

The Patients' Experience of Severe Asthma Add-On Pharmacotherapies: A Qualitative Descriptive Study

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Purpose: Add-on therapies for severe asthma are continually emerging with proven efficacy in randomised controlled trials. To date, however, there are no qualitative studies exploring patients' experiences with these treatments. We aimed to understand the experience of patients who were treated with an add-on therapy for their severe asthma.

Patients and Methods: A qualitative descriptive study was conducted, participants were recruited from the respiratory clinics and databases of a tertiary referral hospital. Participants with treatment-refractory severe asthma (n=20) prescribed an add-on therapy for >4 months (75% mepolizumab; 25% omalizumab, and 25% macrolide) were recruited. Qualitative semi-structured interviews were conducted, with interviews thematically analysed.

Results: Participants' mean (SD) age was 59.5 (15.3) years, and 50% were male. Participants reported 4.5 (2.3) exacerbations in the past year. Asthma Control Questionnaire score was 2.0 (1.4). The monoclonal add-on therapies had been prescribed for a median (IQR) of 12.5 (7.0, 24.0) months. Experience was captured in four emergent themes: "Life is just easier" provided an overall message that the add-on therapy made the participants' life easier in terms of increasing participation, levelling out symptoms, providing more energy and reducing healthcare use. "Prednisone: A necessary evil" was discussed, particularly in terms of dose and dependence and damaging side effects. The theme "worry and hope for the future" referenced treatment non-response or cessation of effect which was discussed by some participants. Finally, "holistic care" was centred on the sentiment that the participant's asthma management and overall health were not related to one aspect or medication alone.

Conclusion: Patients with severe asthma experience vast improvements in quality-of-life and life participation with add-on therapies, but there remains a significant burden related to oral corticosteroids and incomplete treatment responses. Addressing this residual burden is an important area for future research.

Keywords: severe asthma, asthma medications, monoclonal antibody therapies, quality of life, patient experience

Introduction

Severe asthma is a high burden disease with an increased risk of morbidity and mortality,¹⁻⁴ and is associated with quality-of-life impairment.^{5,6} The burden of severe asthma pervades throughout many aspects of life, leading to impairments across physical, emotional, economic and social domains.^{5,7,8} Confounding the treatment of severe asthma is the heterogeneous nature of the disease, with its variable response to treatment, multiple comorbidities and risk factors.⁹

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In recent years, the emergence of add-on therapies for severe asthma has improved clinical outcomes for some people with severe asthma.¹⁰ Monoclonal antibody therapies (mAb) targeting Type 2 inflammatory asthma^{11–13} improves health-related quality-of-life (HRQoL) and asthma control, and reduces acute attacks.^{12,14} Additionally, azithromycin in severe asthma leads to reduced attacks and improved HRQoL.^{15,16} Although these treatments have been shown to be efficacious, residual burden from asthma attacks, ongoing asthma symptoms and quality-of-life impairment remain.¹⁷

Whilst the patient experience of living with severe asthma has been recently explored^{7,8} the experience of people using these medications is not described. Understanding these experiences will aid communication of the potential benefits and limitations of the medications. Therefore, in this study, we aimed to understand the experience of patients who were treated with an add-on therapy for their severe asthma.

Patients and Methods

Study Design

A qualitative descriptive study exploring the experiences of adults with severe asthma in relation to add-on asthma therapies was conducted. Data were collected using semi-structured, in-depth face-to-face interviews with a researcher (VLC), a behavioural scientist, who had no prior relationship with the participants and was not involved in their medical care. Ethical approval was obtained (Hunter New England Human Research Ethics 16/05/8/5.02). This study was conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent prior to study commencement. Participants were informed as part of the consent process that anonymised quotes will be used in possible publications.

Setting

Participants were recruited from the respiratory research database and clinics of a tertiary referral centre in New South Wales, Australia between May 2018 and December 2018.

Participants

Adult (>18 years) participants (n=20), who had a prior confirmed doctor diagnosis of severe persistent asthma, were purposefully recruited. The eligibility for severe

asthma was based on the American Thoracic Society/European Respiratory Society taskforce,¹⁸ including the requirement for maximal high-dose inhaled corticosteroids and a long-acting β_2 -agonist, or requiring frequent oral corticosteroids. A further criterion was the prescription of a novel add-on therapy (omalizumab or mepolizumab or azithromycin) for at least 4 months prior to study entry.

Data Generation

Baseline demographic data were collected prior to the interview including age, age of asthma diagnosis, acute attacks and medical history, and asthma control was assessed using the Asthma Control Questionnaire (ACQ).¹⁹

Semi-structured interviews were conducted to understand the patient experience of using add-on severe asthma medication. Free-speaking was facilitated by open-ended questioning and probing where required. The interview guide was developed with reference to the study aims and a review of the literature^{20–23} by the research team, including expert severe asthma multidisciplinary clinicians (PGG and VMMcD) and a behavioural scientist (VLC). The interview guide covered six core aspects aimed at understanding the experience of add-on therapies in severe asthma (see [supplement](#)).

Participants were assured of confidentiality and informed at the beginning of the interview that they may ask for the recording to be stopped at any time. All interviews took place in a private room, the mean (SD) duration was 37.65 (16.00) minutes. Interviews were stored via password-protected encrypted storage. Interviews were continually evaluated using an iterative process to ensure additional components did not need to be incorporated into the interview guide. Audio-recorded interviews were conducted face-to-face. Pseudonyms were used in place of participant's names to ensure confidentiality.

Analysis

Recordings were transcribed verbatim, anonymised, and entered into NVivo version 12 (QSR International, Doncaster, Australia) for data coding. Thematic analysis²⁴ was performed using an inductive approach. The first analytical step involved familiarising the data by reading and re-reading the transcripts and making initial notes. Following, these data were initially descriptively coded, and then line-by-line using inductive coding. In the third step, codes were categorized and merged based on similar codes from the initial inductive coding. Data were then synthesised into themes and subthemes. Themes and

subthemes were discussed, reviewed and confirmed with co-authors, once consensus was reached, the themes were named to reflect the theme content. Additionally, the emergent themes and subthemes were continually checked against the codes and the original transcripts to ensure they were representative of the interview content.

Results

Participants were mean (SD) 59.50 (15.27) years and 50% male (Table 1). Most (75%) were prescribed Mepolizumab, 25% prescribed omalizumab and 25% using azithromycin (Table 1). The median (IQR) duration of monoclonal antibody therapy was 12.50 (7.00, 24.00) months. Of all participants, 60% had poor symptom control determined by an ACQ>1.5. Half of the included participants were prescribed maintenance oral corticosteroids (OCS), at a mean (SD) dose of 29.45 (38.16) mg.

There were four emergent themes. These themes and their subthemes are displayed in Figure 1. Exemplar

quotes associated with each emergent theme and their associated subthemes are summarised in Tables 2–5.

Theme 1: “Life is Just Easier”

The theme “life is just easier” provided an overall message that the add-on therapy made the participants’ life easier in terms of levelling out symptoms, providing more energy and reducing healthcare use. Participants described three main subthemes in which the add-on therapies had impacted their life. These were “asthma has stabilised”, “participation in life” and “reduced healthcare and medication use” (Table 2). Participants also contrasted their experience of “asthma before the add-on therapy” (Table 2).

Subtheme 1.1: Asthma Has Stabilised

Participants described how the add-on therapy had stabilised their asthma. They described a levelling out of their symptoms, with reductions in the severity of their attacks,

Table 1 Patient Demographics

Patient Demographics	(n = 20)
Age, mean (SD, range)	59.50 (15.27, 21–81)
Male, n (%)	10 (50)
Living arrangement, n (%)	
Living alone	4 (20)
Living with spouse/family	16 (80)
Employment status	
Retired	12 (60)
Not working for medical reasons	4 (20)
Working (full or part-time)	4 (20)
Age of asthma diagnosis, mean (SD)	23.70 (21.59)
Asthma Control Questionnaire	2.05 (1.37)
Past year asthma attacks	4.45 (2.26)
Inhaled corticosteroids (Beclomethasone equivalent units), median (IQR)	2000 (1000, 2000)
Maintenance Prednisone, n (%)	10 (50)
Maintenance Prednisone Dose (mg), mean (SD)	29.45 (38.16)
Novel medication*, n (%)	
Azithromycin	5 (25)
Mepolizumab	15 (75)
Omalizumab	5 (25)
Duration of Monoclonal antibody therapy (months), median (IQR)	12.50 (7.00, 24.00)

Note: *Azithromycin was an add-on therapy to the monoclonal medications.

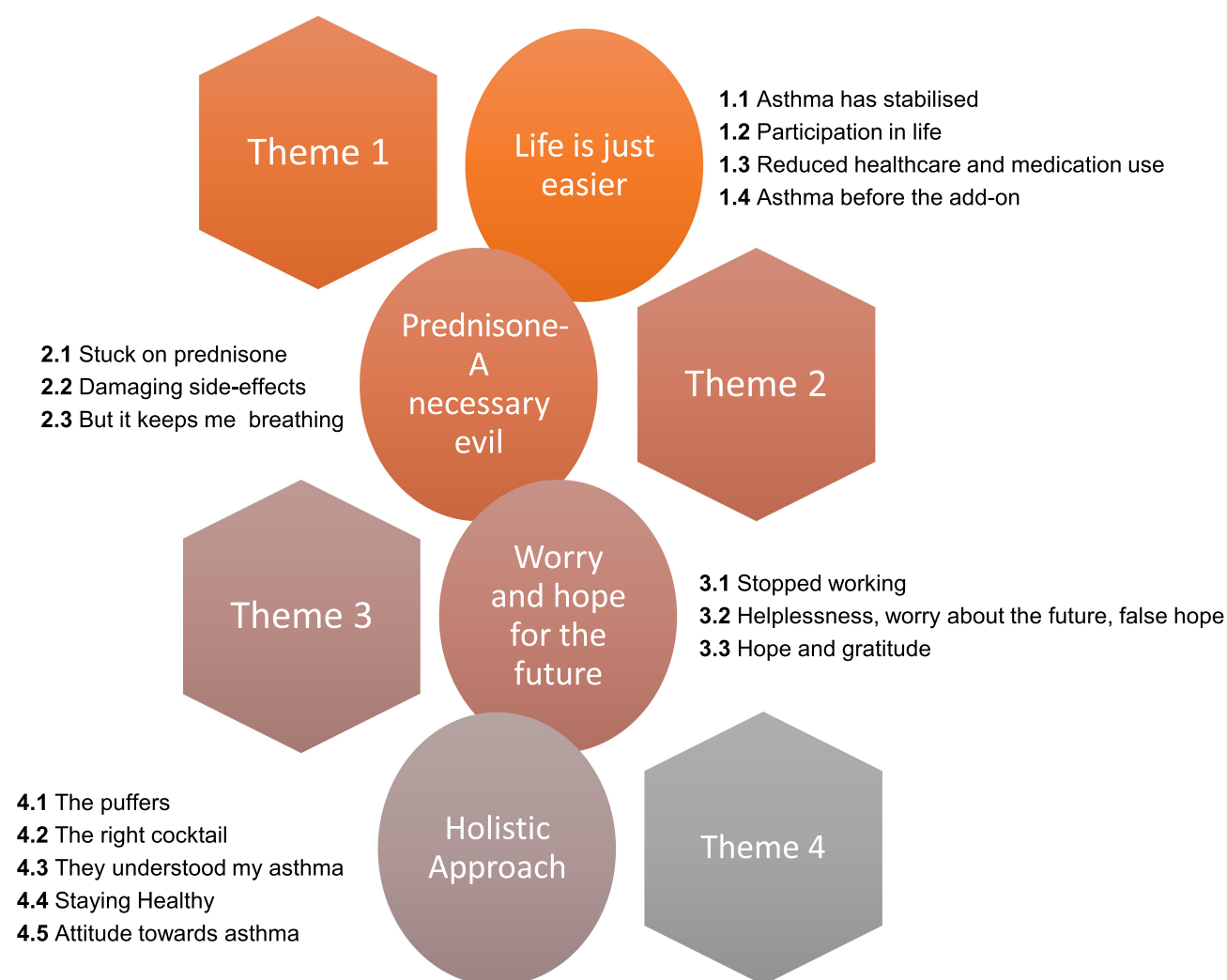


Figure 1 Themes (circles) and subthemes (boxes) for understanding the experience of add-on therapies in severe asthma.

and a reduction in time taken to recuperate from an attack (Table 2). Participants still talked about having symptoms of asthma, including congestion and chest tightness, but that these symptoms were more manageable.

Subtheme 1.2: Participation in Life

Participants described a substantial improvement in quality-of-life. They reported improvements in energy, ability to participate in life and the ability to undertake household chores, which they were unable to complete prior to their medication commencement. Reduction in asthma symptoms was credited by several participants for their quality-of-life improvement (Table 2). “The other thing is just the quality of life is just so much better. Sleeping better. Just not having to be restricted because I am constantly coughing and spluttering away.” Howard, Male, 62.

In addition, an improvement in energy also contributed to the positive experience of the add-on therapies “I feel more alert, I think. I feel bouncier, I’ve got more energy” William, 72, male. The combination between symptom reduction and increased energy enabled participants to take part in more activities, including going for walks, travelling and doing work around the house. Further, Ian, age 63, male described his experience “In terms of impacting my life, well it means that I can live a normal life, essentially”.

Subtheme 1.3: Reduced Healthcare and Medications Use

Reductions in healthcare and medication use were described by the majority of the participants (Table 2), which was attributed as a positive response to the

Table 2 Theme 1, “Life is Just Easier”

Theme: “Life is Just Easier”	
Subthemes	Exemplars
Asthma has stabilized	<p>“... it's very much stabilised my asthma ... it stopped the exacerbations to the extent that I wasn't locked into that cycle of high doses of Prednisone” Ian, 63, male.</p> <p>“Just a levelling out of symptoms which I think it has done”, Anthony, Male, 72.</p> <p>“I think it's more to do with the severity of asthma attacks, if you want to call it that. The severity, the time taken to recovery; which is - to recover, rather, is something that until I actually started to piece together what I was - what was happening, I wouldn't have thought of it” – Clyde, male, 57.</p> <p>“It levels the symptoms out. Instead of having those ups and downs, I still get tight but yeah, it's levelled it”. Jane, 61, female.</p> <p>“I was taking all the other medication, and I was not getting any better. I was staring, and I was thinking ... you are not going to live too much longer ... then it changed [after I took Nucala], and it is not the cough that is better; it is the effort”. Nicholas, male, 77.</p> <p>“It eliminates the condition. Well, it does not eliminate the condition but eliminates the intensity of the condition.” Ian, 63, male.</p>
Participation in life	<p>“I've gone from none, to 90% better ...” Nicholas, male, 77.</p> <p>“The other thing is just the quality of life is just so much better. Sleeping better. Just not having to be restricted because I'm constantly coughing and spluttering away”. Howard, Male, 62.</p> <p>“At that point it was just a dramatic change [when I started the medication], I could walk around and I could talk, you know, because even 30% lung function I couldn't even hold normally a sentence properly”. Rhonda female, 56.</p> <p>“It [Nucala] gives me longer running time. It's like unleaded petrol versus the leaded version. It can go further. You can do more things and you can go a bit harder” Jennifer female, 61.</p> <p>“It's not earth-shattering but it does give you a degree of comfort, it does give you the ability to do more things ...” Clyde, male, 57.</p> <p>“I can mow a lawn without stopping, or just stopping one or two times; if I can take the rubbish out, if I can prune a tree, if I can wash the car, help the wife shopping, if I can do those without the major discomfort that I used to have, whilst there is still discomfort, it is nowhere near as uncomfortable as it used to be, if I can put it that way”. Clyde, male, 57.</p> <p>“Having azithromycin and Nucala, I think, as I said, is making my life so that I am able to live it.” Helen, female, 76</p>
Reduced healthcare and medication use	<p>“The main thing I've noticed is that with me not coming to hospital, I think I would've been in hospital more times if I didn't have it”. Diane, female, 66.</p> <p>“Before I started taking it [the add-on] I was using the Ventolin quite a bit. Since I've started on that [the add-on therapy] I haven't used it half as much”. [sic] Harold, male, 81</p> <p>“Now I'm not taking any Ventolin at all which is quite amazing.” William, Male, 72.</p> <p>“I think it's kept me out of hospital. That's the main thing I have noticed”. Diane, Female 66.</p> <p>“I used to use my Butamol four puffs every four hours. Now I'm down to two puffs, morning and night ... when I get sick, yeah. I take that less [prednisone] too-” Jennifer, Female, 61.</p> <p>“I used to have Prednisone [all the time]; like the last few months I really haven't - I haven't had as many - near as many the number of issues [of Prednisone] as I did have with, say, for six to 10 months previous”. [sic] Clyde, male 57.</p>

(Continued)

Table 2 (Continued).

Theme: “Life is Just Easier”	
Subthemes	Exemplars
Asthma before the add-on	“I mean I was trying to work at lung function that was within the 30% range and I had been there for over six months. Life had just ground to almost a halt.” Rhonda female, 56. “I was having so many exacerbations ... I had enough Prednisone in six months to qualify for the 12 months, probably twice as much if I need it”- Albert, Male 58 “I’ve got fruit trees and things, but not - I couldn’t look after them properly ... I can’t do the housework”. Margaret, Female, 70 “It was the last stop. You know, we had tried at that time all the puffers that were out, you know, [the doctor] tried [Spiriva] but that actually made me worse. You know, I’ve done all of the current puffers that there were, I mean there’s more that have come out since but tried all of them still. But yeah, I was on everything that there was and nothing.” Rhonda female, 56. “I was feeling lousy [from asthma], like I could barely get myself up, like I was dragging myself, and I had always been a person who my motto was why burn the candle at both ends when you burn it in the middle to.” Rhonda, female, 56

medication. Participants described the need for fewer emergency department and general practitioner visits. They also talked about less Salbutamol and Prednisone use (Table 2). However, not all participants were able to reduce their oral corticosteroids (examined in the theme “Prednisone- A necessary evil”).

Subtheme 1.4: Asthma Before the Add-On

Participants described what life was like before they were commenced on their add-on therapy (Table 2). They described the need for high OCS use, frequent attacks and limitations to life.

Theme 2: “Prednisone – A Necessary Evil”

Despite the perceived effectiveness of add-on therapies prednisone use was a concern for the majority of participants, with subthemes emerging around the frustration of being “stuck on prednisone”, concerns for the “damaging side-effects”, and acceptance “but it keeps me breathing” (Table 3).

Subtheme 2.1: Stuck on Prednisone

The inevitability of having to continue to take prednisone was discussed. Some participants described unsuccessful reduction attempts, and being caught in a cycle of reducing prednisone, then increasing again (Table 3). When asked

about the medication they were currently taking, Rhonda, female, 56 said

... I’ve been stuck with [prednisone] for the five and a half years, that I just can’t get off. We even have problems getting me below 20 milligrams ... below 20 usually causes an exacerbation. Even though you technically can cut by five milligrams, supposedly if we try and cut me at five milligrams I can end up in hospital.

Subtheme 2.2: Damaging Side-Effects

Concerns around the damaging side-effects of prednisone were described by over three quarters of the participants. Exemplars are presented in Table 3. Side-effects were described across multiple body systems - “I have osteoporosis, the broken bones, the cataracts, mood swings, puffiness, the works ... I need it to keep me alive, but it’s not a nice thing.” James, male, 45. Furthermore, participants expressed how side-effects impaired their quality-of-life, with one participant explaining

I hate steroids. They’re just brutal. I’m so against them. Just how you feel on them, you’re just - you can’t sleep. Your body’s [SIC] so exhausted from being sick with asthma, but you’re just awake; the fluid in my legs, my feet, that’s also there. I don’t know the long-term side-effects of steroids, that scares me a lot. They’re just - to me, I call them a Band-Aid.

Naomi, female 34.

Table 3 Theme 2, “Prednisone: A Necessary Evil”

Theme 2: Prednisone: A Necessary Evil	
Subthemes	Exemplars
Stuck on prednisone	<p>“I think I might have tried once [to reduce prednisone] and the symptoms I had started to reappear. I'm just not prepared - because I know what it's like when I was in that cycle of massive doses of Prednisone, weaning yourself off massive doses and wean yourself off ...” Ian, male, 63.</p> <p>“When I was taking the high dose of Prednisone you had a little period of time where you think you can do everything and anything and then when you start reducing it, because you have to because you feel so blah, and then I couldn't do it. I'd reduce it and for a little period of time I couldn't do anything much and then I had to take them again and for a few days.” Margaret, female, 70.</p> <p>“Well, yeah I know the side effects and I guess - yeah, you consider it, but once again if I wasn't on the little bit of prednisone I'm on, I know I go backward. I really don't have a lot of choice I guess; it's either live for now or live for later. My biggest thing is to just try to keep it to its minimum I need. Other than that, I really can't do much.” Michael, male, 48.</p> <p>“... it's really affecting me because I've been on it for so long already. I don't know what's going to happen in the next five or 10 years because of the prednisone because it's just really destroying my body pretty quick over the last five years mainly, hasn't it, I've really gone downhill for the bones and that, haven't I? ... It's actually overtaking the asthma problem now is the side effects from it. [prednisone]” James, male, 45.</p>
Damaging side effects	<p>“Because I think that was associated to the weakening of the bones. There was a stage where I leaned over to pat mum's cat on the lounge and I pressed some ribs against a handle and I cracked a rib.” Howard, 62, male.</p> <p>“I hate Prednisone because number one you get the moon face. Number two I find it hard to sleep on it and I don't know whether that just gets in your brain and you just keep on thinking I'm not going to sleep because I've got this drug. It just - I get aches and pains with it ... I just get pains in my back with it and yeah flushed cheeks and all sorts of things. The last lot I had, I was starting to feel really agro and that's not me. I really hate that drug.” Judy, female, 66.</p> <p>“I've broke my feet all the time. It's not just from - it's just from normal walking on them. I wake up in the morning and I'll be in a lot of pain and that - my knees, my hips, my elbows. I've just come out - I broke my wrist from it from doing hardly anything. I was doing a barbecue, just the tongs and I managed to break my wrist. So just very annoying and it's getting really depressing as it goes on now.” James, male, 45.</p> <p>“Well I mean I think the majority of the side effects of Prednisone have happened now. Don't forget your skin, it's like tissue or like it can bruise very easily and had a few damage results. Like my shins, it's like that ... touch and ... [it rips right open]” William, male, 72</p> <p>“I worry about the Prednisone, because of the side effects, there's three big side effects ... cataracts, osteoporosis and diabetes. I worry about the ongoing use of that.” Ian, male, 63.</p> <p>“Well I put on tons of weight ... it's starting to affect my eyes” Rebecca, female, 21.</p> <p>“I go a bit - sleep deprivation, overeating - well, appetite enhancement, fluid retention. I tend to go a little bit funny in the head. I nearly drove a car off the side of the hill one time because of it ... I don't think very straight when I'm on it.” Albert, male 58.</p> <p>“Well, bad experience, I had prednisone for quite a long time, quite a high dosage of that, and I suffered severe depression. At my lowest, never, ever, ever thought I'd feel the way I did.” Naomi, female, 34.</p>
But it keeps me breathing	<p>“It keeps me breathing. That's the only thing I can say I like about it”. James, male, 45.</p> <p>“[The GP] tried to tell me to knock it off [the prednisone], but it was the only thing that I could get a bit of relief with”. Harold, male, 81.</p> <p>“I knew it was never a good thing to be on and I always wanted to get off it. My wife in particular saying, oh don't increase your Prednisone? I keep on saying well ... Well what do you want me to do? Do you want me to collapse on the floor and cough and splutter all day and whatever and not be able to do anything?” William, male, 72</p> <p>“At this point in time [the benefits of prednisone outweigh the negatives]. There's no other - there's nothing else available”. Ian, male, 63.</p> <p>“... that's a last resort. That's when I'm crook, when I need that one”. Diane, female, 66.</p>

Table 4 Theme 3, “Worry and Hope for the Future”

Theme 3: Worry and Hope for the Future	
Subthemes	Exemplars
Stopped Working	<p>“I tried that [Xolair]. I was on that for quite a while too - quite a while, something like two years ... That just stopped working. Those blood tests started not being right.” James, male, 45</p> <p>“I just feel like I get tighter a bit more often now than when I first went on it.” Jane, female, 64.</p> <p>“I didn’t feel like it [Nucala] was working, it made me sick ... So I’m like, there’s no point taking these if they don’t work.” Rebecca, female, 21</p> <p>“But once I got over the headaches because they slowly got better it started working really well and I felt good about myself. Then it just all of a sudden just didn’t work and I was like well, that was ... that.” Rebecca, female, 21</p> <p>“I think, for the first eight months, I think it changed a lot. I was quite able to - I felt that I was kind of living a normal life, which was amazing. But in the recent three, four months, I don’t think it’s helped me a lot at all.” Naomi, female, 34.</p>
Helplessness, worry about the future, false hope	<p>“I don’t know. And nobody can tell me, is good to take it for ten years. But I don’t know. Maybe in another year, maybe another dose, and [the doctor] will say we have to stop, I don’t know? And when I mention it, they say, well, let’s take it for one year, but there is some irritation, how of how long I can be taking it.” Nicholas, male, 77.</p> <p>“I’m starting to give up a bit [that something new will come along] ... I think I’m pretty well the way I’m going to be all the time” James, male, 45.</p> <p>“There is a concern and it’s not a resistance as such. It’s more it’s done as much for me as it can do, yeah, because the asthma attacks are not quite as - how do you say it? They’re not as severe, nowhere near it, nowhere near it, but that first year that I was on it, especially the second six months, it was just wonderful.” Jane, female, 64.</p> <p>“[Do you worry about the long-term side effects?] Sometimes I don’t think I’ll live long enough to be worried. I don’t think I’m going to end up to be a terribly old person really.” Rhonda, female, 56.</p> <p>“What am I going to do when they find out that it’s not working [Xolair], what’s the next thing?[it worries me] ... because I feel like it’s plateauing [the effect of the medication]. I guess I’m afraid of that creeping back. Is there going to be something else? It’s like I can distinctly remember having my first Ventolin and it was a miracle. It took me about six months to really appreciate Xolair and that was wonderful. Now what?” Jane, female, 64.</p> <p>“I’m sure at some stage I will develop a total - it will become inefficient at combatting what - the job its doing now. So - but - I’m hoping I run out of time before that happens.” Anthony, Male, 72.</p> <p>“We were just, when we were told about this new drug it was sold to us as a miracle thing that was ... we expected, I wanted to at least have some improvement ... and maybe not get off the steroids but lower the dosage with some of the other medication we might’ve been able to ditch. But it hasn’t eventuated.” Rebecca, female, 21.</p>
Hope and gratitude	<p>“When I started to get it years ago, asthma, there was no medication. I was told that was all in my mind and I was just stressing too much, even though I was crawling up the back steps. The fact that you have medication, I bow to the medical world.” Helen, female, 76</p> <p>“[The clinician] was saying that they’re starting to look at perhaps strategies to wean people off Prednisone who are on these targeted severe asthma treatments. So, maybe somewhere down the track. Ten years ago, there was no such thing” Ian, 63.</p> <p>“I’m all for giving everything a go, definitely. I had really high hopes for the mepo (Mepolizumab), I still do, but I have lost a lot of hope, and my quality of life has definitely dropped in the last four months.” Naomi, female, 34.</p> <p>“If your illness, or your chronic illness is bad enough, and if the medications you’re using are having an impact but not a broad impact, then if something was made available that was going to - I’m loathe to use the word, dramatically, but improve your quality of life, dependent on what form of asthma or COPD you have, then I wouldn’t hesitate in trying it; and that’s probably overall the reason I like to engage in these trials because somewhere, sometime, there’s got to be an answer to the discomfort that you go through.” Clyde, male, 57.</p>

Table 5 Theme 4, “Holistic Approach”

Theme 4: Holistic Approach	
Subthemes	Exemplars
The puffers	<p>“Sometimes I wish the Ventolin would just open the airways just a little bit more. But I don’t go over the dosage. What I do if I’m quite clogged, then I get the nebuliser out and take the heavier ones.” Helen, female, 76</p> <p>“No [I don’t like the puffer], the puffer is the thing that - so sometimes they make you cough and coughing can sometimes set you off for ages, even though its making me better.” Rhonda, female, 56</p> <p>“Ventolin is one thing that relives you.” Rhonda, female, 56</p> <p>“Seretide is important. Even though I’m on the Xolair I think that Seretide is still very important - it’s focussed.” Jane, female, 64</p> <p>“Ventolin, that was just a miracle to have an instant reversal, because when I was young it was an instant reversal. It was for many, many, many like several decades. You’d have a puff and - you’d be wheezing your head off; have a puff and you’d get on with it. It was as if you’d never had a tightness at all- [but it] and when you’re - I guess for somebody that’s never had asthma, but you know what it’s like, so that struggling to breathe and then [gasp] ...” Jane, female, 64</p> <p>“I find the puffers have been good. You know, I sort of keep out of trouble but if I get a chest infection then that’s when the cortisone and the antibiotics come in.” Anthony, male 72</p> <p>“[Symbicort and Ventolin] just kept me bubbling along at a reasonable level I think”, Judy, female, 66</p>
The right cocktail	<p>“It’s a combination I think [of medication]. Yes, and I think it’s also the help that you get. There is a place to go to get help” Helen, female, 76.</p> <p>“The problem is, most of these drugs I also understand they’re not short-term. It’s not like taking Panadol and they kick in in four hours and it’s that sort of dose, most of these are cumulative ... you’ve got to be taking it continuously to get any effect or have it built up, so it’s not just take it now and maybe take it in three days, they don’t work like that.” Rhonda, female, 56.</p> <p>“So, it’s hard - when you are doing all these different things [treatments] it’s hard to separate what’s - what is causing that effect” Anthony, male, 72</p> <p>“I think that each one I’ve mentioned has had its own impact in certain ways. To tie it down to one - so it’s like a combination has worked.” Michael, male, 48.</p> <p>“It [the add-on medications] just seems to - how would you - complement or help or ... help the others” Melissa, female, 41</p>
They understood my asthma	<p>“[My GP was] absolutely phenomenal, he’s up to date on all the research when I was getting sick so he would do things and so when I got sick, I then had to wait for a specialist. I got that specialist and he actually said that my GP is so good that there’s actually nothing he could do for me.” Rhonda, female, 56.</p> <p>“They understood my asthma [the doctors]. They understood that, that inhibited capacity to breathe. What triggered it was really the eosinophil count.” Jane, female, 64</p> <p>“... go to a proper respiratory person ... and then take the time with the puffers and follow the bloody - what you’re told and give them the time. A lot of people miss doses; and that’s not only for asthma drugs, that’s for all drugs and they wonder why they don’t work.” Michael, male, 48.</p> <p>“... before I was diagnosed ... I went to different doctors and it’s like, here’s a Ventolin puffer, take that mate, you’ll be right; out the door ... the doctor I’ve got now, he was the only one that took some interest and hospitalised me and got me on the right track. So yeah, find the right doctor.” Michael, male, 48.</p>
Staying healthy	<p>“Quite obviously I can’t expect that medication to have any lasting improvement on my health if I don’t lose weight; hence the exercise classes that I’m currently in, or the diet that I’m currently on. You know, I try to be more proactive after I’ve got myself into a - well, I’ll say a shitful [sic] state, to try to at least lose the weight, give myself half a chance.” Clyde, male, 57.</p> <p>“I guess I’ve always tried to remain as active as I can ...” Judy, female, 66</p> <p>No one else [will take care of your health] - you know, your doctors and all of that are only your coaches kind of thing, that’s the way I put it as a physio. Like I used to say, I can give you the exercises, but no one is going to do them and no amount of treatment that I do here is really the treatment; the real treatment is what you do at home.” Rhonda, female, 56.</p> <p>“I’ve always been one to do as much exercise, because I think the worst thing you can do is sit down. So, I keep moving as much as possible.” Helen, female, 76</p> <p>“I take it as prescribed and add to it. I think [the doctor] knows I do that and I’m going to do that whether you say I can or I can’t, good, bad or otherwise, because I know how I feel. I know that that’s what I need to do and that’s - is it arrogant?” Jane, female, 64.</p> <p>“I do not know why [people miss their medication]. It’s just silly. Really, if you want to stay out of hospital you have got to take your medication. They give them to you for a reason, not to put in the drawer. You have got to take them.” Diane, female 66.</p>

(Continued)

Table 5 (Continued).

Theme 4: Holistic Approach	
Subthemes	Exemplars
Attitude towards asthma	"I guess the only thing that I would say is when I do come across people who have had similar sorts of issues, number one most of them seem to be a lot worse than me and I do try to stay - you know exercise a bit, I do try to make sure I have the medications. It does impact on my life and how I live it because there are things that I have to do. But I just find if I can keep on doing these things and stay healthy and exercise, then hopefully you know my lungs are not going to cark it on me before anything else." Judy, female, 66 "Yeah, you just don't think about, it's called staying alive, really. You know, in my category of asthma that's pretty much what it is, so you do what you do, you know?" Rhonda, female, 56 "I think when you've been sick for a long time and like I said, you evolve to be able to do. I've always been like a doer; so it's just like, well it has to be done so [we're going to have to get] it done some way. I guess, when you work for yourself and when it just has to be done, some people can say well I can't do anything and just stick with that; oh, I'm not capable of doing it, so I just won't do it. Where I'm one of the people, well we got to get it done." Michael, male, 48

Subtheme 2.3: But It Keeps Me Breathing

They acknowledged, however, a trade-off between the side-effects of prednisone for the benefits. Participants acknowledged that prednisone was an effective medication, and implied that often it was their only option “But it’s a necessary evil so I put up with it”. Anthony, male, 72. Additionally, prednisone was described as a “safety net” by one participant and another described it as a “last resort” (Table 3).

Theme 3: Worry and Hope for the Future

The theme “worry and hope for the future” centred around the anxiety that some participants felt when their current add-on therapies did not provide or sustain the disease control that they wanted. Several participants described how their add-on therapies had “stopped working”. Additionally, some felt like this medication was their last hope and expressed feelings of “hopelessness, worry about the future, or false hope”. However, others remained hopeful that there would be new asthma discoveries.

Subtheme 3.1: Stopped Working

Reduced efficacy or treatment non-response was discussed by some participants (Table 4). James, male, 45, expressed frustration at not being able to reduce the prednisone. “No. That’s [the problem]. We haven’t been able to reduce it [the prednisone]. We tried to not long ago [to] step down. I – we tried – as far as I got was 20 milligrams from 25 but I got sick, so we had to put it back up.”

Naomi, female, 34, who had expressed that the add-on therapy had enabled her to lead a normal life, indicated that the medication was no longer helping her asthma, “I think, for the first eight months, I think it changed a lot. I was quite able to – I felt that I was kind of living a normal life, which was amazing. But in the recent three, four months, I don’t think it’s helped me a lot at all.”

Subtheme 3.2: Helplessness, Worry About the Future, False Hope

Some participants expressed worry about the unknown future around some aspects of their medication, for example, not knowing how long they needed to be on the medication. They feared that the medication was losing or would lose its effectiveness (Table 4), with one participant stating,

“At this stage – certain periods through your life, they give you these drugs and say is it going to work? It appears to work at the time ... [then they don’t work anymore]”, William, male, 72.

Further, Jane, female, 64 described, “I’d like to know that there’s something in the pipeline, but that’s a security issue ... I have concerns, very real and very consistent ... ” There was additional concern around not knowing what the future will hold in terms of their severe asthma, and this was limiting to their life.

“Just not knowing, like you want to get a full-time job but not knowing if you can hold it because you don’t know if you’re going to get sick that night or you’re going to be well” Rebecca, female, 21.

Subtheme 3.3: Hope and Gratitude

Some participants expressed a sense of hope for the future in terms of new discoveries (Table 4). Helen, female, 76, recalled “When I started to get it years ago, asthma, there was no medication. I was told that was all in my mind and I was just stressing too much, even though I was crawling up the back steps. The fact that you have medication, I bow to the medical world”.

Theme 4: Holistic Approach

“Holistic approach” (Table 5) was centred around participants expressing that it is more than their add-on therapies that contribute to their disease management. The sub-themes describe the role of other medications (use of their “puffers”), as well as the getting “the right cocktail” of medication. In addition to their pharmacological treatments, participants also expressed the importance of having access to the right healthcare team, and knowledge of what they can do to control their asthma and stay healthy.

Subtheme 4.1: The Puffers

Participants talked about the importance of their other asthma medications in addition to their add-on therapies. Overall, the majority of people felt that the puffers kept them going and the add-on therapy gave them the extra boost.

Subtheme 4.2: The Right Cocktail

Whilst participants were enthusiastic about the effect their add-on therapy had on their asthma symptoms and life (Table 2), they also recognised that finding “the right cocktail” of medication was important. There was a recognition that their add-on therapies provided add-on value as part of their existing asthma management strategies (Table 5). Ian, male, 63 illustrates, “I don’t believe I could just survive on mepolizumab alone. Clearly, Prednisone on its own at 5 milligrams is not enough. It probably would be if I stuck at 50 milligrams a day, but that would be a pretty horrific dose. Yeah, so I think it’s all part of a collective.”

Subtheme 4.3: They Understood My Asthma

Some participants expressed the importance of having access to expert clinicians for their overall severe asthma management, as well as being able to get access to new treatments (Table 5). They credited that it was important to

“find the right doctor” and how important their healthcare team was in understanding their asthma.

Subtheme 4.4: Staying Healthy

Some of the participants talked about the importance of staying healthy. Participants spoke about the importance of diet, exercise, medication adherence, as well as being informed about their disease (Table 5).

Subtheme 4.5: Attitude Towards Asthma

Some participants demonstrated a stoic view towards their asthma (Table 5). This included people not wanting others to perceive them as sick, or impaired. “Then yeah, it’s really important to me to be normal. I don’t want anybody to ever perceive me as being an invalid. I don’t like to be seen as a person with a weakness or a sickness, or whatever label you want to put on it. I have to manage it so that you don’t know.” Jane, female, 64.

Discussion

This study encapsulated the patient experience of using new add-on therapies for the treatment of severe asthma. Overwhelmingly participants spoke about how their add-on therapy had positively improved their life. These novel data provide insight into the patient experience beyond that of patient and clinician-reported outcome measures used in clinical trials. We highlight the positive response to treatment and describe the ongoing concerns of patients. Importantly, patients described how the new treatments integrate as a component of a holistic asthma management approach.

The improvements in patient-perceived quality-of-life reported in this study are consistent with the clinical trials of add-on therapies; however, improvements in quality of life were only modest in randomised controlled trials,^{12,14,16} whereas the experiential description from patients suggests a far greater improvement. The reasons for this are unclear. It may be that quality-of-life questionnaires used in clinical trials²⁵ do not adequately capture the experience of people with severe asthma, or may not ask the questions that are of most important to people with severe asthma. The use of fit for purpose severe asthma patient-reported outcome measures may provide greater sensitivity.²⁰

The theme “participation in life” may also provide important insights in this regard, as participation, meaning increased participation in everyday activities, such as social and physical activities and improved relationships,

was highly valued by participants. In another study exploring outcomes that matter to patients with severe asthma, wanting to be more physically active was rated as one of the most important outcomes from a patients' perspective;²⁶ however, this outcome is infrequently assessed. Physical activity is a complex construct and can relate to participation as well as activity/functional limitations.²⁷

Participants in this study contrasted their experience of living with severe asthma before they received their add-on therapy. These limits to life have been described in previous studies.^{7,8,20} The themes described in this study extend current knowledge about the patient experience by specifically exploring the impact of novel add-on asthma therapies from a patient's perspective. From their perspectives, these therapies were able to bring back a normal level of function, such as participating in simple household tasks, like mowing the lawn. Additionally, in previous literature, participants have focused on the negative emotional and physical side-effects of severe asthma treatment.^{7,8} In the current study, the side-effects of add-on therapies were scantily mentioned.

The use of oral corticosteroids however remained a major concern for people with severe asthma.^{20,28,29} In this regard, our study mirrored the previously outlined concerns of patients and illustrated that oral corticosteroids use remains a significant problem despite add-on therapies.³⁰ In this current study, participants detailed the damaging consequences of long-term oral corticosteroid use and the inability to wean from this treatment despite mAbs or macrolide therapies. This caused frustration for some as they felt deflated about being "still stuck on prednisone". Whilst participants described the negative aspects of oral corticosteroids in terms of their side-effects, it was acknowledged by some participants that it was an essential part of their severe asthma management. These data highlight the importance of oral corticosteroid minimisation and the need for oral corticosteroid stewardship in treating severe asthma.³¹

The impact of treatment and future options was an important consideration. A subset of participants described that their severe asthma add-on therapy had just "stopped working" or had reduced efficacy. Fear and panic in relation to living with asthma has been previously described;²⁰ however, in this study, some participants expressed hopelessness in relation to the likelihood of new medication discoveries, with some "starting to give up a bit" that new medications would come along. Lack of response to treatment is a frustration that is shared by other chronic

respiratory diseases, such as chronic obstructive pulmonary disease.³² Additionally, some participants resigned that they were "pretty well the way I'm going to be all the time". This view was not shared by all, with some people expressing hope for new discoveries. Engaging in discussions with patients about their expectations of treatment, their perception of efficacy and potential new developments may help allay some of these concerns.

Another insightful finding was that participants acknowledged their add-on therapies were only a component of their disease management. They talked about the importance of holistic management and having access to the right clinical team and their other asthma medications in managing their disease, describing the add-on severe asthma therapy as providing additional support. This is consistent with current guidelines for the management of severe asthma.^{33,34} A systematic review using qualitative data⁷ highlighted the importance of autonomy from a patient's perspective in managing their symptoms, acquiring knowledge on treatment options and their relationship with health care providers. The findings of this study are complementary to those of Eassey et al⁷, with participants describing the importance of what they can do to manage their disease as well as the importance of the right health care team. Given the reported rates of poor treatment adherence in severe asthma³⁵ and the limited use of self-management strategies, such as written action plan,³⁶ the recognition from participants that a comprehensive programme of care is necessary is important and further understanding from patients with severe asthma, may improve these critical aspects of care.

This study provides important understandings of the patient experience of novel add-on therapies. Using rich qualitative data we have provided detailed experiences from a diverse range of participants to assist in understanding the real-world experiences of people with severe asthma with add-on therapies. Our data present a diverse range of experiences from $n=20$ participants, while this sample is small in quantitative research it is considered appropriate for qualitative designs. We also recognise some limitations. At the time of this study, there were only two mAb therapies available for prescription in Australia. Since this study was conducted an additional mAb therapy has become available, with several others available overseas. We, therefore, have been unable to capture the patient experience of all available mAbs. Further, as it was the aim of the study to understand the experience of patients who were treated with an add-on

therapy for their severe asthma we have not sampled to cater for subgroup analyses that may provide further novel information. Further research could focus on sampling to include subgroups of interest, such as different types of mAbs, duration of medication or age of prescription. A strength of this study was that there were a broad range of participants interviewed, who were at varying stages since treatment initiation.

Conclusion

This study provides insight into the patient's experience of add-on severe asthma therapies which has previously not been described, and cannot be gained from efficacy trials. Understanding these experiences will aid communication of the potential benefits and limitations of these add-on medications. Discussion points between clinicians and patients can include, what a patient can expect from their new treatment based on real-world experiences, whether the treatment will be able to reduce their oral corticosteroids, and the place of these therapies in the asthma management strategy. They can also guide discussion around alternative treatment in cases of reduced treatment efficacy or non-response. These data also highlight the importance of effectively capturing the patient experience.

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