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ORIGINAL RESEARCH

Severe Asthma Questionnaire (SAQ) and Asthma Control Questionnaire (ACQ) as Early Predictors of Biologic Response in Severe Asthma

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Background: Biologic therapy in asthma can be life-changing and affect health-related quality of life, but symptoms are rarely used in the assessment of response.

Aim: To examine the change in health-related quality of life and asthma control between starting a biologic and assessment of biologic response, assessing whether this change can provide early prediction of eventual clinical response at 12 months.

Methods: A service evaluation of severe asthmatics initiating a biologic at the Royal Devon NHS trust between 2019 and 22. Health-Related Quality of Life (Severe Asthma Questionnaire) and asthma control (Asthma Control Questionnaire-6) was captured at baseline, 8 weeks, 16 weeks and 12 months. Patients were classified as responder or non-responder using NICE Criteria for biologic response. Independent samples *t*-tests were used to determine statistical difference in change from baseline patient reported outcome measure scores between responder and non-responders.

Results: One hundred and eight initiations (103 patients) of biologic therapy were included. At 8 weeks and 16 weeks, responders had greater improvement in Severe Asthma Questionnaire & Severe Asthma Questionnaire Global compared to non-responders ($p<0.05$). Improvement in Asthma Control Questionnaire only achieved significance between all-responders and non-responders at 16 weeks ($p<0.05$).

Conclusion: This study provides evidence of the early and sustained improvement in health-related quality of life and symptoms after starting biologic therapy. The findings support the use of the Severe Asthma Questionnaire and the Asthma Control Questionnaire as per the Core Outcome Measures Sets for Severe Asthma (COMSA). We have shown that health-related quality of life and asthma control can assist earlier assessment of response and non-response to biologics.

Keywords: severe asthma, quality of life, patient reported outcomes, patient-centred, biologics

Introduction

Asthma affects 350 million people worldwide[1] with an estimated 3–10% of people diagnosed with asthma having severe asthma.[2] However, these patients often describe a significant burden of living with severe asthma, accounting for a disproportionate distribution of asthma-associated morbidity and healthcare costs.[3] Advances in targeted biologic therapies have expanded treatment opportunities with recognition of a subgroup of patients that describe life-changing benefits[4] often expressing a multifaceted "response" including a wide range of effects on health-related quality of life (HRQoL).[5]

However, there are still no universally accepted criteria for what constitutes response to biologic therapy in asthma.[6] Research concerning predictors of biologic response have focused on specific biomarkers such as exhaled nitric oxide and eosinophils, traits such as atopy, onset of asthma and nasal polyposis or outcomes important to regulatory bodies such as exacerbation rate, oral corticosteroid use, lung function and asthma control.[7,8] Current definitions are constructed from these outcomes but fail to include any measures of HRQoL.[9] Whilst clinicians and regulators often focus on

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exacerbations and oral steroids, patients are more concerned with the burden of living with severe asthma and consistently rank improvement in HRQoL as one of the most important goals of treatment.[10]

To address these issues, the 3TR international working group developed a core outcome set for severe asthma to provide consistency and comparability between studies.[11] Collectively termed "Core Outcome Measures for children, adolescents, and adults with Severe Asthma" (COMSA), they included patient reported outcomes (PROs). For adult populations, the Severe Asthma Questionnaire (SAQ) was recommended as the HRQoL measure of choice, with the Asthma Control Questionnaire (ACQ) recommended as the measure of asthma control.

We conducted a service evaluation to examine the change in asthma HRQoL and asthma control between initiating a biologic treatment and assessment of biologic response, usually at 12 months. We examined whether the SAQ and ACQ can provide early prediction of clinical response in a clinically useful manner. The aim was to more accurately capture the burden of living with severe asthma and its treatment as well as providing clinically useful data that may not be measured by other PROs. We also provide a preliminary comparison between the SAQ and ACQ to assess if there was any difference in their ability to predict response.

Materials and Methods

Using clinic records, retrospective data were collected from patients initiating biologic therapy for severe asthma between January 2019 and May 2022 within a single UK specialist severe asthma centre (Royal Devon University Hospital Trust). This clinical data, including the SAQ and ACQ, were recorded in clinics as part of routine practice for enrolment within the UK severe asthma registry with consent from our patients. This consent included the use of patient data for research and service evaluation purposes. This project underwent independent review facilitated by the Research and Development Department of the Royal Devon. It was deemed to be a service evaluation and not research. As such, additional ethical approval was deemed unnecessary.

To be included in the analysis, patients needed to have complete baseline data, 12 months of follow-up data and have had completed at least the SAQ or ACQ at 8 weeks (measured between 4–10 weeks), or 16 weeks (measured between 12 and 28 weeks), after starting their biologic treatment. This included those switched due to non-response. Patients who received more than one biologic treatment during the study period have separate data points for each biologic initiation. If failure to biologic therapy was assessed before 12 months, they were still included within the data set.

Response and Remission

Severe asthma was defined by ERS/ATS definition,[12] and biologic prescribing decisions were undertaken within a complex asthma multi-disciplinary team adhering to National Institute of Clinical Excellence (NICE) criteria.[13] Response to biologic therapy was based on NICE criteria, defined as a $\geq$ 50% reduction in exacerbations or $\geq$50% reduction in maintenance oral corticosteroid use.[14] Non-responders are defined as patients who did not meet either of these criteria. This is a composite response criterion based upon the Benralizumab[15] and Mepolizumab[16] NICE criteria of "clinically meaningful" reduction in severe exacerbations and continuous oral steroid, and the Dupilumab[17] NICE criteria defining this reduction as $\geq$50%. The NICE criteria of Omalizumab[18] does not define response. Whilst there is variation between definitions of response between biologics from NICE, we applied these criteria to all biologic reviews.

The delphi super-responder criteria was applied to the responder group,[9] defined as $\geq$3 of 3 major criteria and 3 minor criteria, of which at least 2 must be major criteria. Major criteria were exacerbation elimination at 12 months, improvement in ACQ $\geq$ 1 (2x MCID) and cessation of oral steroids. Minor Criteria were 75% exacerbation reduction, overall ACQ score $\leq$1 and $\geq$500mL improvement in FEV1. We judged patients on physiological doses of steroid due to secondary adrenal insufficiency at 12 months as having eliminated oral corticosteroid (OCS) use. This dose was assumed to be <5 mg of prednisolone with evidence of adrenal insufficiency in cortisol measurements. Clinical remission criteria were also applied to the cohort, defined as elimination of exacerbation and maintenance OCS use, overall ACQ score $\leq$1 and $\geq$100mL improvement in FEV1.[19]

Patient Reported Outcomes

HRQoL was measured using the SAQ and asthma control was measured using the ACQ-6, both in paper format. The SAQ comprises 16 items that measure quality of life within the last 2 weeks. The SAQ score is the mean of the 16 items (1–7) with higher scores indicating better quality of life. The minimum clinically important difference (MCID) is 0.5.[20] The SAQ-global (1–100) is the final question in the SAQ and assessed over a 0–100 point scale, with higher scores indicating better quality of life. The MCID is 11.[20] ACQ-6 is a six-item questionnaire designed to measure asthma symptoms. The questionnaire is scored by the mean of all items (0–6) with higher scores indicating poorer control. The MCID is 0.5.[21]

Statistical Analysis

Baseline demographics and PRO scores were compared between responders and non-responders using independent samples T tests. Fisher's Exact Test was used in cases where proportions of patients needed to be compared between responders and non-responders. We tested whether change in response to a PRO was significantly different between responders and non-responders using independent t-tests, where change from baseline to follow-up on the PROs was calculated. Effects sizes as Hedge's g (*g*) are presented for all comparisons. This effect size statistic is interpreted the same way as Cohen's D where 0.2 is considered small, 0.5 is medium and 0.8 large.[22]

Results

Data were collected from 108 initiations of biologic therapy. This included 103 patients with 5 patients starting two different biologic therapies at different times during the study period (Table 1). Baseline clinical variables are given in Table 2. Eighty-eight percent were classified as responders, 20% achieved clinical remission and 40% were classified as super-responders, whereas 12% were non-responders. Sixty-four percent of responders were able to become exacerbation free with no need for maintenance OCS use above physiological levels, however only 34% were also able to obtain good asthma control (ACQ < 1.5). Most demographic factors did not differ significantly between responders and non-responders. However, responders were significantly more likely to have nasal polyps and higher FENO in the last 12 months than non-responders. Non-responders had significantly more hospital admissions in the last 12 month compared to responders. Non-responders scored significantly worse on the SAQ global and ACQ at baseline compared to responders.

Table 1 Demographics and Prescribed Biologic Treatments at Time of Initiating Treatment with Biologic

	All Biologic Initiations (N=108)[#]	**Responders (N=94)**	**Non-Responders (N=14)**	**Responders vs Non-Responders Significance *P***
Age *years* Mean (range)	53 (18–78)	54 (18–78)	49 (19 –72)	0.13
Bmi Mean (range)	31 (17–54)	30 (17–54)	33 (23–54)	0.13
Female N (%)	57 (53)	48 (52)	9 (60)	0.18
Ethnicity – White British	104 (96)	90 (96)	14 (100)	
Omalizumab	19 (18)	15 (16)	4 (29)	
Mepolizumab	12 (11)	11 (12)	1 (7)	
Benralizumab	71 (66)	62 (66)	9 (64)	
Dupilumab	6 (5)	5 (5)	1 (7)	

Notes: [#] 5 patients were switched between biologics during the study period, with 3 patients being present in both non-responder and responder groups. 1 patient was a responder but was switched to a more effective treatment whilst 1 patient failed to respond to both biologics.

Table 2 Clinical Variables for Patients Undertaking Biologic Initiations

	All Biologic Initiations (N =108)	**Responders (N=94)**	**Non-Responders (N=14)**	**Responders vs Non-Responders Significance *P***
N (%)				
Receiving Maintenance Ocs	66 (61)	58 (62)	8 (57)	0.37
Age Of Onset **Child** **Adult**	 49 (45) 59 (55)	 40 (43) 54 (57)	 9 (64) 5 (36)	0.40
History of Atopy **Present** **Absent**	 54 (50) 54 (50)	 45 (48) 49 (52)	 9 (64) 5 (36)	0.39
Nasal Polyps **Present** **Absent**	 28 (26) 80 (74)	 28 (30) 66 (70)	 0 (0) 14 (100)	0.01*
Smoking History **Current** **Ex** **Never**	 4 (4) 31 (29) 73 (67)	 3 (3) 27 (29) 64 (68)	 1 (7) 4 (29) 9 (64)	0.76
Mean Pack Years (Current/Ex Smokers)	13.14	12.16	19	0.12
Mean *Range*				
Daily Maintenance Ocs (Mg)	13.70 *2–40*	14.00 *2–40*	20.63 *5–40*	0.23
Exacerbations In Previous 12 Months	7.4 0–30	7.1 *0–26*	10.00 *0–30*	0.15
Hospital Admissions In Previous 12 Months	1.8 0–20	1.3 *0–10*	5.0 *0–20*	0.02*
(N)				
Blood Eosinophils	0.56 0–3.5	0.57 (90) *0–3.5*	0.48 (13) *0.24–0.90*	0.24
Feno (PPB)	58 3–300	62 (90) *4–300*	32 (13) *3–108*	0.03*
(N) and Mean *SD*				
FEV1 (L)	2.2 (106) 0.78	2.2 (92) *0.73*	2.14 (14) *1.08*	0.42
FEV1%PRED	71 (106) 19.97	72 (93) *19.24*	66 (14) *24.42*	0.14

(*Continued*)

Table 2 (Continued).

	All Biologic Initiations (N =108)	**Responders (N=94)**	**Non-Responders (N=14)**	**Responders vs Non-Responders Significance *P***
SAQ (1–7)	3.6 (108) *1.23*	3.64 (94) *1.22*	3.0 (14) *1.20*	0.05
SAQ-GLOBAL (0–100)	50 (108) *20.66*	49 (94) *20.36*	35 (14) *19.00*	0.008*
ACQ (0–6)	3.1 (106) *1.27*	3.0 (94) *1.26*	4.0 (12) *1.14*	0.005*

Note: *p<0.05.

All patients had SAQ and ACQ data at baseline and either 8 or 16 weeks. Ninety-four percent of patients had SAQ and ACQ data at 8 weeks (average 8.0 weeks) and 67% of patients had SAQ or ACQ data at 16 weeks (average 17.7 weeks). Responders mean SAQ and SAQ global scores increased at 8 weeks and continued to increase at 16 weeks and 12 months whereas non-responders mean SAQ and SAQ global scores remained suppressed throughout (Figure 1a–c).

The change scores, tests of significance and effect sizes are shown in Table 3. Change in SAQ score was significantly greater for responders compared to non-responders at 8 weeks, 16 and 12 months showing a clinically meaningful difference between the group by 8 weeks, and more than 3 X MCID at the latter two time points. Change in SAQ global score was also significantly greater for responders compared to non-responders at all three time points, with a difference of 3 X MCID at 16 weeks and more than 2 X MCID at 12 months.

Change in ACQ score was significantly greater for responders compared to non-responders at 16 weeks and at 12 months but not 8 weeks (p = 0.761). The average difference in ACQ scores between the groups at 16 weeks was 2 x MCID and 3 X MCID at 12 months.

There was a trend for the SAQ and SAQ-global to detect change earlier than the ACQ, but effect size at 12 months was similar for all three questionnaires.

There was considerable variance in magnitude of improvement in PROs at all time points (Table 4). Responders displayed a heterogenous magnitude of improvement with a proportion failing to achieve 1x MCID. However, this proportion declined by 16 weeks with a general trend to improved HRQOL and asthma Control at 12 months. Most non-responders failed to achieve greater than 1 MCID improvement at all time points.

Discussion

Current guidelines use the criteria of exacerbations and OCS use for assessment of biologic response. These guidelines fail to assess benefit as perceived by the patient. This real-world study demonstrates how application of the COMSA can be used to assess response to biologic treatment. Our data has shown clinically significant changes from baseline in mean SAQ and SAQ global and ACQ scores as early as 8 weeks into biologic treatment with continued benefit up to 12 months. Our findings indicate that HRQoL improvement can be rapid and imply that the benefit of these treatments is more than just due to exacerbation and systemic steroid reduction.

Our data suggest that most of the change in HRQOL and asthma control for responders occurred within the first 6 months of treatment, and that earlier assessment of biologics using SAQ & ACQ could help identify non-responders quicker, facilitating timelier discussion around appropriate biologic switching.

Individual patient response within these groups varied substantially. The heterogenous magnitude of change in PRO scores within the response group demonstrates the multifaceted response that patients have described in previous

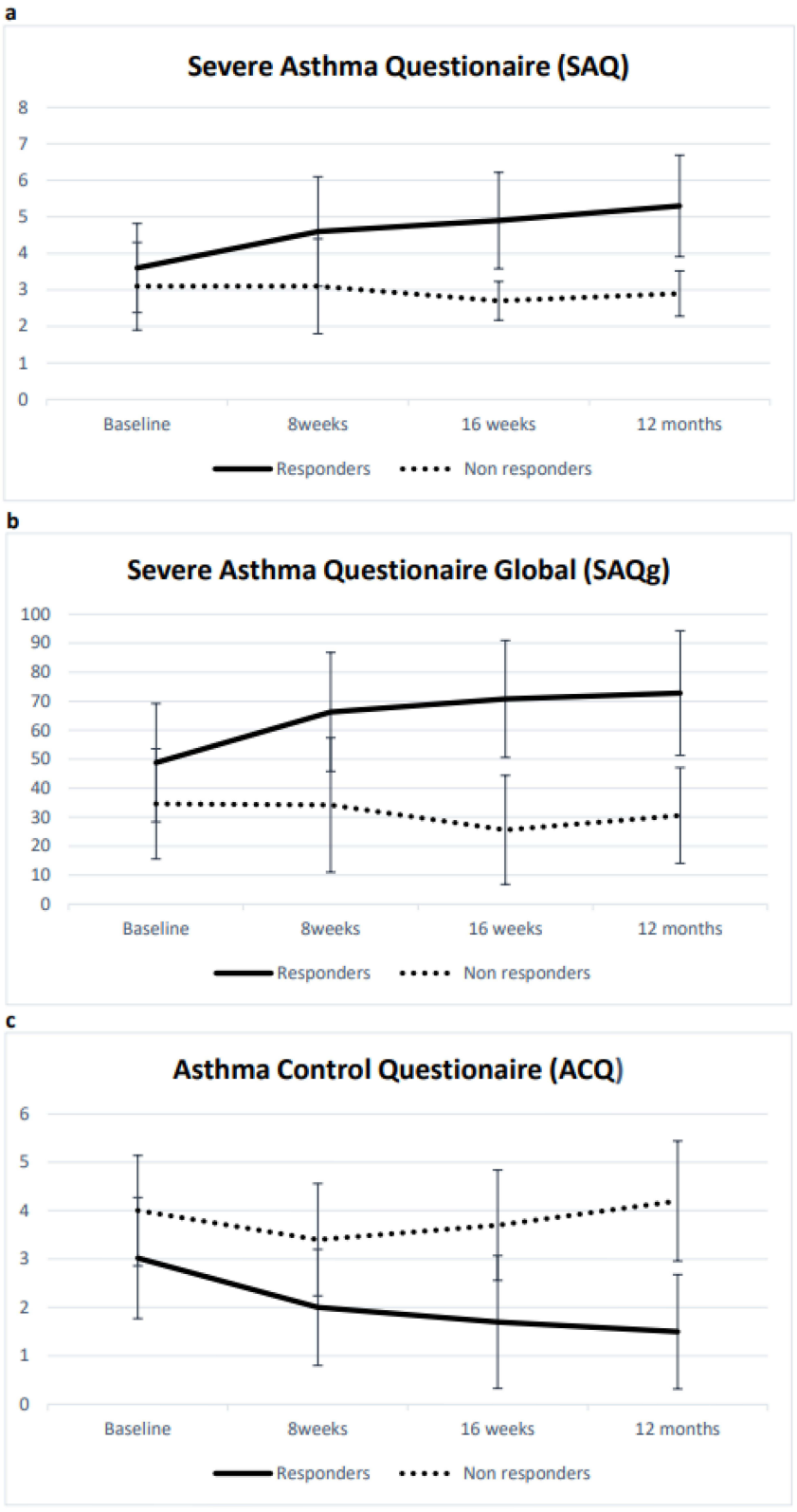

Figure 1 (**a**–**c**) The average scores for each PRO at 8 weeks, 16 weeks and 12 months for responders and non-responders.

Table 3 Mean Change in Scores From Baseline with n (Number of Biologic Initiations with Completed PRO Data at That Time Point) and SD (Standard Deviations), for Questionnaires at Three Time Points, Comparing Responders and Non-Responders

		Responder Mean Change from Baseline Score (a)	N	SD	Non-Responder Mean Change from Baseline (b)	N	SD	Difference in Mean Change in Score from Baseline Between Responder and Non-Responder	Significance (P value) [a] vs [b]	Effect Size (g)
SAQ	8 weeks	0.99	89	1.34	0.09	13	1.35	0.91	0.025	0.67
	16 weeks	1.32	64	1.39	−0.48	8	0.76	1.80	< 0.001	1.34
	12 months	1.52	80	1.5	−0.25	9	1.14	1.77	< 0.001	1.2
SAQ Global	8 weeks	17.36	89	20.19	0.77	13	23.26	16.59	0.008	0.8
	16 weeks	23.56	64	20.86	−10	8	11.95	33.56	< 0.001	1.67
	12 months	20.90	81	21.75	−6.67	9	20.46	27.57	< 0.001	1.27
ACQ	8 weeks	−1.05	89	1.24	−0.93	11	1.13	−0.12	0.76	0.09
	16 weeks	−1.48	62	1.38	−0.3	6	0.92	−1.18	0.045	0.87
	12 months	−1.35	81	1.27	0.21	7	1.11	−1.57	0.002	1.24

Table 4 % of PRO Scores for Responders and Non-Responders That Achieved Their Respective MCID at Each Time Point. The Response Rate of PRO for Each Time Point Is Given as a Percentage of Responders or Non-Responders That Provided PRO Data Respectively

Change in Respective PRO as Multiples of MCID		SAQ			SAQ Global			ACQ		
		8 weeks	16 weeks	12 Month	8 weeks	16 weeks	12 Month	8 weeks	16 weeks	12 Month
Responder (n=94)	< 1x MCID	41%	30%	25%	43%	30%	31%	31%	18%	28%
	1–2x MCID	11%	17%	19%	19%	19%	26%	19%	18%	10%
	2–4x MCID	25%	17%	29%	27%	34%	30%	31%	34%	36%
	> 4x MCID	23%	36%	37%	10%	17%	13%	19%	31%	26%
	Total n (%) of Responder	**88 (94)**	**64 (68)**	**79 (84)**	**88 (94)**	**64 (68)**	**80 (85)**	**88 (94)**	**62 (66)**	**80 (85)**
Non- Responder (n=14)	< 1x MCID	79%	88%	60%	71%	100%	78%	36%	67%	63%
	1–2x MCID	7%	13%	10%	21%	0%	11%	9%	0%	13%
	2–4x MCID	0%	0%	30%	0%	0%	11%	27%	33%	25%
	> 4x MCID	14%	0%	0%	7%	0%	0%	27%	0%	0%
	Total n (%) of non-responder	**14 (100)**	**8 (57)**	**10 (71)**	**14 (100)**	**8 (57)**	**9 (64)**	**11 (79)**	**6 (43)**	**8 (57)**

studies.[5] Furthermore, there was a group of responders for whom the SAQ and ACQ scores did not change by more than one MCID between baseline and 12 months. This indicates that either these patients perceived no clinically meaningful improvement in HRQOL and asthma control, or that their perceived control and HRQOL was already very good at baseline. These findings support the use of multiple outcome measures for the assessment of response as HRQOL and Asthma control may not predict response in isolation.

Within our cohort, 1 responder had failed to respond to two previous biologics but met 12-month criteria for response in exacerbation reduction of 10 to zero with Benralizumab. However, they continued to have very poor QoL and airflow obstruction with continued maintenance OCS use. The MDT decided to undertake a switch to Dupilumab via an early access scheme with resulting improved HRQOL and asthma control and sustained clinical remission. The response of this patient demonstrates that traditional outcomes based on exacerbations alone may not be adequate in matching the right biologic with the right patient to achieve the best outcome.

Limitations

This was a service improvement project from a single severe asthma centre in the UK which, whilst allowing us to capture real-world data, naturally lacks randomisation and could be open to sampling bias. Larger prospective studies in more diverse, ethnic and cultural populations are required to confirm our results. However, all UK severe asthma centres provide a standardised multi-dimensional assessment to optimise all treatable traits prior to considering high-cost therapies.[13] Whilst our sample size was not powered to draw any comparisons between biological therapies, a trend for the SAQ to respond faster than the ACQ was observed.

Currently, guidelines advise a 16-week assessment for omalizumab and a year assessment for all other biologics in the UK.[14–18] There were responders within our study who had assessments as early as 20 weeks into treatment. Whilst we gave a subsequent annualised exacerbation rate, 16 weeks is too short time frame to assess response, and we often extend this assessment within our local clinical practice. However, the differing assessment points makes homogenisation of biologic data problematic.

Our study period encompassed the advent of the covid pandemic and lockdown within the United Kingdom. Clinical practice changed over this timeframe and can account for some of the variance within our data time points and missing PRO responses. The pandemic also limited our ability to directly supervise steroid weans. Our regional practice also moved towards starting homecare and self-administration of biologics earlier for patients after 3 months of treatment enabling a patient-centric approach to treatment administration. However, this change limited our ability to collect data directly from patients at 16 weeks. PRO data collection through other methods, such as mobile apps, may aid in future studies. The Severe Heterogenous Asthma Research Collaboration, Patient-centred is currently developing the Patient Coach app that will aid future collection of the patient experience of severe asthma.[23]

Our cohort had significantly poorer asthma control, asthma quality of life and healthcare utilisation that could have affected our response rate and magnitude of improvement in HRQOL and control. However, the response rate was comparable to other real-world studies.[24] Furthermore, due to the nature of PROs, a single timepoint for data collection can be affected by ill health such as infections or exacerbations at the time of collection. Single time point data collection can therefore lead to inaccurate or inappropriate treatment decisions in the context of an overall improved quality of life over the course of treatment.

Conclusions

This study provides the first evidence of assessment of biologic response using the patient-centred outcome measures recommended in COMSA, specifically the SAQ. Patients that responded to biologic medication achieved significant improvements in asthma quality of life and control as early as 16 weeks, that was sustained over 12 months, compared to patients that did not respond to these treatments. Larger studies are required to help us understand the impact of HRQOL on our patients and help us direct better patient-centric therapy.

By using the SAQ and ACQ as core outcome measures alongside other established response outcomes as described in COMSA, clinicians and patients may be able to predict response earlier than 12 months, expediting targeted and potentially more effective biologic choices. These results demonstrate the significance of the patient's perspective in assessing their response to a treatment.

Ethics

This work adheres to the ethical principles set out in the Declaration of Helsinki.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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References

1. Mukherjee M, Stoddart A, Gupta RP, et al. The epidemiology, healthcare and societal burden and costs of asthma in the UK and its member nations: analyses of standalone and linked national databases. *BMC Med*. 2016;14(1):113. doi:10.1186/s12916-016-0657-8
2. von Bülow A, Kriegbaum M, Backer V, Porsbjerg C. The prevalence of severe asthma and low asthma control among Danish adults. *J Allergy Clin Immunol Pract*. 2014;2(6):759–767.e2. doi:10.1016/j.jaip.2014.05.005
3. Foster JM, McDonald VM, Guo M, Reddel HK. "I have lost in every facet of my life": the hidden burden of severe asthma. *Eur Respir J*. 2017;50(3):1700765. doi:10.1183/13993003.00765-2017
4. Lanario JW, Cartwright L, Jones RC, Sayers R, Hyland ME, Masoli M. "Life-changing": the experience of super-responders to biologics in severe asthma. *BMC Pulm Med*. 2022;22(1):445. doi:10.1186/s12890-022-02241-2
5. Coleman C, Khaleva E, Rattu A, et al. Narrative review to capture patients' perceptions and opinions about non-response and response to biological therapy for severe asthma. *Eur Respir J*. 2023;61(1):2200837. doi:10.1183/13993003.00837-2022
6. Khaleva E, Rattu A, Brightling C, et al. Definitions of non-response and response to biological therapy for severe asthma: a systematic review. *ERJ Open Res*. 2023;9(3):00444–2022. doi:10.1183/23120541.00444-2022
7. Clark VL, Gibson PG, McDonald VM. What matters to people with severe asthma? Exploring add-on asthma medication and outcomes of importance. *ERJ Open Res*. 2021;7(1):00497–2020. doi:10.1183/23120541.00497-2020
8. Kroes JA, Zielhuis SW, van Roon EN, ten Brinke A. Prediction of response to biological treatment with monoclonal antibodies in severe asthma. *Biochem Pharmacol*. 2020;179:113978. doi:10.1016/j.bcp.2020.113978
9. Upham JW, Le Lievre C, Jackson DJ, et al. Defining a severe asthma super-responder: findings from a delphi process. *J Allergy Clin Immunol Pract*. 2021;9(11):3997–4004. doi:10.1016/j.jaip.2021.06.041
10. Ainsworth B, Chatburn E, Bansal AT, et al. What bothers severe asthma patients most? A paired patient–clinician study across seven European countries. *ERJ Open Res*. 2023;9(3):00717–2022. doi:10.1183/23120541.00717-2022
11. Khaleva E, Rattu A, Brightling C, et al. Development of core outcome measures sets for paediatric and adult severe asthma (COMSA). *Eur Respir J*. 2022;61:2200606.
12. Chung KF, Wenzel SE, Brozek JL, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J*. 2014;43(2):343–373. doi:10.1183/09031936.00202013
13. National Institute for clinical excellence. Asthma: diagnosis, monitoring and chronic asthma management. 2017.
14. National institute for clinical excellence. Tezepelumab for treating severe asthma. 2023.
15. National institute for clinical excellence. Benralizumab for treating severe eosinophilic asthma. 2019.
16. National institute for clinical excellence. Mepolizumab for treating severe eosinophilic asthma. 2021.

17. National institute for clinical excellence. Dupilumab for treating severe asthma with type 2 inflammation. 2021.
18. National institute for clinical excellence. Omalizumab for treating severe persistent allergic asthma. 2013.
19. Menzies-Gow A, Hoyte FL, Price DB, et al. Clinical remission in severe asthma: a pooled post hoc analysis of the patient journey with benralizumab. *Adv Ther*. 2022;39(5):2065–2084. doi:10.1007/s12325-022-02098-1
20. Masoli M, Lanario JW, Hyland ME, et al. The Severe Asthma Questionnaire: sensitivity to change and minimal clinically important difference. *Eur Respir J*. 2021;57(6):2100300. doi:10.1183/13993003.00300-2021
21. Juniper EF, O′byrne PM, Guyatt GH, Ferrie PJ, King DR. Development and validation of a questionnaire to measure asthma control. *Eur Respir J*. 1999;14(4):902. doi:10.1034/j.1399-3003.1999.14d29.x
22. Cohen J. A power primer. *Psychol Bull*. 1992;112(1):155–159. doi:10.1037/0033-2909.112.1.155
23. Severe Heterogeneous asthma research group patient centered. SHARP program of work. 2023. Available from: https://europeanlung.org/sharp/programme-of-work/. Accessed Jun 19, 2023.
24. Hansen S, Von Buelow A, Soendergaard MB, et al. Clinical response and remission in patients with severe asthma treated with biologic treatment: findings from the nationwide Danish severe asthma registry. In *0501 - Airway Pharmacology and Treatment*. European Respiratory Society; 2022:3553.