

A qualitative study of the impact of severe asthma and its treatment showing that treatment burden is neglected in existing asthma assessment scales

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Abstract

Background People with severe asthma experience significant respiratory symptoms and suffer adverse effects of oral corticosteroids (OCS), including disturbed mood and physical symptoms. OCS impacts on health-related quality of life (HRQoL) have not been quantified. Asthma HRQoL scales are valid as outcome measures for patients requiring OCS only if they assess the deficits imposed by OCS.

Aims The aim of this study was to compare the burden of disease and treatment in patients with severe asthma with items in eight asthma-specific HRQoL scales.

Methods Twenty-three patients with severe asthma recruited from a severe asthma clinic were interviewed about the impact of their respiratory symptoms and the burden of their treatment. The domains from a thematic analysis of these interviews were compared with the items of eight asthma-specific HRQoL scales.

Results In addition to the burden caused by symptoms, ten domains of OCS impact on HRQoL were identified: depression, irritability, sleep, hunger, weight, skin, gastric, pain, disease anxiety, and medication anxiety. Some

patients experienced substantial HRQoL deficits attributed to OCS. Although all HRQoL scales include some OCS-relevant items, all eight scales fail to adequately assess the several types of burden experienced by some patients while on OCS.

Conclusion The burden of OCS in severe asthma is neglected in policy and practice because it is not assessed in outcome studies. Existing asthma HRQoL scales provide an overly positive estimation of HRQoL in patients with frequent exposure to OCS and underestimate the benefit of interventions that reduce OCS exposure. Changes to existing measurement procedures are needed.

Keywords Severe asthma · Difficult asthma · Quality of life · Treatment burden · Assessment

Introduction

Health-related quality of life (HRQoL) is one of several outcome measures used to inform treatment guidelines and economic decision-making for the treatment of asthma. HRQoL scales are important amongst outcome measures in that they inform whether treatment is worthwhile from the perspective of the patient [1], a perspective that includes the burden of disease and the burden of treatment. The quantitative results from such scales depend on the type and relative frequency of the items in the domains that make up these scales. For example, asthma-specific HRQoL scales tend to be more sensitive to change than generic scales [2, 3]. Generic scales include items in domains that may be unaffected by a particular disease and therefore are unlikely to change following treatment. Furthermore, asthma-specific scales include asthma-distress items that may be missing from a generic scale. In order to

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make valid decisions from the results of an HRQoL scale, the items of the scale should match the experiences of the population that are relevant to the purpose for which the scale is being used. That is, the scale should be content valid for its intended purpose. In addition, the balance between items in different domains is important in that a domain with relatively few items can add little to the overall effect of the scale.

Asthma varies in severity, and increased doses or types of medication are required for the more severe patients. The majority of patients with asthma have mild-to-moderate disease, and the potential to be well controlled with inhaled corticosteroids and bronchodilators. These medications are targeted to the lung, have a small systemic profile, and iatrogenic effects are uncommon. However, severe asthma is a much more heterogeneous condition and is increasingly recognised as qualitatively different from mild-to-moderate asthma. These patients are more challenging to manage, have frequent exacerbations, and are more likely to require treatment with oral corticosteroids (OCS). OCS are a systemic form of treatment and, although highly effective in achieving asthma control, have well-recognised iatrogenic effects. Side effects include osteoporosis (causing bone fractures), and diabetes, as well as weight gain and a 'Cushingoid' appearance where the face becomes very fat. OCS may be prescribed for severe patients during the frequent exacerbations which are an indicator of their poor asthma control, and some severe patients may be prescribed additionally a maintenance dose. Thus, whereas mild and moderate patients receive no or very occasional treatment with OCS, severe patients may receive a large cumulative exposure resulting from frequent episodes of high dose OCS, sometimes supplemented with a daily maintenance dose.

If the HRQoL deficits of asthma vary only in degree between mild, moderate, and severe patients, then a scale that has shown to be valid for mild and moderate patients should also be valid for patients with severe asthma—assuming that items are chosen to avoid floor or ceiling effects. By contrast, a scale that is valid for mild or moderate patients would not be valid for severe patients if either of the following occurred. (a) Severe asthma patients have uniquely different types of HRQoL deficits compared with mild and moderate patients that require assessment by dimensions irrelevant to mild and moderate patients. (b) Items that are relevant to severe patients are excluded from the scale because they so infrequently endorsed by mild or moderate patients. If a scale is not valid for a particular subset of the asthma population, then use of that scale in clinical trials to evaluate treatment effectiveness will, within that population, produce erroneous and misleading results.

All published asthma HRQoL scales contain items relating to the burden of asthma (i.e. activity restriction and the emotional impact of asthma), and some include one or more items relating to the impact of treatment. The impact of OCS is known to be far greater than the impact of other asthma treatments [4, 5], and therefore, severe patients, i.e. those exposed to high doses of OCS, are likely to have a greater treatment burden than other patients. OCS are known to have direct effects on mood (e.g. depression, suicidal ideation, and anxiety), as well as physical effects (e.g. bone fractures and weight gain) that also can have psychological implications [6–8]. It is unclear whether the burden of treatment is adequately measured by existing scales. If existing scales fail to assess the impact of OCS on HRQoL, then this will lead to overestimation of the effectiveness of OCS and underestimation of the benefit of steroid-sparing treatments.

The aim of this study was to characterise the burden of asthma and its treatment in severe asthma patients and to determine the extent to which items in existing asthma-specific scales provide a valid assessment of the patient experience.

Methods

Patients were recruited from a specialist severe asthma clinic at Derriford hospital, Plymouth, UK. Patients are referred to this specialist clinic if their asthma remains uncontrolled despite high levels of preventative (primarily inhaler) medication. Such patients will experience or have experienced frequent asthma exacerbations requiring some form of emergency treatment. Data collected in 2012 at this clinic showed that seven out of the 30 patients (23 %) prescribed maintenance OCS were non-adherent when plasma prednisolone and cortisol levels were measured.

A convenience sample of 53 patients was identified from patient records, provided with study information, and invited to contact the clinic if they wished to take part. Patients were eligible if they were either on or had previously taken a maintenance course of oral steroids, and were selected for inclusion with the aim of achieving a range of different age groups and social backgrounds.

An open style of interviewing was adopted which followed the lead taken by the patient in the conversation. After an initial history taking to put the patient at ease, the following general questions were asked:

- What is your experience of having asthma? How does it affect your life?
- What is your experience of asthma medicines? How effective are they are and do you experience side

effects? The interviewer specifically asked about OCS and the effects of OCS on mood.

- What is your experience of treatment at the asthma clinic?

The interviewer (MH) was experienced in holding focus groups and interviews with mild and moderate patients and was an author of asthma-specific HRQoL scales [12, 16], but was unfamiliar with severe patients. An iterative procedure for interviewing was adopted. General questions were asked at the beginning of the sequence, but as patients raised particular issues, these issues were referred to specifically for later patients. An open questioning style was used where patient responses determined subsequent questions and with an overarching aim of providing a therapeutic environment for patients to unburden themselves. The questions and the style of conversation were individualised to the characteristics of the patient and therefore not identical between patients. The number of patients interviewed was determined by content saturation, that is, when the interviewer felt that no new themes were being identified.

The interview took part in a quiet room in a building near, but entirely separate from, the hospital. Audio from interviews was recorded and transcribed verbatim, anonymised, and analysed by thematic analysis. The thematic analysis was realist and inductive in orientation [9]. All four authors read the transcribed interviews, made annotations, and tentatively identified themes. Agreement was reached on the selection and naming of themes through constructive discussion where the authors brought their different experiences and specialisms to the agreed final decision. Patient comments relating to each domain were drawn up collaboratively by two raters who searched the total transcript file electronically for word fragments relating to each theme (e.g. searching for ‘depress’ to find words relating to depression) and synonyms and then copying the relevant section of conversation to a working table of comments for each domain, where all comments relating to each of the OCS domains were recorded by patient number. Clinic records were used to provide measures of lung function, adherence, medication, and body mass index. Ethical approval and written informed consent were obtained.

To compare the topics identified from the interviews with common assessment practice, eight asthma-specific HRQoL scales were examined, of which six are those referred to in an international consensus document on asthma outcome assessment [10]. These are the Juniper Asthma Quality of Life Questionnaire (AQLQ^{Juniper}) [11]; the mini-AQLQ [12]; the Living with Asthma Questionnaire (LWAQ) [13]; the St George’s Respiratory Questionnaire (SGRQ) [14]; the Marks Asthma Quality of Life

Questionnaire (AQLQ^{Marks}) [15]; and the Asthma Questionnaire which is in two forms: the 30-item AQ30 and a 20-item subset, the AQ20 [16]. We supplemented these six with two additional scales: The Asthma Bother Profile (ABP) [17] was developed for clinical use, where side effect concerns are relevant to adherence, and has additionally been used as an outcome tool [18, 19]. The asthma-specific quality of life scale (ASQLS) [20] is a recently published scale, the development of which involved extensive qualitative research on asthma HRQoL domains.

Results

Patient characteristics

Fifty-three patients were identified as suitable for interview; 40 patients were contacted, 28 agreed to take part, 23 were interviewed, and five were not interviewed because of difficulty finding a mutually convenient time before the study was complete. Twelve patients declined to take part for several reasons, including work commitments, child care, and health. Patients are labelled P1–P23 in order to interview. Characteristics of the 23 patients interviewed are shown in Table 1. There were 19 females and four males in our sample which is a strong bias towards females compared to the overall clinic and severe asthma populations. Twelve patients of the 15 patients were prescribed maintenance oral steroids and had been tested in the clinic for levels of blood cortisol of whom 11 were fully adherent and one partially adherence—a rate slightly better than that of the clinic, but substantially better than reported elsewhere [21].

Results of the thematic analysis

The content of interviews revealed two overarching themes: the *impact of asthma* and the *impact of medication*. Impact of asthma could be divided into three domains: *activities*, *emotional impact*, and *hospitalisation*. OCS created the greatest impact on patients; patients reported only minor effects of other medications for their asthma or for other conditions. The effects of OCS could be divided into ten domains: *depression*, *irritability*, *sleep*, *hunger*, *weight*, *skin*, *gastric*, *pain*, *disease anxiety*, and *medication anxiety*.

Impact of asthma

All patients experienced some degree of activity restriction, activity avoidance, and emotional impact of those restrictions. For example, walking problems were not limited to walking up a hill as might be the case with mild

Table 1 Characteristics of the 23 patients

Patient number	Gender	Age	Age at diagnosis	BMI	FEV1%	Current oral steroid dose mg/day
1	F	50	7	21.7	50	7.5
2	F	44	7	30.5	73	5
3	F	45	7	29.8	46	5
4	M	70	64	32	33	10
5	M	53	31	35.4	69	25
6	F	54	13	28	71	25
7	F	49	21	29	81	15
8	F	54	29	24	67	0
9	F	54	20	36.2	55	6
10	M	66	48	25	69	10
11	F	60	30	53	71	0
12	F	56	2	31.2	64	0
13	M	59	7	32	23	0
14	F	28	17	24.9	69	0
15	F	56	–	40.5	81	0
16	F	43	7	24.9	32	0
17	F	63	2	25	30	5
18	F	28	7	26.2	48	30
19	F	32	1	25.3	70	0
20	M	66	52	27.5	67	7.5
21	F	49	42	38.8	90	20
22	F	64	7	25.6	70	5
23	F	29	7	45.2	83	60

FEV1% is a measure of lung function expressed as a percentage of the predicted value for the patient

BMI body mass index

or moderate patients (P8: Going to university has been really tricky because, walking with my friends... They walk fast and they talk and I'm like... Trying to keep up). A third domain of hospitalisation was reported by 19 patients. These patients disliked being in hospital, and the associated treatment required. P1 estimated she had been in hospital 17 times in the previous year; P20 reported a year of 13 hospitalisations. Hospitalisation affected working life (P2: I lost my job, I was medically discharged because I was in and out of hospital). The unpredictability of asthma in this population disrupts working life (P19: I can't work because my condition is so unpredictable). The effect of hospitalisation affected child care, including the time after leaving hospital when parents had to resume child care though not entirely well (P23: of course when you come out of hospital, because they've done you a favour it's like, "I'm out of hospital, I'll have the boys back"). The words 'panic' or 'fear' were used in relation to asthma by P2, P3, P7, P10, P18, P21, and P23 (e.g. P18: It's trying to try breathe at the same time, then the panic sets in).

Impact of medication

Patients reported side effects only in association with OCS. Other asthma medication was perceived to have no or trivial effects; a finding that contrasts with mild or moderate patients.

Depression P1, P10, and P15 experienced severe depression and attributed it to the effect of steroids (P1: "I know I was never depressed before I started on steroids"; P10 "I can't tell you how much I hate being on them because of the depression"). P15, P16, and P19 reported the onset or increase in depression when reducing their OCS dose, and P10 reported that depression extended beyond the period in which they took OCS (P10: "it seems to last a good couple of weeks when I've come off them, even if I tail them off gently"). P5 and P8 reported depression but attributed it to their increased weight (P5: "I suppose it's where a lot of my depression comes from: because you get fat, your clothes don't fit"). P6 and P23 experienced depression but were unsure whether or not it was caused by OCS, asthma, or some other factor.

Irritability Irritability caused by OCS was reported by P1, P2, P5, P6, P10, P16, P19, P20, P21, and P22. (P10: "[I'm] Like a Rottweiler on heat! I am oh, it's worse than any menopausal or premenopausal or anything like that. My poor husband I've cried, I've said, I wish I was dead, you'd be better off without me"; P16: "I've been more irritable since I've been on steroids.").

Sleep disturbance Sleep disturbance due to the arousing effect of OCS was reported by P6, P7, P9, P12, P15, P19, P21, and P22. (P6: "I never sleep properly when I am on steroids"). P6 and P19 reported being easily woken (P6: "any sound wakes me up"). P9 and P15 reported not sleeping at all during the first night of a course of OCS (P15: "I don't sleep. I'm just hyper"). P17 reported that she used to experience sleep disturbance but had become used to it, and P20 reported sleep disturbance caused by severe hunger that she attributed to OCS. Sleep disturbance was linked to an ability to rest or relax (P6: "Even though you're tired, you can't relax").

Hunger and disturbed eating patterns Increased levels of hunger due to OCS were reported by 16 of the 23 patients (P1, P5, P6, P7, P8, P9, P10, P14, P15, P16, P18, P19, P20, P21, and P22). P22 reported hunger on 40 mg, but not 5 mg prednisolone. P1 and P8 reported that the hunger was associated with a feeling of sickness (P8: "I get to feeling sick all day... it's a really, really weird combination"), and both of these patients reported vomiting due to overeating (P1: "the amount of times I've been physical sick because

of it, it's a complete nightmare"). P16 reported eating things she did not like when on OCS. P5 and P9 reported hunger for about 1 week after terminating OCS.

Impact of weight gain and change in facial appearance Fourteen patients mentioned weight gain as a problem. P3, P14, P17, and P22 reported that they had not experienced weight gain and only slight weight gain was reported by P19. Patients reported that their increased weight was embarrassing (P5: "My weight thing is the big thing. It sounds so stupid, but I've had years of people going on about how fat I am"). P2 showed the interviewer a picture of herself before being put on steroids so as to demonstrate to the interviewer how her face had become fat (P2: "Until then, 12 months ago I looked like this"—shows interviewer photograph of her face taken before being put on steroids, which to the interviewer looked substantially different).

P6, P15, and P23 reported that the increased weight made the effects of asthma worse (P6: "It doesn't help the breathing does it, when you've got more to carry.... Am I wheezing because I'm wheezing, or am I wheezing because I am carrying all this excess weight?". P15: "Obviously, the more weight you're carrying the more breathing problems you're having. So it's a Catch-22").

Impact of skin thinning P10, P16, P18, P20, and P23 reported bruising easily, and P16 and P18 reported that they modified their behaviour to avoid bruising (P16: "I've got to be careful where I walk. You know like little handles on doors, corners on things ... I do just bump into things because I sometimes don't think properly where I'm going. But a door handle will give me a bruise").

Gastric problems P4, P5, P7, P8, P9, and P12 reported stomach bloating, P7 and P9 reported wind, and P8 and P9 reported constipation. P4, P8, P12, and P16 reported stomach pain.

Pain Two types of pain were reported: (a) pain resulting from the fractures and bone deterioration resulting from OCS-induced osteoporosis, and (b) pain due to other mechanisms. P1, P2, and P21 reported pain attributed to fractures. P11, P15, and P19 reported pain when their OCS were reduced (P11: "If I suddenly went off prednisolone completely now, as I have done in the past, you find that all sorts of aches and pains come back". P15: "I cannot manage without the maintenance dose. I can't let [husband] touch me because my skin feels as if it's all bruising". P19: "If I take them off quickly, I get pain—really awful pains in my joints and muscles.... Basically, if someone just touches me, it hurts—I mean everywhere"). Note: this

symptom would appear to be similar to the central sensitisation found in fibromyalgia [22].

Anxiety about future disease course P5, P6, P10, and P16 expressed concerns about the future (P5: "I mean I just worry that I wouldn't be around with my kids when they're little". P6: "Yes I do worry, you know, asthma kills, it does. You do worry about it sometimes").

Medication anxiety P4, P5, P6, P8, P9, and P13 expressed concerns about the long-term effects of OCS (P4: "I feel that it's poisoning my system". P9: "I'm getting immune to them I think").

Additional comments

Some patients indicated that OCS had a greater impact on their lives than asthma symptoms, and this issue was then explored for selected patients. In response to a time trade-off question, P2 indicated she would trade 15 years of life if she did not need to take OCS with asthma symptoms remaining constant, P4 would trade "a little" and P9 and P16 would trade 10 years. However, the question was found difficult by some patients (P15: "I have no idea how to answer that question"). Six patients were asked to rate the impact of OCS on a 10-point scale where 10 = "makes my life a misery". The ratings were P6: 7; P9: 8; P10: 9–9.5; P15: 4; P16: 9 or 10; P19: 5. Some patients reported delaying the start of OCS and delaying visiting the clinic when they knew they were deteriorating, but otherwise reported that they adhered to inhaled and maintenance oral doses. All patients reported high satisfaction with the care they were given.

Summary of qualitative study

The type of impact of OCS varied between patients. Ten patients reported irritability, five reported depression directly attributed to the use of steroids, and a further two reported depression as a consequence of weight gain (note that this is the patient's report rather than established aetiology). Eight patients reported sleep disturbance due to the arousing effects of OCS, with a further one patient reporting sleep disturbance due to the effects of hunger. Of the 14 patients reporting hunger, two reported vomiting due to overeating, and one reported indiscriminate eating. OCS had an impact on patients' lives also when the dose was reduced or discontinued, with three patients reporting pain sensitisation under these circumstances, and three reporting depression. Three patients reported that the increased weight caused by OCS exacerbated their asthma symptoms. Symptoms are also reported to arise when OCS dose

Table 2 Number of questions in eight ASQLSs corresponding to each of the ten domains of OCS impact

Domains	Number/23 reporting problem	AQLQ ^{Juniper}	MiniAQLQ	LWAQ	SGRQ ^b	AQLQ ^{Marks}	ABP ^c	AQ30 ^d	ASQLS
No. of items in questionnaire		32	15	68	50/76	20	18	30	112
Activity limitation ^a	23	10	7	35	26	8	8	15	52
Emotional impacts ^a	23	4	1	19	11	4	4	8	43
Asthma symptoms	23	12	4	0	8	3	1	4	0
Depression	7	0	0	1	0	1	1	0	0
Irritability	10	0	0	1	0	0	0	1	0
Sleep	8	3	1	4	1	1	1	1	5
Hunger	16	0	0	0	0	0	0	0	0
Weight	14	0	0	1	0	0	0	0	0
Skin	5	0	0	0	0	0	0	0	0
Gastric	7	0	0	0	0	0	0	0	0
Pain	6	0	0	0	0	0	0	0	0
Disease anxiety	4	0	1	1	0	2	1	0	2
Medication anxiety	6	2	1	1	1	0	0	1	4
Non-specific items about medication ^e		0	0	5	3	2	0	0	6

AQLQ^{Juniper}: Asthma Quality of Life Questionnaire [10]; MiniAQLQ: Mini Asthma Quality of Life Questionnaire [11]; LWAQ: Living with Asthma Questionnaire [12]; SGRQ: St Georges Respiratory Questionnaire [13]; AQLQ^{Marks}: Asthma Quality of Life Questionnaire [14]; AQ30: Asthma Questionnaire-30 [15]; ABP: ABP [16]; and ASQLS: Asthma-specific quality of life scale [19]

^a Some questionnaire items have both activity and emotional content but are counted once only

^b The SGRQ has 76 questions, but they are scored as 50 items. Note that the ‘impacts’ category in the SGRQ is not identical to the emotional impacts classified here

^c The ABP has an additional seven management items

^d The AQ20 has 20 items comprising a subset of the AQ30

^e These items typically involve embarrassment or inconvenience with inhaler medication

is reduced—three patients reporting depression and three (partially overlapping) reported pain sensitisation when a burst of OCS is tailed off.

Comparison with existing asthma-specific HRQoL scales

All eight HRQoL scales contain items assessing the impact of asthma symptoms in the domains of activities and emotions. No scale contains any items specifically referring to hospitalisation. Table 2 shows the number of items in each of the eight asthma-specific HRQoL scales that potentially could measure the impact of OCS in each of the ten OCS domains of impact identified in this study. All of the existing scales had items relating to sleep disturbance. Sleep disturbance can arise for at least two reasons—due to breathlessness/cough and due to the arousing effect of oral steroids (or less commonly, due to increased hunger). The sleep items of four of the scales (including the AQLQ^{Juniper} and the mini-AQLQ) are worded in such a way that either cause would be reported. Depression was not assessed in either the AQLQ^{Juniper} or mini-AQLQ, but was assessed in some other scales (see Table 2). Depression was a major

impact in some patients and is a recognised side effect of OCS. Depression in asthma can result from three causes—depression due to limitations caused by asthma symptoms; a direct effect of OCS on depression; and the indirect, depressive effects of altered body image and self-concept. For those scales where depression is assessed (i.e. LWAQ, the AQLQ^{Marks}, and the ABP), any cause of depression would elicit a patient response.

It is possible that the HRQoL deficits resulting from OCS are assessed by non-specific items relating to the general negative effect of medication and medication anxiety on HRQoL. Neither the mini-AQLQ nor the AQLQ^{Marks} have items relating to medication. The SGRQ has two items, and the ASQLS has one item relating to the effect of medication on life. Other scales had items relating to medication embarrassment or bother, but not to their impacts. The AQLQ^{Juniper} has one item relating to concern about use of medication, but not related to impact. Only the LWAQ has an item that could relate to weight gain, and none have items relating to hunger or disturbed patterns of eating, the impact of skin thinning, gastric problems, and pain. Irritability was found to be a common and troubling

symptom, but only the LWAQ and the AQ30 have items that measure this aspect of the patient's experience, and then only by referring to restlessness and an inability to relax.

Discussion

The impact of OCS is entirely or almost entirely neglected in the scales most frequently used in clinical trials (ACLQ^{Juniper} and mini-AQLQ). Other asthma-specific HRQoL scales contain items that could detect some of the OCS impacts, but the number of items doing so in relation to the total number of items is small. As the score of an HRQoL scale depends on the sum of items, the number of items in each domain determines to what extent that domain influences outcome. If there are few or no items relating to the deficits caused by OCS, then these deficits will be under-represented in the scale score. The issue of balance between the number of items in different domains also relates to the balance between different domains of asthma disease deficits and is one reason why scales should be selected for their utility in the specific context of use: a horses for courses approach [23].

Our findings show considerable overlap with another qualitative study [4] that reported OCS side effects of depression, gastric problems, sleep, hunger and weight gain, and irritability and mood swings, but did not report the effects of pain and pain sensitisation and depression associated with OCS withdrawal or skin-related problems. One other study reported side effects but without specifying what these are [5]. The present study differs from those other two studies [4, 5] in that the patients in this study appear to be more satisfied with the information they have been given. In contrast to these other studies, patients in our sample did not complain about lack of information and were highly satisfied with the quality of care given at the clinic. One small study [24] has explored patients' perception of asthma-specific HRQoL scales and showed that patients reported omissions of content as well as irrelevance. While some items will inevitably be irrelevant to some patients, the existence of omissions is concerning.

Limitations of this study include the iterative and individualised method of interviewing, which, while having advantages in an exploratory study, could affect the frequency of different kinds of reporting—and so the figures in Table 2 should be interpreted cautiously. For example, the effects of OCS withdrawal were first reported by P11, and so this issue was explored with subsequent patients; earlier patients may have experienced withdrawal without reporting it. Adherence and treatment satisfaction were higher in this sample than reported elsewhere [4, 5], so patients may have a higher burden of OCS symptoms due

to better adherence compared to other centres. The patients' attribution of symptoms to OCS may or may not represent the true aetiology of these symptoms, but whether true or not is likely to impact on adherence, and can therefore have an impact on asthma control.

The reason that side effects of OCS in asthma-specific HRQoL scales are neglected in severe asthma can be understood from an historical perspective. The first paper on the treatment of asthma by OCS [25] was published in 1958, long before HRQoL assessment became routine in clinical trials. Inhaled asthma medications (inhaled bronchodilators and inhaled corticosteroids) that had a safer side effect profile were developed shortly afterwards. The first HRQoL trial of an asthma medication [26], published in 1991, was a comparison between two inhaled bronchodilators (i.e. alternative treatments for mild and moderate patients). Subsequent to that date, alternative inhaler medications for mild/moderate asthma were evaluated by HRQoL scales, most commonly the AQLQ^{Juniper}. In the mid 1990s, a new class of drug was developed, a monoclonal antibody, that targeted inflammatory pathways in a more specific way than steroids. Although expensive and administered by injection, these drugs are effective in sparing patients from OCS exposure and are therefore suitable for severe patients. The first paper to evaluate the HRQoL benefits of a monoclonal antibody in asthma [27] followed convention and used the AQLQ^{Juniper}. However, the present study shows that none of the existing HRQoL scales adequately measure the burden of OCS. As a consequence, such scales (a) underestimate the impact of severe asthma on HRQoL because they neglect to add in the burden of OCS treatment and (b) underestimate the benefit of new medications that reduce the need for OCS treatment, because scales do not have items that are sensitive to OCS sparing. Of the existing scales, the AQLQ^{Juniper}, which is the scale of choice by convention, is particularly unsuited to the severe asthma population (see Table 2). Although it has three sleep items, the questions are worded so as refer to disturbance caused by asthma or asthma symptoms and so may not be endorsed by patients whose sleep is disturbed by the arousing effects of OCS.

Strategies for the future

There are several strategies [28] for remedying this current unsatisfactory situation, but they all involve the development of new items that measure the quality of life deficits imposed by OCS. These items could be used either as a stand-alone scale or as an additional module to be included within an existing scale. If existing asthma-specific scales are deemed to fail to measure the burden of severe asthma, it would also be sensible to develop new symptom-burden items as an additional module or as part of a new asthma-

specific scale for severe asthma. Whichever method is used, the question of balance between item domains or between asthma symptom-burden versus OCS symptom-burden questionnaires remains paramount. For purposes of health resource allocation, it is necessary to have an overall HRQoL score for each patient, and so, whether it is the combination of items within a questionnaire or the combination of two questionnaires, the method of combination is important to the overall score. Further research is needed both for the development of new OCS burden items and to understand how the burden of the treatment of asthma should be combined with the burden of the treatment in asthma so as to produce an overall score that informs treatment and resourcing decisions.

Conclusion

Existing asthma-specific scales underestimate the burden of severe asthma and underestimate the benefits of steroid-sparing agents. This underestimation is important because the high cost of modern steroid-sparing agents requires accurate quality of life assessment to inform decision-making. Improved assessment procedures are needed to provide accurate information on which treatment and resourcing decisions are made.

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