[183], Kobayashi et al. (2013)[184], Johnston et al. (2006)[185], Johnston et al. (2016)[177], Graham et al. (1982)[169], Graham et al. (2001)[186].
SRS (2018)[46]	**Recommendation** Not provided. Noted regarding the treatment of asthma exacerbations in emergency care: Ipratropium bromide and short acting β_2 agonist are associated with fewer hospitalisations and greater improvement in PEF and FEV1 compared with short acting β_2 agonist alone.[159] **Strength of recommendation and Level of evidence** Not provided **Key references** Rodrigo et al. (2005) [159]	**Recommendation** Not discussed **Strength of recommendation and Level of evidence** N/A **Key references** Not discussed	**Recommendation** Primary care: Antibiotics should not be prescribed unless there is clear evidence of chest infection. **Strength of recommendation and level of evidence** Not provided **Key references** Not provided

Key: BTS/SIGN – British Thoracic Society/Scottish Intercollegiate Guidelines Network; ED – emergency department; FEV1 – forced expiratory volume in one second; GEMA - Guía Espanola para el Manejo del Asma; GINA – Global Initiative for Asthma; ICU – intensive care unit; IV – intravenous; LTRA – leukotriene-receptor antagonist; mcg – microgram; mg – milligram; min – minute; N/A – not applicable; NACA – National Asthma Council Australia; NVALT – Dutch Association of Pulmonologists; NVL – National

Care Guidelines (Germany); PEF – peak expiratory flow; (p)MDI – (pressurised) metred dose inhaler; RRS – Russian Respiratory Society; SINA – Saudi Initiative for Asthma; SRS – Swiss Respiratory Society; SFMU/SRLF - Societe Francaise de Medecine d'Urgence, the Societe de Reanimation de Langue Francaise.

3.7 Recommendations relating to secondary topics of interest

Seven secondary topics of interest for guideline recommendations were highlighted by the GDG. A matrix of recommendations relating to these secondary topics included by the guidelines is provided in Table 12.

Table 12 Matrix of secondary topics of interest addressed in the included guidelines

	GINA (2024)[52]	NVALT (2024)[54]	NVL (2024)[53]	SINA (2024)[49]	GEMA (2023)[47]	NACA (2022)[51]	RRS (2022)[48]	BTS/SIGN (2019)[50]	SFMU /SRLF (2019)[45]	SRS (2018)[46]
FEV1 for detecting and or assessing an acute asthma attack and to inform hospital referral and/or admission	✓	✓		✓	✓	✓		✓		✓
FeNO for detecting and or assessing an acute asthma attack		✓								
Respiratory rate for assessing severity of an asthma attack	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Use of nebulised magnesium sulphate	✓	✓	✓		✓	✓		✓	✓	
Use of IV fluid regimes							✓	✓		
Use of nebulised furosemide								✓		

Key: BTS/SIGN - British Thoracic Society/Scottish Intercollegiate Guidelines Network; FeNO - Fractional exhaled Nitric Oxide; FEV1 – forced expiratory volume in one second; GEMA - Guía española para el manejo del asma; GINA - Global Initiative for Asthma; IV – intravenous; NACA - National Asthma Council Australia; NIV – non-invasive ventilation; NVALT - Dutch Association of Pulmonologists; NVL – National Care Guidelines (Germany); RRS - Russian Respiratory Society; SFMU/SRLF - Société Française de Médecine d'Urgence/Société de Réanimation de Langue Française;; SINA - The Saudi Initiative for Asthma; SRLF -; SRS - Swiss Respiratory Society.

3.7.1 FEV1 for detecting and or assessing an acute asthma attack and to inform hospital referral and or admission

Seven guidelines address the use of FEV1 values (predicted or personal best) in the detection or assessment of acute asthma attack, and consequently its use in informing the appropriate care setting, though cut-off values were not consistent across the literature, with sources of evidence rarely outlined.[46, 47, 49-52] GINA (2024) recommends considering discharge from the ED for patients whose FEV1 is 60-80% after initial treatment and continuing treatment in the ED for those whose FEV1 is less than 60%.[52] GINA (2024)[52] also recommends that providers hospitalise patients whose pre-treatment FEV1 is less than 25% and those whose post-treatment FEV1 is less than 40%.[64] GEMA (2023) cites FEV1 values to denote severity of exacerbation, where FEV1 greater than 70% is considered a mild attack, FEV1 less than 70% is considered moderate, while FEV1 less than 50% is considered severe.[47] BTS/SIGN (2019) mentions that assessment of lung function by PEF is more convenient than FEV1 in the acute situation, and recommends that lung function (including FEV1) be closely monitored for exacerbations in the ED.[50] NACA (2022) notes that, when conducting secondary assessment of acute asthma exacerbation, FEV1 predicted or personal best of greater than 50% indicates mild/moderate exacerbation (when other criteria are met), and FEV1 of less than or equal to 50% indicates severe exacerbation.[51] NACA (2022) also notes that, when measured one hour after initial treatment has been provided, hospital admission should be considered where FEV1 is less than 60% predicted or 50% of usual, if known (consensus recommendation).[51]

NVALT (2024) indicates that, if practical, spirometry (or inflammatoryometry) may be considered selectively for risk assessment in a patient experiencing asthma exacerbation. However, the guideline notes that, due to lack of evidence, no advice can yet be given on whether and when to use these lung function measurements. While SINA (2024) does not specify FEV1 cut-off values to inform the detection or assessment of acute exacerbation, the guideline does state specify deteriorating lung function (FEV1 and or PEF) as a criterion for ICU referral.[49]

3.7.2 Fractional exhaled Nitric Oxide for detecting and or assessing an acute asthma attack

One guideline references the use of FeNO in the assessment of acute asthma exacerbation. NVALT (2024) sought to review evidence regarding the place of lung function measurement with a FeNOmeter in the diagnosis of adults with an asthma exacerbation, specifically in the first two hours after presentation to the hospital. However, the guideline reports that no data were found.[54]

3.7.3 Respiratory rate for assessing severity of an asthma attack

All 10 included guidelines refer to respiratory rate for assessing severity of exacerbation. Six guidelines classify an exacerbation as severe where respiratory rate is greater than 25 breaths per minute,[47, 48, 50, 51, 53, 54] while three guidelines classify an exacerbation as severe where respiratory rate is greater than 30 breaths per minute.[45, 49, 52] SRS (2018) specifies an exacerbation with a respiratory rate of greater than 30 breaths per minute may be classified as severe or life threatening, requiring immediate transfer to acute care.[46]

3.7.4 Use of nebulised magnesium sulphate

Few guidelines recommend the use of nebulised magnesium sulphate for use in acute asthma. BTS/SIGN (2019) states that nebulised magnesium sulphate is not recommended for treatment in adults with acute asthma (Grade of recommendation A) and SFMU/SRLF (2019) states that magnesium sulphate should probably not be administered routinely to adult patients with severe asthma exacerbation (GRADE 2−, strong agreement).[50] GINA (2024) reports that RCTs excluding patients with more severe asthma showed no benefit with the addition of nebulised magnesium compared with placebo in the routine care of asthma exacerbations in adults and adolescents (Evidence level B).

NVALT (2024) cites a trial (Goodacre et al., 2014)[140] that found no evidence that nebulised magnesium sulphate was more effective than placebo.[54] In contrast, GEMA (2023) allows for inhaled magnesium sulphate in case of treatment failure,[47] citing a recent Cochrane systematic review (Knightly, 2017)[187] showing beneficial effects of inhaled magnesium sulphate added to short-acting β_2 agonist or short-acting β_2 agonist plus ipratropium bromide in reducing hospital admissions (mostly from the ED) and mild improvement of pulmonary

function. NVL (2024) also cited Knightley (2017), stating that the guideline development group was unable to derive a benefit for the inhalation of magnesium sulphate for hospitalisation from the available data, with several studies of low to modest level of proof yielding discordant results. NACA (2022) does not include a recommendation on the use of nebulised magnesium sulphate; the guideline states that its use as an add-on treatment to salbutamol and ipratropium may achieve small improvement in lung function and reduction in hospital admission rates in acute asthma, noting that this has not been clearly demonstrated in studies at time of guideline development.[51]

3.7.5 Use of IV fluid regimes

Two guidelines refer to the use of IV fluids in the management of acute asthma exacerbation in adults.[48, 50] BTS/SIGN (2019) states that there are no controlled trials, observational or cohort studies of differing fluid regimes in patients with acute asthma, but that some patients require rehydration and correction of electrolyte imbalance, for example hypokalaemia can be caused or exacerbated by β2 agonist and or steroid treatment and must be corrected.[50] Conversely, RRS (2022) states that IV fluid regimens are not recommended.[48]

3.7.6 Use of nebulised furosemide

Only BTS/SIGN (2019) discusses the use of nebulised furosemide in acute asthma exacerbation,[50] citing a review of three small trials that failed to show any significant benefit of treatment with nebulised furosemide compared to β2 agonists (Level of evidence 1+).[188]

4. Discussion

4.1 Overall summary

Ten guidelines that contained recommendations on the primary topics of interest to the *Management of Acute Asthma Attacks in Adults* GDG were included in this review.[45-54] Acute asthma exacerbation was the primary focus of only two guidelines,[45, 54] while a further eight guidelines featured recommendations relating to acute asthma exacerbation as part of a guideline focusing on asthma diagnosis and management more broadly.[46-53] No guideline was identified which provided recommendations on all 14 primary topics of interest to the GDG. Secondary topics of interest that were frequently addressed included the use of lung function assessments such as FEV1 and respiratory rate to classify severity of exacerbation in the management of acute exacerbation. Recommendation strength and the level of evidence underpinning recommendations were not always outlined. The overall quality of the included guidelines varied, though three of the guidelines (BTS/SIGN (2019),[50] NVL (2024),[53] and NVALT (2024)[54]) were rated as consistently high quality, with regard to overall quality assessment score and under each of four core domains assessed. Two of these high-quality guidelines were recent publications (2024),[53, 54] while correspondence with the BTS/SIGN guideline developers indicates that there is no current plan to update the acute management aspects of the BTS/SIGN (2019) guideline.[50]

4.1.1 Primary topics of interest addressed in current Irish guideline

Nine of the 14 topics of interest identified by the GDG are currently addressed in NCG No. 14.[32] Seven topics map to existing guideline recommendations and two topics (chest X-ray and antibiotics) map to good practice points.[32]

The use of PEF measurement as an indicator to inform referral of care was discussed by nine of the included guidelines. Specific cut-off values differed between guidelines, and few guidelines cited either sources of evidence or a degree of certainty for the values reported. Both NACA (2022)[51] and NVALT (2024)[54] indicated that insufficient evidence exists to support the use of PEF values to inform care setting, making no recommendation on PEF as a referral criteria, and in the case of NACA (2022),[51] noting that it is not well-studied. Sources of evidence cited indicated no emerging evidence was identified in relation to this primary

topic, though no guideline noted whether a topic-specific search was conducted. Notably, international guidelines broadly indicated treatment in the acute care setting where PEF is less than or equal to 50% predicted. This differs from that indicated in the current Irish national guideline, which recommends that admission to hospital is advised in patients whose peak flow is less than 75% best or predicted after initial treatment.

Use of chest X-ray and imaging in treating acute asthma was discussed in ten guidelines.[45-54] In line with NCG No. 14, five guidelines state that chest X-ray is not routinely recommended.[46, 49, 50, 52, 53] Particular circumstances for use of chest X-ray mentioned in the international guidelines include:

- complicating or alternative cardiopulmonary process[46-53]
- lack of response to treatment[45-47, 50, 52]
- life-threatening acute asthma attack[47-50]
- ventilation requirement.[48, 50]

Of note, five guidelines[46, 47, 49, 52, 54] did not indicate the strength or level of evidence. The other four guidelines[45, 48, 50, 51] indicated strength or level of evidence tended to be low or consensus. The most frequently referenced paper[63] was published over 30 years old and there is no indication of emerging evidence on this topic in the international guidelines.

Though four guidelines addressed the use of oxygen-driven versus air-driven compressors,[45, 49-51] only one (BTS/SIGN, 2019) provided guidance specifically relating to a primary care setting. BTS/SIGN (2019)[50] recommends that nebulisers for giving β_2 agonist bronchodilators should preferably be driven by oxygen in settings including primary care, owing to the risk of oxygen desaturation while using air-driven compressors.[50] SINA (2024) also recommends the use of oxygen-driven nebulisation over air-driven, though the guideline does not specify the care setting to which this recommendation applies.[49] However, NACA (2022), specifies that in the initial management of severe exacerbations, air-driven nebulisation of pharmacological treatment is recommended unless oxygen therapy is required.[51] Additionally, NACA (2022) outlines a scenario whereby a switch from oxygen-driven nebulisation to air-driven nebulisation may be considered in secondary care.[51] Notably, SFMU/SRLF (2019) state that

a systematic search of the literature did not yield evidence to support the use of oxygen over air as an aerosol carrier gas.[45] No emerging evidence was cited across guidelines.

The use of heliox was addressed by six guidelines,[45, 48, 50-53] with all recommending against the use of heliox in the management of acute attack. This is judged to be in agreement with the current Irish guideline, which recommends against the use of heliox in acute exacerbation management outside of a clinical trial setting.[32] Guidelines did not cite any emerging evidence, and the lack of evidence of clinical benefit to support the use of heliox was often noted, though no guidelines specify conducting a topic-specific search to identify relevant evidence.

Eight guidelines refer to the use of NIV for acute asthma exacerbation.[45-48, 50-52, 54] Notably, three guidelines do not provide a recommendation on its use, citing insufficient evidence on the use of NIV.[45, 46, 52] NVALT (2024)[54], who conducted a systematic topic-specific search in 2021, recommends against the use of NIV due to lack of evidence. Four guidelines indicate possible circumstances the use of NIV could be considered.[47, 48, 50, 51] Similar to NCG No. 14, BTS/SIGN (2019) indicated that NIV should only be considered in ICU or equivalent clinical setting.[50] Five[45, 50-52, 54] out of eight guidelines cited the same systematic review[111] published in 2012. Where strength of evidence was provided on this topic, it ranged from consensus statement [50, 51] to weak.[48]

The use of anticholinergics as an addition to β_2 agonists in the treatment of acute exacerbation was recommended by nine of the included guidelines,[45, 47-54] which is in agreement with the recommendation set out in the current Irish guideline.[32] While SRS (2018) did not make a specific recommendation on the use of anticholinergics as an add-on treatment,[46] the guideline did note evidence in support of their use. Certainty of supporting evidence was high, where reported. No emerging evidence was noted.

Nine included guidelines recommend against the routine use of IV β_2 agonist therapy for acute attacks,[45-47, 49-54] with six of these outlining conditional recommendations for use, including where other interventions have failed, or where the inhaled route is not possible.[47, 49-51, 53, 54] No emerging evidence of note was cited by the guidelines, with the most recent topic-specific search for this primary topic carried out in 2022. Included guidelines concur with the recommendation around IV β_2 agonists outlined in the current Irish guideline.[32]

The use of IV magnesium for acute exacerbation was addressed by all included guidelines, with recommendations broadly in agreement with that outlined in the current Irish guideline;[32] all but one guideline[54] indicated that IV magnesium may be used in the management of severe exacerbation, with some guidelines specifically noting that use is appropriate when other treatments have failed. NVALT (2024), having conducted a systematic topic-specific search conducted in 2022, were more restrictive in their recommendation, stating that the use of IV magnesium may be considered only to avoid, or shorten the duration of, mechanical ventilation.[54] An RCT by Goodacre et al. (2013)[140] was noted to be most recent supporting evidence cited across guidelines.

The use of antibiotics in acute asthma is discussed in nine guidelines.[45-53] In line with the NCG No. 14, all nine guidelines indicate they should not be used routinely in acute asthma unless indicated for signs of infection. Five guidelines referenced antibiotic use in "respiratory", "lung" or "chest" infection or pneumonia.[45-48, 52] Five guidelines indicated that antibiotics should only be used if the infection is bacterial.[45, 48, 50, 51, 53] There was a range in the strength of recommendations from strong or high[45, 53] to weak.[48]

4.1.2 Primary topics of interest not addressed in current Irish guidelines

Five primary topics of interest in this review are not addressed in the current national clinical guideline of the management of acute asthma attack,[32] specifically the use of respiratory rate as an indicator to inform referral to the appropriate care setting and the use of LTRAs, IV aminophylline, high-flow oxygen, and ECMO as interventions in acute asthma attack.

Five guidelines provided specific respiratory rate cut-off values to inform referral from primary care to hospital in the event of acute exacerbation, though guidelines conflicted as to whether 25 or 30 breaths per minute is considered an appropriate measure for referral. BTS/SIGN (2019)[50] and NVL (2024),[53] both rated as high-quality guidelines, cited the lower value of 25 breaths per minute as an indicator of referral, with BTS/SIGN (2019) providing a grade of recommendation B to support its recommendation.[50] The underlying evidence for these values were rarely cited, indicating little evidence relating to this primary topic. None of the guidelines provided a specific respiratory rate to inform ICU admission.

All six of the included guidelines that discussed the use of LTRAs were in agreement against their use as an add-on treatment in the management of acute attack,[47, 48, 50-52, 54] with a systematic review by Watts et al. (2012)[162] noted by a number of guidelines. The most recent topic-specific search was conducted in 2022 for the development of NVALT (2024),[54] which found no studies demonstrating clinical benefit in acute attack on specified endpoints of interest. No emerging evidence was identified in this search.

The use of IV aminophylline for acute asthma attacks was addressed by six guidelines.[48-52, 54] Five guidelines, including two deemed high-quality, either advised against use, or advised conditional use, such as where exacerbation is life-threatening, and other treatments have failed.[48, 50-52, 54] All note the potential for adverse events with the use of IV aminophylline. Overall, guidelines provided a high certainty of evidence in support of these recommendations.

Guidelines that provided recommendations or guidance on the use of high-flow oxygen for the management of acute severe exacerbation were in agreement that controlled flow oxygen was preferable to high-flow oxygen. Of note, NACA (2022) noted that delivery of high-flow oxygen via nasal cannulae is increasingly common practice in Australian emergency rooms, despite sparse evidence to support its use.[51] A topic-specific search of NIV conducted in 2022 by NVALT (2024)[54] identified three studies published in 2019,[86] 2020[87] and 2021[88] which indicate that any clinical benefit of high-flow nasal cannula over conventional oxygen therapy is very uncertain in acute asthma. While NVALT (2024) could not recommend its use,[54] these more recent publications, when considered alongside apparent increasing use in Australian settings,[51] would appear to indicate an evidence base may be developing around this topic.

While the use of ECMO was not addressed by the current Irish national clinical guideline, neither was it addressed in many of the included guidelines in this review. Two guidelines that did address the use of ECMO (BTS/SIGN, 2019[50] and NVL, 2024[53]) were perceived to be of high quality, with both conditionally indicating that ECMO may have a role as a rescue treatment where exacerbation is near-fatal, though BTS/SIGN (2019) indicates a low level of certainty in this recommendation.[50] The third guideline that addressed ECMO (SRFMU/SRLF, 2019)[45] indicates that its use may be considered in specific cases after consultation with

clinical experts, but interestingly notes that ECCOO_2 may be an alternative treatment option, given that it may be more convenient and accessible.[45] While guidelines cited few sources of evidence in relation to ECMO, it should be noted that the most recent topic-specific search reported (conducted by BTS/SIGN (2019)[50] included literature published in 2018.

4.1.3 Secondary topics of interest addressed in the included guidelines

Secondary topics of interest in this review varied with regard to how they were addressed in the included guidelines. Some secondary topics, such as the use of FeNO in the assessment of exacerbation, nebulised furosemide and IV fluids, were rarely addressed by the included guidelines. Where nebulised furosemide and IV fluids were addressed, guidelines noted a lack of demonstrable clinical benefit. While a greater number of guidelines discussed the use of nebulised magnesium sulphate, some guidelines provided recommendations against its use, classifying the available evidence underlying the recommendations as being of relatively high level. Where guidelines addressed the use of FEV1 to classify severity of exacerbation or to inform appropriate care setting, inconsistency was found in the values reported. Similarly, values relating to the use of respiratory rate in the assessment of severity of exacerbation varied between guidelines.

4.2 Implications

The results of this review should be interpreted with consideration of a number of limitations. This review sought to identify relevant clinical guidelines on the management of an acute asthma attack in adults (aged 16 years and above) that are currently in use internationally. However, clinical guidelines are typically not included within electronic databases. As such, a considerable effort was made to include a diversity of sources in addition to the electronic searches. While an extensive grey literature search was conducted to identify eligible guidelines, a truly comprehensive search of the grey literature is difficult.

This review also provides a summary of the recommendations, advice and good practice points, as outlined in the included guidelines, in addition to a summary of the sources of evidence underpinning the recommendations. The findings need to be considered alongside the rigour of overall approach taken to guideline development, including the EtD framework taken to reach recommendations. Quality appraisal of the included guidelines considered the methodological approach to guideline development, which was often not reported with a

high degree of granularity. Guidelines that rated highly in the quality appraisal provided detailed methods which would enable a reproducible search of the literature, clearly outlined evidence underpinning recommendations, and described robust EtD processes.

Moreover, it is important to clarify that the purpose of this review was not to conduct a systematic review of the clinical effectiveness of the topics of interest, nor does the evidence summarised in this review represent the totality of the evidence that exists relating to these topics. Evidence presented is that which was considered important during the guideline development processes of the included guidelines. Given that topic-specific searches were not conducted for all primary or secondary topics, it is possible that further evidence may exist that could contradict, or further support, recommendations made within the included guidelines.

Considering all of the above, the review has identified two guidelines that were published recently that were rated high-quality, namely NVL (2024)[53] and NVALT (2024),[54] which provide a comprehensive overview of their guideline development processes. However, neither guideline provides recommendations on all 14 primary topics of interest to the GDG.

Based on the evidence and recommendations provided by all included guidelines, the recommendations are broadly (i) in favour of the addition of anticholinergics to β_2 agonists in the treatment of acute asthma attacks, (ii) against the use of LTRAs in the management of acute asthma attacks, and (iii) against routine use of chest X-ray, heliox, IV β_2 agonists, antibiotics, and IV aminophylline, with specific pre-conditions noted for the use of chest X-ray, IV β_2 agonists, and antibiotics.

Inconsistencies were noted relating to several primary topics of interest, specifically the use of PEF or respiratory rate to inform level of care, IV magnesium sulphate, high-flow oxygen, ECMO, NIV, and oxygen-driven versus air-driven compressors in the management of exacerbation. Inconsistency was observed across guidelines on the use of PEF or respiratory rate to inform level of care, both in the values noted and sources of evidence cited, with certainty in this evidence rarely specified. None of included guidelines reported conducting topic-specific searches to inform these values. While guidelines agree on the conditional use of IV magnesium sulphate in the management of severe acute asthma attacks as an add-on therapy or where other interventions have failed, there appears to be inconsistency as to the

conditions under which its use should be considered. While guidelines imply that the use of conventional-flow oxygen is preferred over the use of high-flow oxygen in the management of acute attack, two guidelines note emerging evidence around,[54] and increased use of,[51] high-flow oxygen. The use of ECMO is referenced by three guidelines only,[45, 50, 53] two of which from 2019 and 2024 advise consideration where exacerbation is life-threatening, or where rescue is required,[50, 53] and one from 2019 which suggests that $ECCO_2R$ may be preferential to ECMO based on expert opinion.[45] Guidelines noted a lack of available literature, though the most recent topic-specific search for ECMO was conducted in 2018 by BTS/SIGN (2018).[50] NIV is discussed in eight guidelines but there is lack of agreement among the guidelines. The position of the guidelines varies, with three[45, 46, 52] not providing recommendations due to paucity in evidence; one guideline[54] recommending against its use; and four guidelines[47, 48, 50, 51] outlining its possible use in specific circumstances. Lastly, the use of oxygen-driven or air-driven compressors was discussed by only four guidelines,[45, 49-51] of which only one specified their recommendation related to a primary care setting. Guidelines differ as to recommendations relating to oxygen-driven delivery, and few sources of evidence were cited to support recommendations.

4.3 Conclusions

Overall, this review presents international recommendations and underpinning evidence related to key topics of interest to the Management of an Acute Asthma Attack in Adults guideline development group and indicates key areas where evidence may be emerging. A comparison of the current Irish guidelines and international guidelines suggests that NCG No. 14's Recommendation No. 5 (75% PEF cut-off for admission) may benefit from revisiting, and that the evidence for part of Recommendation No. 9 (oxygen-driven nebulisation in primary care) may be lacking. Other existing Irish recommendations of interest to the GDG appear to be in line with current international recommendations. In terms of primary topics of interest to the GDG that are not currently covered in Irish guidelines, international guidance does offer recommendations around respiratory rate to inform referral to acute care; otherwise, primary topics not currently recommended in Irish guidance are likewise not recommended or recommended against in international guidelines. In line with best practice in evidence-based guideline development, the findings of this review will inform the next steps for the update to NCG No. 14.

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