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Scottish Airways Research Network (SARN) Delphi Consensus on pre-biologic assessment, clinical remission and post-remission management in severe asthma

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Abstract

Introduction: Scotland's severe asthma multidisciplinary teams and prescribing recommendations may contribute to variation in biologic decisions. We sought expert consensus on pre-biologic assessment, clinical remission and post-remission management through the Scottish Airways Research Network (SARN).

Methods: A scientific committee developed 28 statements across these three domains. Thirty specialists from 15 centres rated statements using a five-point Likert scale. Consensus was predefined as >75% agreeing or strongly agreeing. Statements requiring revision were considered in Round 2.

Results: Twenty-four panellists completed Round 1 (80% response), achieving consensus on 15/28 statements (53.6%); 23 completed Round 2 (76.7% response), achieving consensus on 10/13 revised statements (76.9%). Pre-biologic assessment should include treatment optimisation, comprehensive phenotyping, type 2 biomarkers, exacerbation history, comorbidities and patient characteristics. Clinical remission should generally be assessed after at least 12 months and comprise freedom from maintenance oral corticosteroids, absent or minimal symptoms, no severe exacerbations, stable lung function, normalised asthma-related quality of life, and patient-healthcare professional agreement. Improved lung function, reduced airway inflammation and treatment burden, and normalised airway hyperresponsiveness were desirable but not mandatory. No consensus was reached on a specific Asthma Control Questionnaire threshold for remission or restricting biologic access among current smokers not participating in smoking cessation. Dosing-interval extension or discontinuation should not be routine but may be considered for selected patients with sustained remission under specialist supervision, shared decision-making, close monitoring and a rapid restart plan.

Conclusion: This Scottish Delphi study provides a pragmatic framework to support equitable, consistent decisions on pre-biologic assessment, remission and treatment de-escalation.

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BJL reports grants, personal fees (consulting, talks and advisory board), other support (attending ATS and ERS) from AstraZeneca; grants, personal fees (talks and consulting) and other support (Attending ATS ,ERS and BTS) from Sanofi/Regeneron, personal fees (consulting, talks and advisory board) from Niox in relation to the submitted work; personal fees (talks and consulting), grants and other support (attending ERS and BTS) from Chiesi, personal fees (consulting and talks) from Lupin, personal fees (consulting) from Glenmark, consulting fees from Propeller Bio, Belenos, Pfizer , Bambusa ; Equipment from Vitalograph, Lothar Medtec, Thorasys ; and the son of BJL is presently an employee of AstraZeneca.

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Abstract

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Results: Twenty-four panellists completed Round 1 (80% response), achieving consensus on 15/28 statements (53.6%); 23 completed Round 2 (76.7% response), achieving consensus on 10/13 revised statements (76.9%). Pre-biologic assessment should include treatment optimisation, comprehensive phenotyping, type 2 biomarkers, exacerbation history, comorbidities and patient characteristics. Clinical remission should generally be assessed after at least 12 months and comprise freedom from maintenance oral corticosteroids, absent or minimal symptoms, no severe exacerbations, stable lung function, normalised asthma-related quality of life, and patient-healthcare professional agreement. Improved lung function, reduced airway inflammation and treatment burden, and normalised airway hyperresponsiveness were desirable but not mandatory. No consensus was reached on a specific

Asthma Control Questionnaire threshold for remission or restricting biologic access among current smokers not participating in smoking cessation. Dosing-interval extension or discontinuation should not be routine but may be considered for selected patients with sustained remission under specialist supervision, shared decision-making, close monitoring and a rapid restart plan.

Conclusion: This Scottish Delphi study provides a pragmatic framework to support equitable, consistent decisions on pre-biologic assessment, remission and treatment de-escalation.

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Introduction

Severe asthma affects an estimated 5-10% of individuals with asthma and is associated with disproportionate morbidity and treatment burden.¹ The ERS/ATS definition is principally treatment-based, encompassing asthma that requires high-dose inhaled corticosteroids (ICS) plus a second controller to prevent loss of control, or that remains uncontrolled despite such therapy.² Although clinically pragmatic, this definition does not fully capture the biological heterogeneity of severe asthma or the degree of persistent airway inflammation, both of which are central to the selection of targeted therapy. A structured pre-biologic assessment is therefore essential. This should confirm the diagnosis; identify and address modifiable factors such as suboptimal adherence, incorrect inhaler technique and ongoing exposures; and optimise comorbidities and background treatment.¹ Alongside exacerbation history, biomarkers of type 2 (T2) inflammation can help inform biologic eligibility.¹

The advent of biologic therapy has shifted the ambition of severe asthma management beyond disease control, with clinical remission emerging as an achievable on-treatment goal for some patients.³ However, considerable uncertainty remains regarding how remission should be defined. A recent systematic review and meta-analysis of 25 studies identified 68 reported definitions of clinical remission, of which 48 were unique, with particularly marked variation in symptom and lung function criteria.⁴ This heterogeneity limits comparisons between studies and impedes the implementation of remission as a consistent and clinically meaningful treatment target. In parallel, standardised approaches are required to guide cautious treatment de-escalation in patients who achieve sustained disease control or clinical remission.¹

In the United Kingdom, severe asthma is managed through a multidisciplinary team (MDT) approach,⁵ typically involving respiratory physicians, specialist pharmacists and specialist nurses. These MDTs oversee the assessment of patients and the initiation and monitoring of biologic therapy. In England and Wales, regional MDTs commonly make decisions regarding biologic treatment for patients referred from surrounding hospitals. In Scotland, however, MDTs are organised at the individual hospital level rather than regionally, with each centre operating its own severe asthma MDT. This less regionalised model may result in subtle variation in how MDTs assess patients being considered for biologic therapy. There is currently no standardised documentation template, allowing each MDT to reach its own consensus based on local practice. For example, one MDT may prioritise the patient's T2 biomarker status, when selecting a biologic, whereas another may place greater emphasis on clinical phenotype or specific treatment goals, such as improving impaired lung function, provided the relevant licensing and eligibility criteria are met.

Scotland provides a distinct context for severe asthma care. It has a population of approximately 5.55 million, with healthcare delivered through a devolved NHS comprising 14 territorial health boards across a geographically dispersed mixture of urban, rural and island populations. Specialist severe asthma services and biologic prescribing are organised locally or regionally, commonly through MDTs, although service configuration may vary between health boards. NHS prescriptions are also free at the point of dispensing in Scotland, unlike England, although prescriptions are likewise free in Wales, removing direct prescription charges for maintenance asthma treatment. The participation of clinicians from 15 centres therefore provides broad insight into asthma care across this distinctive national healthcare system, while also allowing potential variation in local service organisation and decision-making to be captured.

Biologic prescribing in Scotland is also subject to several important nuances. Although the National Institute for Health and Care Excellence (NICE) provides clear guidance on the use of biologic therapies for asthma, medicines used within NHS Scotland require approval by the Scottish Medicines

Consortium (SMC).⁶⁻¹⁰ SMC recommendations broadly align with those issued by NICE but include subtle differences in prescribing and eligibility criteria. Consequently, a consensus specifically developed for NHS Scotland is needed to promote equitable, consistent and transparent decision-making across severe asthma MDTs.

Accordingly, this study used a Delphi process to establish expert consensus on pre-biologic assessment, the definition of clinical remission, post-remission management and approaches to treatment de-escalation in severe asthma. The panel comprised members of the Scottish Airways Research Network (SARN), representing 15 centres with expertise in severe asthma management across Scotland.

Methods

This study used a Delphi methodology to establish expert consensus on pre-biologic assessment, the definition of clinical remission, and post-remission management in severe asthma. The Delphi method is a structured consensus-building technique designed to enable a panel of experts to address complex questions through a series of iterative surveys.¹¹ It has been applied across a wide range of disciplines and is particularly valuable in healthcare when robust empirical evidence is limited, existing guidelines are insufficient, or knowledge remains uncertain or incomplete.¹² By combining qualitative feedback with quantitative assessment of agreement, the Delphi process facilitates the systematic refinement of expert opinion. Its essential components include the selection of an appropriate expert panel, the development and administration of structured surveys, and repeated rounds of review and feedback until consensus is reached.

The iterative nature of the Delphi method is intended to progressively reduce variation in expert opinion and facilitate consensus. The process is underpinned by three key principles: participant anonymity, controlled feedback, and statistical aggregation of group responses.

A scientific committee comprising six expert respiratory physicians was established to oversee the study. During an initial meeting, the committee discussed and clearly defined the scope of the survey. Drawing on the available literature and their clinical expertise, the committee subsequently developed a preliminary list of candidate statements. These were reviewed and refined to minimise redundancy and ensure clarity and consistency of wording before inclusion in the first-round questionnaire (Round 1; R1).

The R1 questionnaire comprised 28 statements across three principal domains: pre-biologic assessment, the definition of clinical remission, and post-remission management in severe asthma. R1 was administered using Microsoft Forms (Microsoft Corporation, Redmond, WA, USA) between 5 and 17 July 2026. An initial email invitation was followed by two reminders, sent one week after launch and 48 hours before the closing date. It was distributed to a panel of 30 members of the Scottish Airways Research Network (SARN), comprising consultant respiratory physicians (n=23), senior nurses (n=3), senior pharmacists (n=2), and asthma fellows undertaking a higher research degree in asthma (MD or PhD; n=2). All panellists had sub-specialist expertise or research experience in asthma.

Panellists rated their level of agreement with each statement using a five-point Likert scale: 1, strongly disagree; 2, disagree; 3, neither agree nor disagree; 4, agree; and 5, strongly agree. High consensus was defined a priori as >75% of respondents rating a statement as either 4 or 5.¹³ The scientific committee then conducted an interim analysis of the R1 responses, including the quantitative ratings and qualitative feedback. The scientific committee did not have access to identifiable individual responses during the consensus process. Based on these findings, a second-round questionnaire (Round 2; R2) was developed, focusing on priority statements requiring further consideration,

clarification, or reassessment. No additional statements were generated based on first-round feedback.

Before R2, panellists received the anonymised aggregate R1 results, including the number and proportion selecting each response option on the five-point Likert scale. All 30 originally invited panellists, including members of the scientific committee and regardless of whether they had participated in R1, were invited to review and rate the revised R2 statements. R2 was administered using Microsoft Forms between 22 July and 4 August 2026, following the same invitation and reminder schedule.

Results

The board developed 28 statements, which were distributed anonymously to a panel of 30 experts. In R1, 24 experts responded, corresponding to a response rate of 80% (**Table 1**). Consensus was achieved for 15 of the 28 statements (53.6%) (**Figures 1-3**). There was broad agreement on pre-biologic assessment, although consensus was not reached for several eligibility and treatment-selection criteria. Consensus was also achieved on the definition of clinical remission, which required freedom from maintenance oral corticosteroids (OCS), absent or minimal asthma symptoms and exacerbations, stable lung function, normalisation of asthma-related quality of life, and agreement between the patient and clinician that remission had been achieved. Although stable lung function was considered an essential component, the panel did not support requiring a predefined improvement in FEV₁. Similarly, consensus was not reached on the use of a specific Asthma Control Questionnaire threshold of <0.75. Regarding duration, most experts considered remission to require the absence of exacerbations for at least 12 months, although this statement fell marginally below the predefined consensus threshold. No consensus was reached on whether biologic therapy should be continued, discontinued, or administered at a reduced dosing frequency in patients with severe asthma who had achieved clinical remission. Statements that did not achieve consensus were subsequently revised and carried forward to R2. Given the marked lack of agreement, the board decided not to carry forward the statement requiring a predefined improvement in FEV₁ as a criterion for clinical remission.

In R2, the questionnaire was reduced to 13 statements, with responses received from 23 panel members (response rate, 76.7%). Consensus was achieved for 10 of the 13 statements (76.9%) (**Table 1**) (**Figure 4**), confirming agreement on pre-biologic considerations, the composite definition of clinical remission, and decision-making following initiation of biologic therapy.

The revised statement recommending consideration of escalation to high-dose ICS/LABA, or the maintenance and reliever therapy (MART) equivalent, before adding a LAMA achieved consensus (87%) in R2, with the proviso that treatment should be individualised according to patient phenotype and guideline recommendations. In this context, MART would refer to a patient taking 2 puffs ICS/formoterol twice daily as maintenance plus up to a specified maximum of additional ICS/formoterol reliever puffs per day, consistent with high-dose ICS exposure.¹⁴ Following revision of the two statements concerning FEV₁ and a coexisting diagnosis of COPD when selecting an appropriate severe asthma biologic, both achieved consensus in R2 (91.3% and 87%, respectively), with the caveat that asthma phenotype, type 2 biomarkers, exacerbation history, and relevant comorbidities should also be considered.

Although agreement increased in R2 regarding consideration of biologic therapy for patients actively engaged in a smoking cessation programme, consensus was not achieved (25% in R1 versus 73.9% in R2), even after smoking was contextualised alongside other potentially modifiable risk factors, such as obesity. Regarding the duration required to define clinical remission, the statement specifying a

minimum duration of 12 months received greater agreement and consensus in R2 than in R1 (91.3% versus 75%, respectively). Four statements addressing whether clinical remission should include a clinically meaningful improvement in lung function, a reduction in airway inflammation, a reduction in baseline asthma treatment, and normalisation of airway hyperresponsiveness achieved consensus (87%, 95.7%, 87%, and 95.7%, respectively) after these features were specified as desirable rather than mandatory. **Table 2** synthesises the Delphi findings into a pragmatic framework to support MDT assessment and management of patients receiving biologic therapy for severe asthma. It organises the findings into four clinical domains: pre-biologic assessment, mandatory and desirable components of clinical remission, and management following sustained remission. Given the low level of agreement in R1 (12.5%) and duplication of a previous statement on clinically meaningful FEV₁ improvement, the board elected not to revise or carry forward the statement requiring a predefined minimum improvement in FEV₁ as a criterion for clinical remission.

The revised statement concerning extension of the biologic dosing interval achieved consensus in R2 (87%) after specifying that this approach should be considered only within specialist severe asthma services for carefully selected patients with sustained clinical remission, following shared decision-making and with close clinical monitoring. The board also divided the R1 statement concerning the ACQ threshold for clinical remission into two R2 statements specifying cut-offs of <1.5 and <1.0. Neither achieved consensus (65.2% and 60.9%, respectively), with levels of agreement numerically similar to that observed for the <0.75 cut-off in R1 (66.7%). Finally, the revised statement concerning biologic discontinuation achieved consensus in R2 (95.7%), with the caveat that discontinuation should not be routine but may be considered for carefully selected patients with sustained clinical remission following specialist review and shared decision-making, provided that an agreed monitoring strategy and a plan for rapid re-initiation in the event of relapse are in place.

Discussion

Most statements relating to pre-biologic assessment achieved consensus in R1 (7/11; 63.6%). Notably, 91.7% of experts agreed or strongly agreed that total IgE should be considered when assessing suitability for biologic therapy in severe asthma. Although total IgE measurement is required to determine eligibility for and dosing of omalizumab, baseline total IgE does not predict treatment response.¹⁵ This may reflect the profound suppression of free circulating IgE achieved with appropriately dosed omalizumab across the eligible baseline IgE range. Furthermore, in a post hoc analysis of placebo arms of seven randomised controlled trials (RCT), total IgE was not an independent risk factor for exacerbations after adjusting for blood eosinophil count (BEC) and FeNO.¹⁶ The anti-IL4R α biologic dupilumab has also been shown to reduce exacerbation rates to a similar extent irrespective of allergic status, defined as a baseline total serum IgE level ≥ 30 IU/mL and at least one positive perennial aeroallergen-specific IgE result (≥ 0.35 kU/L).¹⁷ Nevertheless, total IgE remains clinically important as an eligibility and dosing biomarker. When interpreted alongside allergen-specific IgE or skin-prick testing and the clinical history, it helps characterise the allergic phenotype, determines whether anti-IgE therapy is a treatment option, and may prompt consideration of relevant comorbid diagnoses, such as allergic bronchopulmonary aspergillosis. Its inclusion in pre-biologic assessment therefore supports comprehensive phenotyping and preserves access to the full range of potentially appropriate biologic therapies.

For uncontrolled asthma, the Global Initiative for Asthma (GINA) recommends considering either escalation to high-dose maintenance ICS/LABA or the addition of a LAMA to a medium-dose regimen.¹ However, the optimal sequence remains uncertain, and joint British Thoracic Society/National Institute for Health and Care Excellence/Scottish Intercollegiate Guidelines Network (BTS/NICE/SIGN) guidance permits LAMA addition to moderate-dose MART.¹⁸ The guidance also states that “if treatment with

MART using a moderate-dose maintenance regimen does not provide adequate asthma control, the evidence on how best to increase treatment is less clear cut. People whose asthma is uncontrolled at this stage will be using additional doses of ICS/formoterol for symptom relief and will effectively be on high-dose ICS". In two RCTs involving patients receiving at least medium-dose ICS/LABA with an FEV₁ ≤80% predicted, the addition of tiotropium significantly prolonged the time to first exacerbation by 56 days and increased peak FEV₁ by 86-154 mL.¹⁹ In a post hoc analysis of the phase III IRIDIUM study, medium-dose mometasone/indacaterol/glycopyrronium (MF/IND/GLY) improved trough FEV₁ by 88 mL (95%CI 39,137) compared with high-dose fluticasone propionate/salmeterol (FP/SAL).²⁰ The same comparison favoured medium-dose MF/IND/GLY for severe exacerbations (rate ratio 0.71; 95%CI 0.53,0.95). However, this post hoc analysis was not stratified according to the presence of airflow obstruction at baseline. In a post hoc analysis of the TRIMARAN study, 29.4% of patients receiving medium-dose beclomethasone/formoterol/glycopyrronium achieved clinical remission at 52 weeks, defined as no maintenance OCS use or exacerbations, preserved FEV₁, and an ACQ-5 score <1.5.²¹ Treatment escalation should therefore be individualised rather than applied as a mandatory sequence. Taken together, these findings raise the possibility that the presence of airflow obstruction, or raised FeNO, the latter of which reflecting IL-13 mediated inflammation and a potentially greater response to ICS,²² could also guide the choice between de-escalation to medium-dose ICS/LABA/LAMA and high-dose ICS/LABA.

Although evidence supporting baseline FEV₁ as a predictor of biologic response remains weak,²³ comparative data suggest that biologics may differ in their effects on lung function. These differences may, at least in part, reflect differential effects on mannitol airway hyperresponsiveness,^{24,25} mucus plugging,²⁶ and/or airway remodelling.²⁷

To our knowledge, no evidence directly informs the choice of biologic in patients with severe asthma and coexisting COPD. Phase III trials, including BOREAS and NOTUS for dupilumab^{28,29} and MATINEE³⁰ for mepolizumab, support the efficacy of these biologics in specific populations of patients with COPD and may therefore influence treatment selection in patients with both conditions. However, this represents extrapolation from COPD trials rather than direct evidence in patients with coexisting severe asthma and COPD. There remains a paucity of evidence regarding biologic efficacy in current smokers, who have generally been underrepresented or excluded from clinical trials. Most available studies compare never-smokers with former smokers and report no meaningful differences in clinical outcomes.^{31,32} Agreement increased from 25% in R1 to 73.9% in R2 after the statement was reframed around active engagement with smoking cessation but remained below the consensus threshold. This likely reflects the balance between recognising smoking cessation as an important component of severe asthma management and concerns that making engagement with a cessation programme mandatory could create an inequitable barrier to biologic treatment for otherwise eligible patients. More recent observational evidence from the European SHARP cohort demonstrated comparable reductions in exacerbation frequency following biologic therapy among current, former and never-smokers.³³ We therefore suggest that current smokers should be offered a time-limited trial of biologic therapy with formal response assessment, pending further evidence on whether efficacy is attenuated compared with that observed in former and never-smokers.

Seven of the 13 statements relating to clinical remission achieved consensus in R1. Across both rounds, most panellists agreed that remission should be assessed over at least 12 months, which is reasonable because this period captures seasonal variation in asthma activity.³⁴ Although stable lung function was accepted as a mandatory criterion, a separate statement requiring a clinically meaningful improvement in lung function did not achieve consensus. This may reflect the need for a pragmatic definition, as some patients have limited scope for improvement because of preserved baseline lung

function or irreversible airflow obstruction. Furthermore, biological and measurement variability and the effort-dependent nature of spirometry may make a universal absolute threshold, such as an FEV₁ improvement of ≥ 100 mL, inappropriate.³⁵ Similarly, reducing baseline asthma treatment burden constitutes good clinical practice,¹ but was not accepted as a mandatory criterion for clinical remission because remission may be achieved and sustained while treatment is continued. Treatment reduction represents a subsequent management decision that should be individualised according to the duration and stability of remission, the risk of relapse and patient preference. Although normalisation of airway hyperresponsiveness is achievable in a proportion of patients receiving biologic therapy,³⁶⁻³⁸ the limited availability of bronchial challenge testing in routine clinical practice precludes its inclusion as a mandatory criterion for clinical remission. Clinical and biological remission, defined by clinically meaningful reductions in FeNO and BEC, may also occur independently of one another.³⁹ Accordingly, biological remission was considered a desirable rather than mandatory component of clinical remission.

Only one of the four statements relating to post-remission management achieved consensus in R1. In patients with severe asthma who have achieved clinical remission on biologic therapy, reduction of ICS/LABA dose, or MART equivalent, should be prioritised before extending the biologic dosing interval. Although no direct evidence establishes whether ICS dose reduction should precede extension of biologic dosing intervals in patients whose asthma is well controlled on biologic therapy, the phase IV SHAMAL study demonstrated that asthma control could be maintained while ICS-formoterol was tapered to medium- or low-dose MART during continued treatment with the anti-IL-5R α biologic benralizumab.⁴⁰ Further evidence is awaited from the phase IIIb ARRIVAL study (NCT06473779), which is evaluating whether patients treated with tezepelumab can reduce background maintenance therapy without loss of asthma control.

Although the absence or near-absence of symptoms was considered a mandatory criterion for clinical remission, the panel did not reach consensus on a specific ACQ threshold after two rounds. This is a substantive negative finding as it directly contradicts published remission frameworks.³ Notably, none of the three ACQ thresholds tested (<0.75 , <1.0 , <1.5) achieved consensus, contrasting with existing remission frameworks that specify ACQ-based cut-offs, and highlighting the need for a MART-adapted symptom measure. This may partly reflect the difficulty of applying a single ACQ threshold in contemporary severe asthma practice. The ACQ was developed and validated in 1999, before the introduction of biologic therapies,⁴¹ and the ACQ-6 and full ACQ-7 include short-acting rescue bronchodilator use, which may be difficult to interpret in patients using ICS-formoterol as both maintenance and reliever therapy.¹ This is therefore an important area for future evidence generation, and a revised iteration of the ACQ that accounts for MART use would be valuable. Furthermore, although validated and reliable, symptom-based patient-reported outcome measures depend on patients' perception and attribution of symptoms. Multimorbidity, including obesity, anxiety, depression and dysfunctional breathing, may mimic or amplify asthma symptoms and adversely affect ACQ scores independently of underlying asthma activity.⁴² Consequently, a single ACQ threshold may lack sufficient specificity to define clinical remission across a heterogeneous severe asthma population.

Finally, consensus was achieved in R2 on revised statements clarifying that biologic dosing-interval extension and discontinuation should not be routine decisions but may be considered within specialist severe asthma services following careful patient selection, shared decision-making, close monitoring, and agreement on a rapid re-initiation plan in the event of relapse. Preliminary evidence suggests that dosing intervals for anti-IL-5/IL-5R α biologics can be extended in selected patients with sustained asthma control or clinical remission.^{43,44} However, the available studies are small, this practice would be off-label, and some patients experience loss of disease control, supporting an individualised

approach with prompt reinstatement of the licensed dosing regimen where required. Moreover, evidence from other immune-mediated conditions suggests that interrupting and subsequently restarting biologic therapy may increase the risk of anti-drug antibody formation.⁴⁵ This association has been demonstrated most clearly with TNF inhibitors, particularly infliximab,⁴⁶ for which intermittent treatment has been associated with greater immunogenicity than scheduled maintenance therapy.

Several limitations should be acknowledged. The candidate statements were generated and revised by the scientific committee rather than through an open-ended first round or formal systematic review, introducing the possibility of statement-selection and framing bias. Response rates were high but incomplete, and because all originally invited panellists were eligible to participate in R2 irrespective of R1 participation, the composition of respondents may have differed between rounds, limiting assessment of within-person convergence. These findings primarily reflect current expert practice within Scottish severe asthma services, providing a pragmatic framework to support consistency of care rather than novel clinical guidance. The Delphi process favours convergence towards prevailing views, and the largely conventional framing of the initial statements may have limited exploration of emerging concepts or alternative perspectives. Nevertheless, areas where consensus was not achieved highlight persisting uncertainty and priorities for further research. Finally, consensus was defined by dichotomising Likert responses.

Future consensus exercises should explore whether earlier introduction of biologic therapy could modify disease trajectory, with any proposed disease-modifying effects requiring prospective evaluation. Greater consideration should also be given to patients with substantial multimorbidity, whose symptom burden and treatment priorities may be inadequately captured by asthma-specific measures alone. Incorporating patient perspectives and broader outcomes, including overall quality of life, functional status and treatment burden, could help define a more comprehensive approach to biologic assessment and guide future research.

This SARN Delphi study provides a first in Scotland pragmatic framework for assessing patients before biologic initiation, defining clinical remission and guiding subsequent treatment decisions in severe asthma. From a national perspective it provides understanding into current MDT practice and the views of expert working groups. Internationally, we hope it will offer insight into how severe asthma care is approached in a nation with smaller regional MDTs. Prospective studies are required to validate these consensus criteria and determine the optimal sequence and safety of treatment reduction in patients achieving remission.

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Table 1 Statements and corresponding levels of consensus achieved during the first (R1) and second (R2) Delphi rounds. Green shading indicates that consensus was achieved, whereas purple shading indicates that consensus was not achieved.

	R1			R2	
R1 Statements	n (%) agreement	Median (IQR)	R2 Statements	n (%) agreement	Median (IQR)
(A) Pre-biologic assessment					
In patients with poorly controlled asthma despite medium-dose ICS/LABA, or an equivalent MART regimen, escalation to high-dose ICS/LABA should be considered before adding a LAMA.	12/24 (50%)	3.5 (3,4)	Escalation from medium-dose to high-dose ICS/LABA or high dose MART regimen should usually be considered before LAMA addition, although treatment should remain individualised according to patient phenotype and guideline recommendations.	20/23 (87%)	4 (4,5)
Patients should generally have an adequate trial of optimised high-dose ICS/LABA, or equivalent MART regime, before biologic initiation, unless this is contraindicated, not tolerated, or clinically inappropriate.	21/24 (87.5%)	5 (4,5)			
Total IgE should be considered when assessing a patient's suitability for biologic therapy in severe asthma.	22/24 (91.7%)	4 (4,5)			
CT-defined mucus plugging should be considered as a treatable trait in severe asthma and may inform biologic selection when	20/24 (83.3%)	4 (4,5)			

interpreted alongside type 2 biomarkers, exacerbation history and comorbidities.					
Relevant comorbidities such as atopic dermatitis or chronic rhinosinusitis with nasal polyposis should influence biologic decision in severe asthma.	23/24 (95.8%)	4.5 (4,5)			
Hospital admission, emergency department attendance, ICU/HDU admission, or previous near-fatal asthma should influence biologic treatment urgency.	24/24 (100%)	5 (4,5)			
Macrolide therapy may be considered in selected adults with severe asthma and persistent exacerbations despite optimised inhaled therapy.	19/24 (79.2%)	4 (4,4)			
Severe asthma assessment should include documentation of socioeconomic factors and barriers to care.	22/24 (91.7%)	4 (4,4)			
Baseline FEV ₁ should be considered when selecting biologic therapy for patients with severe asthma.	13/24 (54.2%)	4 (3,4)	Baseline FEV ₁ should be interpreted alongside biomarkers, exacerbation history and comorbidities when selecting biologic therapy.	21/23 (91.3%)	4 (4,5)
			The presence of concomitant COPD should be considered		

Concomitant COPD should be considered when selecting biologic therapy for patients with severe asthma.	14/24 (58.3%)	4 (3,4)	alongside asthma phenotype, type 2 biomarkers, exacerbation history and relevant comorbidities when selecting biologic therapy for patients with severe asthma.	20/23 (87%)	4 (4,4)
Current smoking status should not preclude biologic therapy in patients with severe asthma who otherwise meet eligibility criteria.	6/24 (25%)	3 (2,3.5)	Current smokers should only be offered biologic therapy if they are actively engaged in a smoking cessation programme, consistent with the management of other modifiable risk factors such as obesity.	17/23 (73.9%)	4 (3,5)

(B) Clinical remission

Clinical remission in severe asthma should be defined using a composite measure comprising multiple clinical criteria.	23/24 (95.8%)	4 (4,5)			
A definition of clinical remission in severe asthma should only be applied after a minimum treatment period of	6 months: 2 12 months: 18 (75%) 24 months: 4 48 months: 0	12 months (12,12)	Do you agree that clinical remission should generally be assessed after at least 12 months of continuous treatment?	21/23 (91.3%)	4 (4,5)
Please indicate the extent to which you agree that each of the following should be included as a criterion in the definition of clinical remission in severe asthma: 1. No ongoing requirement for	23/24 (95.8%)	5 (4,5)			

maintenance oral corticosteroids					
2. Absence or minimal burden of asthma symptoms	24/24 (100%)	4 (4,5)			
3. Absence of severe asthma exacerbations or attacks	24/24 (100%)	5 (4,5)			
4. Stable lung function	20/24 (83.3%)	4 (4,5)			
5. Clinically meaningful improvement in lung function	9/24 (37.5%)	3 (2.5,4)	A clinically meaningful improvement in lung function should be regarded as a desirable outcome of treatment but should not be mandatory for defining clinical remission.	20/23 (87%)	4 (4,4)
6. Reduction in baseline asthma treatment burden, including inhaled corticosteroids and other controller therapies	14/24 (58.3%)	4 (3,4)	Reduction in baseline asthma treatment burden (e.g. inhaled corticosteroid dose and/or other controller therapies) should be considered a desirable outcome of sustained clinical remission rather than a mandatory criterion for defining remission.	22/23 (95.7%)	4 (4,5)
7. Normalisation of airway hyperresponsiveness	9/24 (37.5%)	3 (2.5,4)	Normalisation of airway hyperresponsiveness should be considered a desirable outcome but should not be required for defining clinical remission.	22/23 (95.7%)	4 (4,4)
8. Normalisation of asthma-related quality of life	21/24 (87.5%)	4 (4,5)			

9. Clinically meaningful reduction in airway inflammation	12/24 (50%)	3.5 (3,4.5)	Reduction in type 2 airway inflammation (where elevated at baseline) should be considered a supportive marker of treatment response rather than a mandatory criterion for clinical remission.	20/23 (87%)	4 (4,4)
10. Agreement between the patient and healthcare professional that clinical remission has been achieved	20/24 (83.3%)	4 (4,5)			
In addition to withdrawal of maintenance oral corticosteroids, absence of severe exacerbations and good symptom control, clinical remission should require at least 10% or 100ml improvement in FEV ₁ .	3/24 (12.5%)	3 (2,3)			
(C) Post-remission management					
In patients with sustained clinical remission on biologic therapy, biologic dose-interval extension may be considered in selected cases within specialist care	13/24 (54.2%)	4 (3,4)	In carefully selected patients with sustained clinical remission, extension of the biologic dosing interval may be considered within specialist severe asthma services following shared decision-making and close clinical monitoring.	20/23 (87%)	4 (4,4)
			An ACQ score <1.5 should define good symptom control	15/23 (65.2%)	4 (2,4)

In the context of clinical remission, good symptom control should be defined as an Asthma Control Questionnaire score of <0.75.	16/24 (66.7%)	4 (3,4)	for the purposes of clinical remission.		
			An ACQ score <1 should define good symptom control for the purposes of clinical remission.	14/23 (60.9%)	4 (3,4)
Biologic discontinuation should not be routine but may be considered in selected patients with sustained clinical remission after specialist review, shared decision-making, and a clear monitoring/restart plan.	15/24 (62.5%)	4 (3,4)	Biologic discontinuation should not be routine. In carefully selected patients with sustained clinical remission, discontinuation may be considered following specialist review, shared decision-making, and an agreed monitoring and rapid re-initiation plan in the event of relapse.	22/23 (95.7%)	4 (4,5)
In patients with severe asthma who have achieved clinical remission on biologic therapy, reduction of ICS/LABA dose, or MART equivalent, should be prioritised before extending the biologic dosing interval.	23/24 (95.8%)	4 (4,5)			

ACQ = asthma control questionnaire; COPD = chronic obstructive pulmonary disease; CT = computed tomography; FEV₁ = forced expiratory volume in 1 second; HDU = high dependency unit; ICS = inhaled corticosteroid; ICU = intensive care unit; IQR = interquartile range; LABA = long-acting beta agonist; LAMA = long-acting muscarinic antagonist; MART = maintenance and reliever therapy

Table 2 Scottish Airways Research Network (SARN) criteria for pre-biologic assessment, clinical remission and post-remission management

Pragmatic SARN consensus framework for severe asthma biologic MDTs	
1 Before biologic initiation • Confirm asthma diagnosis and assess alternative/exacerbation mimics • Assess adherence, inhaler technique, triggers/exposures and social barriers • Document exacerbations, OCS exposure, hospital/ED/ICU attendance and near-fatal asthma • Record BEC, FeNO, total IgE and allergen sensitisation • Assess comorbidities: CRSwNP, atopic dermatitis, obesity, breathing pattern disorder, mucus plugging, COPD and bronchiectasis • Optimise inhaled therapy individualising ICS dose and LAMA use according to phenotype and guideline recommendations	2 Clinical remission - mandatory • Assess over a minimum 12-month period • No maintenance OCS • No severe asthma exacerbations • Absence or minimal asthma symptom burden • Stable lung function • Normalisation of asthma-related quality of life • Agreement between the patient and healthcare professional that clinical remission has been achieved
3 Clinical remission - desirable • Clinically meaningful improvement in lung function • Reduction in baseline asthma treatment burden, including ICS and other controller therapies • Normalisation of AHR • Clinically meaningful reduction in airway inflammation	4 After sustained remission • Suggest withdrawal of maintenance OCS first during clinical stability • Consider ICS/LABA or MART-equivalent reduction • Consider biologic interval extension only within specialist severe asthma care • Biologic discontinuation should not be routine • If de-escalating, use shared decision-making, close monitoring, predefined failure criteria and a rapid restart plan
<i>AHR = airway hyperresponsiveness; BEC = blood eosinophil count; COPD = chronic obstructive pulmonary disease; CRSwNP = chronic rhinosinusitis with nasal polyps; ED = emergency department; FeNO = fractional exhaled nitric oxide; ICS = inhaled corticosteroid; ICU = intensive care unit; IgE = immunoglobulin E; LABA = long-acting beta agonist; LAMA = long-acting muscarinic antagonist; MART = maintenance and reliever therapy; MDT = multidisciplinary team; OCS = oral corticosteroids</i>	

Figure 1 Round 1 responses concerning pre-biologic assessment in severe asthma. Horizontal stacked bars show the distribution of responses from 24 panellists across a five-point Likert scale. The vertical dashed line denotes the prespecified 75% threshold; consensus was achieved when >75% of panellists agreed or strongly agreed. Green tick symbols indicate consensus achieved and red minus symbols indicate consensus not achieved. AD, atopic dermatitis; COPD, chronic obstructive pulmonary disease; CRSwNP, chronic rhinosinusitis with nasal polyps; FEV₁, forced expiratory volume in 1 second; HDU, high-dependency unit; ICS, inhaled corticosteroid; ICU, intensive care unit; IgE, immunoglobulin E; LABA, long-acting beta-agonist; LAMA, long-acting muscarinic antagonist; MART, maintenance-and-reliever therapy; SA, severe asthma.

R1 (A) Pre-biologic assessment

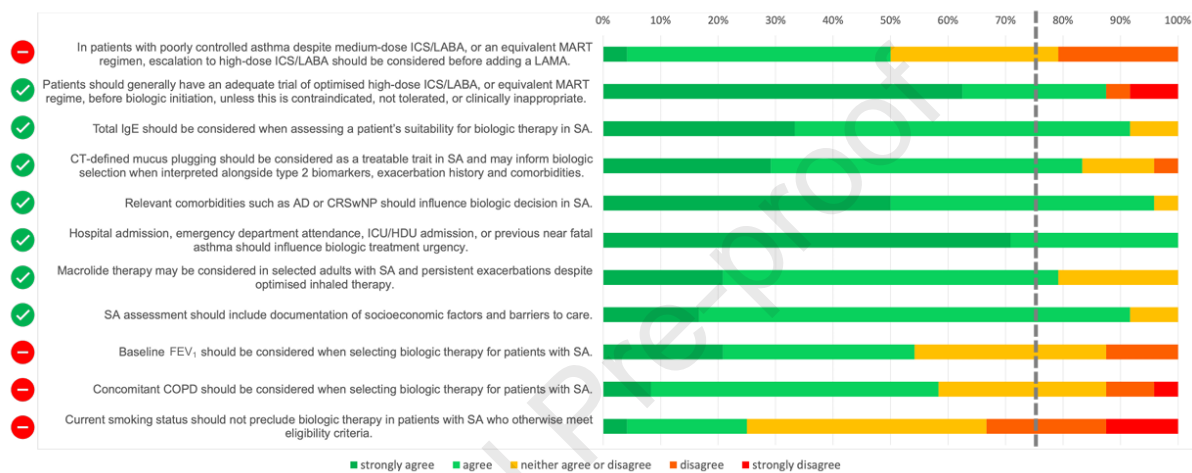


Figure 2 Round 1 responses concerning the definition and assessment of clinical remission in severe asthma. For the question concerning the minimum treatment period before assessing clinical remission, the labelled sections represent the proportion selecting 6, 12 or 24 months; the Likert-scale colour scheme does not apply to this question. ACQ, Asthma Control Questionnaire; AHR, airway hyperresponsiveness; CR, clinical remission; FEV₁, forced expiratory volume in 1 second; ICS, inhaled corticosteroid; SA, severe asthma.

R1 (B) Clinical remission



Figure 3 Round 1 responses concerning post-remission management in severe asthma. ACQ, Asthma Control Questionnaire; CR, clinical remission; ICS, inhaled corticosteroid; LABA, long-acting beta-agonist; MART, maintenance-and-reliever therapy; SA, severe asthma.

R1 (C) Post-remission management

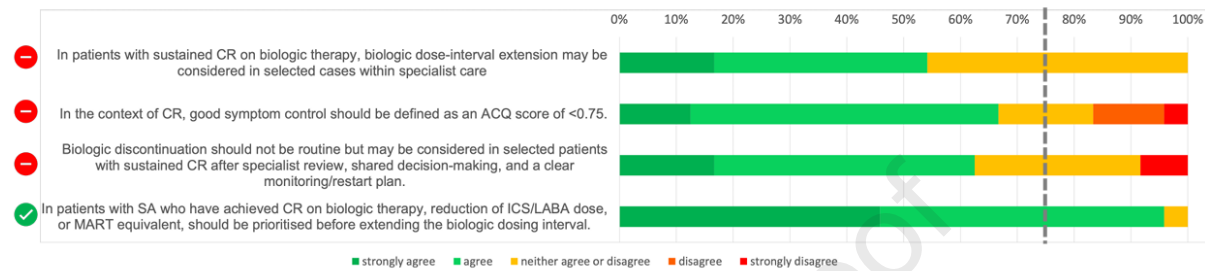


Figure 4 Round 2 responses to revised statements concerning severe asthma assessment, clinical remission and post-remission management.



Ethics declaration

Informed consent and patient details

Written informed consent to take part in the study and to publish the article has been obtained from all participants or their legal representatives. The privacy rights of participants have been observed.

Studies in Human

This study was performed in compliance with relevant laws, regulatory frameworks and guidelines where the research took place.

This study was approved by the West of Scotland Research Committee 4 .

(Approval No. 358976)

Declaration of competing interests:

SJ reports personal fees from AstraZeneca and Chiesi.

Rekha Chaudhuri has received lecture fees from GSK, AstraZeneca, Chiesi and Sanofi; honoraria for Advisory Board Meetings from GSK, AstraZeneca and Celltrion; Consultant to Connect Biopharma; sponsorship to attend international scientific meetings from Sanofi and a research grant from AstraZeneca.

SW reports honoraria and advisory board fees from AstraZeneca.

SD reports personal fees from AstraZeneca (educational sessions) and travel support from GSK.

RG reports personal fees from AstraZeneca and institutional grants from Chiesi.

PS reports personal fees from AstraZeneca, GSK, Lung League Fribourg (Switzerland), Swiss Lung Foundation (Switzerland).

CK reports personal fees (talks and advisory board) and other support (attending ERS) from AstraZeneca and Chiesi.

MP reports personal fees from AstraZeneca, GSK and Chiesi; and other support from AstraZeneca Chiesi, GSK and Sanofi/Regneron (support for conferences).

PL reports personal fees from AstraZeneca, GSK and Chiesi; travel and conference fees from Chiesi.

Arlene Shaw reports personal fees and serving on advisory boards from AstraZeneca.

VS reports personal fees from AstraZeneca and Boehringer Ingelheim; and travel support from GSK.

TF reports honoraria, assistance with travel, conference fees and other funding from Novartis, Chiesi, GSK, AstraZeneca, Boehringer Ingelheim, Pfizer, Teva and Insmed; advisory boards in the previous three years for AstraZeneca and GSK; and is Chair of the Scotland Precision Asthma Group and sat on the UK Precision Asthma Group (AstraZeneca).

BJL reports grants, personal fees (consulting, talks and advisory board), other support (attending ATS and ERS) from AstraZeneca; grants, personal fees (talks and consulting) and other support (Attending ATS ,ERS and BTS) from Sanofi/Regeneron, personal fees (consulting, talks and advisory board) from Niox in relation to the submitted work; personal fees (talks and consulting), grants and other support (attending ERS and BTS) from Chiesi, personal fees (consulting and talks) from Lupin, personal fees (consulting) from Glenmark, consulting fees from Propeller Bio, Belenos, Pfizer , Bambusa ; Equipment from Vitalograph, Lothar Medtec, Thorasys ; and the son of BJL is presently an employee of AstraZeneca.

Rory Chan has been awarded institutional grants from Asthma + Lung UK, Chiesi, AstraZeneca, GSK and Sanofi-Regeneron; served on advisory boards for Vitalograph, Chiesi and AstraZeneca; received personal fees from AstraZeneca, Chiesi, Vitalograph, Thorasys, GSK, Jaeger and Sanofi-Regeneron; and support attending conferences from AstraZeneca, Chiesi, NIOX, Sanofi-Regeneron and Vitalograph.

ME reports conference and travel support from Chiesi, Boehringer Ingelheim and GSK, and personal fees (meeting chair) from AstraZeneca.

CR reports no conflicts of interest.

NP reports no conflicts of interest.

Andrew Smith reports honoraria, assistance with travel, conference fees and other funding from Chiesi, GSK, AstraZeneca and Sanofi and advisory board fees from AstraZeneca and GSK.

Douglas Cowan reports no conflicts of interest.

GM reports personal fees from AstraZeneca.

Alison Copland reports personal fees from AstraZeneca.

WTNL reports no conflicts of interest.

SL reports no conflicts of interest.

CC reports receiving speaker fees from AstraZeneca and GSK and is a member of the PROJECT 50 working group.

DM reports receiving personal fees for talks and training from AstraZeneca and GSK, and travel and accommodation support from AstraZeneca and GSK.

PC reports no conflicts of interest.

JL reports speaker fees from AstraZeneca and Sanofi-Regeneron.

TB reports no conflicts of interest.

PK reports no conflicts of interest.

EC reports no conflicts of interest.