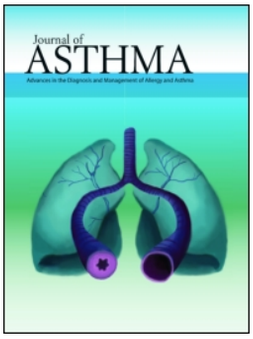

Journal of Asthma

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/ijas20

‘Like a fish on dry land’: an explorative qualitative study into severe asthma and the impact of biologicals on patients’ everyday life

M. B. de Graaff, S. A. Bendien & H. M. van de Bovenkamp

To cite this article: M. B. de Graaff, S. A. Bendien & H. M. van de Bovenkamp (2021): ‘Like a fish on dry land’: an explorative qualitative study into severe asthma and the impact of biologicals on patients’ everyday life, Journal of Asthma, DOI: 10.1080/02770903.2021.1888976

To link to this article: https://doi.org/10.1080/02770903.2021.1888976

© 2021 The Author(s). Published with license by Taylor & Francis Group, LLC.

Published online: 24 Feb 2021.

Submit your article to this journal

Article views: 283

View related articles

View Crossmark data

Full Terms & Conditions of access and use can be found at
https://www.tandfonline.com/action/journalInformation?journalCode=ijas20

JOURNAL OF ASTHMA
https://doi.org/10.1080/02770903.2021.1888976

Taylor & Francis
Taylor & Francis Group

OPEN ACCESS Check for updates

'Like a fish on dry land': an explorative qualitative study into severe asthma and the impact of biologicals on patients' everyday life

M. B. de Graaff, PhD[a], S. A. Bendien, MD[b] and H. M. van de Bovenkamp, PhD[a]

[a]Erasmus School of Health Policy & Management, Erasmus University Rotterdam, Rotterdam, the Netherlands; [b]Department of Pulmonology, Haga Teaching Hospital, The Hague, the Netherlands

ABSTRACT

Objective: In order to provide concrete context to research on biologicals for severe asthma we explore the everyday experiences of patients living with severe asthma and using biologicals.

Methods: We use a multi-method qualitative research-design including existing patient narratives, ten life-history interviews with patients using benralizumab ($N=8$), dupilumab ($N=1$), no biologicals ($N=1$), and with healthcare professionals ($N=2$) in the Netherlands. Our analysis focuses on patients' experiences with the burden of disease and the burden of treatment regarding severe asthma.

Results: Findings show how our respondents experience a high burden of disease (breathlessness, fatigue, exacerbations, loss of family, friends and employment) and treatment (oral corticosteroids' side-effects, dependency, life-style changes). Treatment with biologicals is relatively new for respondents. They mention to be cautious in their embrace of biologicals and in expressing hope for the future. Respondents who react to treatment with biologicals experience relief of both the burden of disease and treatment. They aim to regain their social life and societal participation, a contrast to those for whom biologicals prove ineffective. Biologicals' burden of treatment is experienced as low and minor side-effects are mentioned by three respondents. Respondents appear relatively unconcerned about the lack of knowledge concerning the long-term effects of biologicals.

Conclusions: Effective treatment with biologicals is generally experienced as a cautiously optimistic next step in a much longer and complex process of living with severe asthma. The practical lessons we draw point to managing patients' expectations and the need to pay attention to patients not eligible for treatment with biologicals.

ARTICLE HISTORY
Received 14 September 2020
Revised 14 January 2021
Accepted 8 February 2021

KEYWORDS
Severe asthma; biologicals; burden of disease; burden of treatment; patient experience; benralizumab; qualitative research (Quality of Life; Control/Management)

Introduction

Over the past 15 years, the diagnosis of 'severe asthma' has evolved. According to the current universally accepted definition, severe asthma is: 'asthma which requires treatment with a high dose of inhaled corticosteroids (ICS) plus a second controller (and/or systemic corticosteroids) to prevent it from becoming 'uncontrolled' or which remains 'uncontrolled' despite this therapy (1: p.344) (1). Only about 3–5% of the total asthma population suffers from severe asthma. This relatively small subgroup uses about 60% of the resources for treatment. This is mainly due to their high use of medication (2). Because of these differences, developing from medical and pathological differences, calls have emerged to distinguish severe asthma more explicitly from milder asthma (3).

From the early 2000s specific medicines for asthma called 'biologicals' have emerged (1). Biologicals are monoclonal antibodies that influence the immune system directly by blocking a specific messenger protein, interleukin, that is involved in inflammation processes (biologicals work on immunoglobulin E (IgE interleukin-4 receptor (IL4) (R), interleukin-5 (receptor) (IL5(R)) and interleukin-13 (IL13). Anti-IL-5 reduces eosinophilic inflammation in asthma by inhibition of eosinophil maturation and survival (2). Biologicals are add-on treatments such as omalizumab (Xolair®, 2003, IgE), mepolizumab (Nucala®, 2015), reslizumab (Cinquero®) (2016, IL-5), benralizumab (Fasenra®, 2017, IL-5R), and most recently dupilumab (Dupixent®, 2019, IL4R). Only about 50% of patients with severe asthma meet the criteria for treatment with these biologicals, as this depends on the type of inflammation and which

CONTACT M. B. de Graaff degraaff@eshpm.eur.nl Erasmus School of Health Policy & Management, Erasmus University Rotterdam, Rotterdam, the Netherlands.

© 2021 The Author(s). Published with license by Taylor & Francis Group, LLC.

This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives License (http://creativecommons.org/licenses/by-nc-nd/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited, and is not altered, transformed, or built upon in any way.

interleukins are involved. For patients with severe eosinophilic, T helper type 2 cells (Th2) driven, asthma the addition of biologicals to their treatment has proven to be effective in order to regain control over the disease, such as reducing asthma exacerbations (4). Clinical trials show biologicals having a 'relatively favorable safety profile' (5: p. 747, cf. 6,7). Novel approaches and therapies are needed for patients with severe non-eosinophilic asthma for whom currently available biologicals are not effective.

There is little research published that addresses patients' experiences of living with severe asthma, and to the best of our knowledge, no interpretive research has been executed that explores the use of biologicals for this group of patients (8). Such an exploration is highly relevant in order to provide the necessary lived context to existing technical pharma-economical and epidemiological research on the use of biologicals for severe asthma. In this paper we focus on patients' experiences with biologicals. However, we also pay attention to the experience of living with severe asthma in general at the same time as the experiences with this type of drugs will be connected to patients' experiences with the disease in daily life life and past experiences with treatments.

The literature on the impact of living with chronic conditions, such as asthma, in daily life focuses on the burdens caused by these conditions. Firstly, this literature identifies a burden of disease; the burden of symptoms that patients experience. Secondly, it identifies a burden of treatment; the experience of patients 'new and growing demands to organize and coordinate their own care, to comply with complex treatment and self-monitoring regimes, and to meet a whole range of expectations of personal motivation, expertise and self-care' (9: p0.2). The burden of treatment thus refers to the engagement of patients with their own (chronic) conditions that cannot be cured but rather must be managed.

From the few studies that have been done on experiences of patients we can distill that suffering from severe asthma shows high burdens of disease and treatment, although the experiences of patients are not conceptualized as such in these studies. Applying this conceptualization, we can conclude from these studies that burden of disease is high. Patients find themselves continually short of breath, fatigued, at risk of fearful exacerbations, unable to breathe, and in need of regular medication, while dealing with anxiety and depression (3,10). Besides physical distress, patients report living in fear, experience loss of contact with friends and family, and are unable to work. The latter also causes financial burdens (8,11). Burden of treatment for severe asthma is also high. It includes regular use of medication with (risks of) side-effects, especially oral corticosteroids (OCS), and large lifestyle changes such as weight management, exercise, smoking cessation, and avoiding triggers at work, home, and in everyday social life (8,12–14). The burden of treatment also involves health care utilization, such as repeated hospital visits and stays. Moreover, calls for patient empowerment and self-management can be found in literature on patients with severe asthma (15). As self-management shifts responsibilities to patients, it can further increase the burden of treatment.

This paper focuses on exploring the burden of disease and burden of treatment in patients with severe asthma and treated with biologicals. In doing so, we respond to the call for in-depth insight into the lived experience of severe asthma patients treated with biologicals (8) by reporting on a qualitative study from the Netherlands.

Methods

Our qualitative exploratory research involved two steps: an analysis of patient experience stories and an interview-study with a life-history approach.

Firstly, we analyzed existing Dutch written patient narratives. Eighteen books were selected from the collection of 5409 patient narratives at the library of the Erasmus University Rotterdam[1] using the theme 'asthma'. We excluded eleven books after a first reading of the material, selecting the seven books written by patients living with severe asthma (16–22). We identified two further publications through our interview study (23,24). None of the publications focused on the use of biologicals. However, they did provide us with the opportunity to gain in-depth insight into the experiences of living with the condition.

Secondly, building on the insights gained from the patient narratives, we interviewed patients ($n = 10$) and healthcare professionals ($n = 2$). The patient interviews were approached as "life-histories" in which we gave patients the opportunity to share their own experiences, in their native language (Dutch), without over-structuring the interview (25,26). The researcher used open-ended topics to elicit spontaneous discussion on patient experience in patient's own words. Topics were, except for biologicals, derived from the patient narratives and included: experiences in everyday life, finding a diagnosis, getting treatment. This approach enabled us in our aim to seek diversity in patients' own narratives on daily life with severe asthma and the impact of biologicals. The patient

interviews were supplemented with two interviews with specialized health care personnel (respiratory nurse, pulmonologist). These interviews helped us to contextualize the patient interviews.

For the interviews we purposefully selected patients using a specific biological, benralizumab[2] and included patients who are currently using benralizumab successfully and those that have (recently) stopped. In order to develop a broader understanding of the themes related to the therapeutic area as a whole, we also included patients who use(d) other biologicals and one patient who had no experience with biologicals and was diagnosed with allergic severe asthma. Details on respondents can be found in Table 1.

Respondents were selected from four nonacademic Dutch hospitals with tertiary severe asthma referral centers spread out across the Netherlands. AstraZeneca provided assistance for the selection of hospitals, however the researchers remained fully independent in their decision to adopt or reject the input. Physicians informed patients of the study and the primary researcher contacted them when they expressed the wish to participate. Interviews were, in all cases except for one (P008), executed in the homes of the respondents and lasted between 43 min (P009) and 86 min (P003) with an average of 56 min. Respondents P004 and P005 were interviewed together, and respondent P010 requested his wife to be present during the interview. All respondents consented to have their interview audio recorded, no incentives were offered for participation. Recordings were subsequently transcribed verbatim to enable detailed analysis.

The written patient narratives and interviews were analyzed abductively through iterative thematic reading of the material; moving back and forth between the data and the literature (27,28). The initial coding scheme (available upon request) thematically categorized how respondents give meaning to the burden of severe asthma on their lives, the burden of care and the impact of biologicals. Atlas.ti software was used to aid the analysis. The analysis was jointly done by the first and third author.

This study was given positive ethical advice (MEC-U, W19.113/NWMO 19.05.023), following the guidelines from the Dutch Clinical Research Foundation (DCRF) for non-interventional studies, and was performed in accordance with ethical principles that are consistent with the Declaration of Helsinki, ICH GCPs, GPP and the applicable legislation on Non-Interventional Studies and/or Observational Studies.

Results

In this section, we first discuss the burden of disease and the burden of treatment of living with severe asthma before we comment on the lived experiences with using biologicals. Table 2 provides an overview of the main findings.

Burden of disease: dealing with symptoms

Our empirical results on patients' experiences of the burden of disease align with the existing literature. An important part of this burden consists of having trouble breathing:

> '*… like a fish on dry land, yes, that's how I feel. Hoping for air, everything in my whole body tries to just catch this tiny little breath of air*' (19: p.206).[3]

Breathlessness and other symptoms like coughing can reach high severity and frequency. Patients refer to being identified by their symptoms:

> '*Also, in my work, they said: 'I do not know the name of that lady, but that is the lady who always coughs, So… yes, that's what they said of me. I am known as 'that lady who coughs so much*' (Respondent P009).

Severe asthma can be complicated by severe exacerbations which are difficult for the respondents to control. They are described as intense and fearful

Table 1. Overview of respondents.

Respondent	Gender	Year of birth	Education (Dutch level)	Biologicals (effect*)
P001	Woman	1965	Secondary vocational education (MBO)	benralizumab (responder)
P002	Woman	1972	Secondary vocational education (MBO)	omalizumab (non-responder), benralizumab (non-responder)
P003	Woman	1963	Secondary vocational education (MBO)	mepolizumab (non-responder), benralizumab (decreasing response)
P004	Man	1954	Higher professional education (HBO)	dupilumab (responder)
P005	Woman	1956	Higher professional education (HBO)	none (non- eosinophilic severe asthma)
P006	Woman	1968	PhD (Doctor)	benralizumab (responder)
P007	Man	1970	Higher professional education (HBO)	omalizumab (non-responder), benralizumab (responder)
P008	Woman	1968	Secondary vocational education (MBO)	benralizumab (responder)
P009	Woman	1952	Secondary vocational education (MBO)	benralizumab (responder)
P010	Man	1951	Primary education (Basisonderwijs)	benralizumab (responder)
A001	Pulmonologist			
A002	Pulmonary nurse-specialist			

*Effect as mentioned by the respondent during the interview.

Table 2. Overview of the main findings.

Themes	Findings
Burden of disease	Dealing with symptoms and their unpredictability, low-energy, large consequences for social life and societal participation, struggling with general incomprehension of society.
Burden of treatment	Long process of diagnosis, 'muddling through' care, high dependency on medication, focus on self-management.
Biologicals	Learning about this treatment option through specialist, low burden of treatment including limited worries on long-term effects and dependencies. Decreasing burden of disease by regaining lost social life and societal participation when effective. Burdens potentially increase when not effective.

experiences. Severe exacerbations and prolonged extreme breathlessness may require respondents to be hospitalized for weeks, sometimes leading to recurrent hospitalizations. Some respondents and authors have been hospitalized for more than 15 times. This is experienced as very frustrating, and the sheer frequency appears to influence care-seeking:

> *'I just want to be normal, just live … I refuse any admittance because I just don't want to let my health ruin another year, I want to stop worrying about my health!'* (19: p.67).

To 'just live' is difficult for respondents. At the time of the interview, some respondents still had regular paid employment (P004, P006, P007), or have continued working until retirement, but most were not able to do so. The impact on other aspects of social life can also be large. With symptoms being unpredictable and energy-levels low, respondents shared many examples concerning the importance of controlling triggers in order to avoid exacerbations. Avoiding asthma triggers has strong consequences for respondents' social life and societal participation. Many respondents share the same emotional experience, like losing friends and family because of having to deal with triggers affecting their symptoms, such as the use of perfume or smoking tobacco. Respondents mention that they struggle with people's incomprehension of the severity of their asthma and, as a consequence, do not disclose their illness easily. P007 is adamant in his determination with which he states not to be open about his disease, he does not want to appear sick and weak:

> *'People are though, the only one being hurt is me, because people say: '[P007] is the klutz of the neighborhood, we will ask someone else to help' […] so I just didn't say anything anymore, so I am involved and my life remained intact'* (P007).

Burden of treatment: the diagnosis and managing treatment

Whereas respondents seek ways to regain control and autonomy in their everyday lives, treatment for severe asthma is often insufficient. Respondents (except for P005 and P010) share an experience in exhibiting symptoms of asthma throughout their lives but have only recently been diagnosed with 'severe eosinophilic asthma'. They tell stories that generally consist of patients and healthcare professionals 'muddling through' symptoms and exacerbations with prednisone, anti-biotics, etcetera – for most of our respondents, culminating in receiving benralizumab. Biologicals can play a part in this diagnostic process for patients:

> *'I have always accepted that I had asthma, okay, and I am very happy that now, in fact, it has the stamp of this is it and nothing else. You can say that the syringe* [benralizumab] *is effective for me, but first, see if it really works for me* […] *after two injections I had something like, this oh yes this is it, finally'* (P001).

The realization of P001 is the final step in a long diagnostic process. Nonetheless, respondents appear to have a strong sense of trust in their current healthcare professionals. Regular checkups, controls and advice are deemed important – even though such tests are found to be strenuous themselves. Respondents who appear more able and willing to navigate their own healthcare also often appear critical of care professionals. Especially issues in the communication between specialists and patients can be experienced as increasing the burden of treatment, for instance, when specialists such as P007's ENT specialist and pulmonologist do not consult one another.

In the stories of patients, regular use of different kinds of medication is another prominent part of the burden of treatment. Respondents mention always needing to have a stock of medication readily available and share feelings regarding dependency. Some respondents have a rather ambivalent relationship to their medications and treatments, whereas others seem to be more straightforwardly at ease with it. Oral corticosteroids (OCS), prednisone, are mentioned more explicitly either as something that kept them going despite all odds or as medicine to be avoided – mainly because of the side effect of feeling bloated. Respondents also mention treatment with a strong focus on self-management techniques, for example, by practicing breathing and inhaler-techniques or creating an exacerbation plan with the nurse (A002). Respondents mention learning such self-management principles, linked to a more holistic perspective of a

patients' life, rather effectively in revalidation centers. This is also simultaneously experienced as a very intense step: removing oneself from existing routines in everyday life is an integral part of the treatment.

Respondents generally state to adhere to their prescribed treatment, while at the same time giving ample examples of moments in which they have taken matters into their own hands. This can consist of using complementary medicine, but it is also expressed as learning to feel your own body and predicting flares, to such an extent that respondents argue against the doctor if necessary:

> *'Yes, I had a fight with that new doctor who said: 'no, I am against prednisone'. Yes, I said you can be, but I have an agreement,* [with her regular GP] *I feel my own body. 'Well yes, I will give you antibiotics', the doctor said, and I said: 'You can do it but on the weekend, I'll call* [my GP] *immediately, so then I got* [prednisone] *anyway'* (P001).

This new doctor made the self-management effort of this respondent more difficult. This shows how patients can struggle to engage healthcare professionals in meaningful ways, and how such management is very much interaction between different actors. Interestingly, our interviews where the spouse of the patient was present as well (P004/P005 and P009) show how 'self' management is a shared rather than individual effort; P005 seems to follow his wife in her efforts, and P001 reasons with her family, and her daughters, all the time.

Living with biologicals: cautiously embracing the last straw

Our respondents talk about the use of biologicals in the context of their experiences regarding the burden of disease and treatment. They have generally just recently learned of the existence of biologicals, mostly through their specialist. Respondents with relevant education and experience (such as P006) do mention to have researched possible treatments on Google and Pubmed. Other patients also heard about this treatment option through the national patient organization for asthma (Longfonds) or the media, - such as reports on the 'magic drug' from Bennie Jolink [regional celebrity folksinger]. Most respondents appear hopeful but reasonably sober in their expectations about biologicals. Their emotions, hopes and expectations are also actively managed by healthcare professionals.

Most respondents have recently started using biologicals, sometimes in an experimental setting that requires quite some work from the respondents. However, respondents tend to be rather opaque about the actual use of biologicals; if it is about a shot, they must visit the hospital every now and then and extensive training is not required. This indicates a lower burden of treatment:

> *''The first time I got it I had to wait for two hours because you can get side effects and […] then you get the medicine a month later again, because it is every month, and then you just see your lung values going up. Once you see more lung capacity without having increased my medication, I think: 'hey, that's funny stuff. It works!'* (P007).

For some respondents, the monthly visits are also a comforting affair. It is nice to have tests and controls, and the meetings with the specialist or nurse can be encouraging. The relatively new concept for patients to inject themselves at home is accompanied by some worries about less frequent controls at the hospital. Hence, this next step in treatment, intended to alleviate the burden of treatment, might for some patients in fact increase it.

The respondents for whom benralizumab is working well are positive about the effects - it allows them to reboot their social life and societal participation. The main positive effect they mention is to be able to significantly reduce or stop the use of prednisone. According to respondents, that effect is usually achieved directly after the first injection. Interestingly, the common reaction is not elation when able to do something new, but instead, it is about regaining what has been lost. This experience is joyful to respondents, but also rather precarious; it is contextualized within their existing experiences of the burden of disease and treatment. Most respondents continue to need prednisone and inhalers and need to continue making lifestyle changes. In that sense, biologicals are really an 'add-on' treatment, an extra but important 'last straw' to be grasped with both hands (wife of P010). However, successful treatment with biologicals is not the case for all respondents. Respondent P002, for instance, mentions her frustration that the biologicals do not really seem to affect her:

> *'Inhalers and the other medication did not do much anymore, so then we searched for another possibility.* [omalizumab] *came into the picture, so for five years I had that, but I was admitted to the hospital quite a few times* […] *And that was also the only biological so far because I have had five or six, which I think helped me* […] *but good, in November I will start a new one'* (P002).

P002 has been taking biologicals since becoming available, generally to no avail. Still, she does pin her hopes on the next and new biological (dupilumab).

Perhaps because of this 'last straw' approach to the biologicals, only three respondents talk explicitly about side effects of biologicals such as heavy sweating (P008). Almost all respondents are aware of the lack of scientific understanding of the long-term effects of the use of biologicals. They do not seem to worry too much about them despite the potential life-long dependency, only the possibility that it negatively affects the immune system is mentioned. Instead, their focus is on the present: respondents mention for instance that they are simply happy to be able to go on a holiday (P003).

Discussion

Little is written about the way patients with severe asthma experience the burden of disease and treatment, and even less is known about how these patients consider treatment with biologicals (8). Our findings show that patients with severe asthma experience a high burden of disease. This burden moves beyond the boundaries of the experience regarding the symptoms (shortness of breath, coughing, fatigue, etc.) to difficulties with (intimate) social interaction and societal participation (13–15), and includes living with incomprehension and in fear (8,29). The burden of treatment appears similarly high and to consist of the regular use of, and dependency on, medication with risks of side-effects combined with large lifestyle changes. Dependency on, and side effects of, OCS dominate how respondents discuss their treatment (6,12,13). Treatment burden also includes many interactions with healthcare professionals and repeated (emergency) visits to hospitals and revalidation centers. Generally, our respondents show high trust in the professionals currently treating them and we have found relatively few moments of tension between lay and expert knowledge that might compound frustration and uncertainties – although comprehensive information is not accessible to all severe asthma patients (30–32). A good relationship with professionals, partners and friends can alleviate burden of treatment. In cases where such relationships are harder to find respondents feel they have to take matters in their own hands. This potentially heightens the burden of disease.

Severe asthma patients' self-management is generally dominated by ideas of adherence and control derived from evidence-based clinical guidelines (33–35). However, based on our results, we support the call to reconsider the nature of self-management, the asthma action plans that are meant to support it and to thoroughly value the patient's daily life experience. Intentions and initiatives from doctors and health care institutions, concerning shared decision-making, self-management, home treatment and monitoring by E-Health, may thus not always be in line with the patient's needs or wishes. This is especially important because the main impetus for patient self-management is to enhance autonomy in everyday life and gain control over their disease (15).

Biologicals are meant to serve as add-on medication and if they are effective, appear to significantly lighten the burden of treatment (8,13). We indeed find that, when effective, the positive impact on both the burden of disease and treatment can be high. However, most of our respondents appear cautious in their embrace of biologicals and in expressing hope for the future. This may be related to their turbulent patient journeys. Respondents' tentative position to biologicals appears to be justified considering that for some respondents, biologicals do not seem to be effective or the effects diminish over time. These patients resume an everyday life dominated by severe asthma. To return to such a situation might even increase the experienced burden of disease and treatment. This group of patients continues to be rather invisible to the broader public and to be at risk of social isolation. The efficacy of biologicals potentially further obscures this group as clinical attention is drawn to the success of these new treatment options. It seems important to ensure that a concrete focus on improving the burden of disease and treatment in the everyday lives of all patients, including patients with non-Th2 inflammation, suffering from severe asthma is maintained.

Limitations and future research

In this research we conducted an exploratory qualitative study with a small sample size. Such a design proves effective for exploring commonalities in patient's experience and narratives, but is limited in for instance, comparisons between different sub-groups of patients suffering from severe asthma. Future research should consider to detail differences between experiences of patients of different educational backgrounds or between responders and non-responders to biologicals as we could only provide indications of variation. Also, most of our respondents are using benralizumab and exhibit a positive response to treatment, our results may be biased on these issues and future research could consider more variation in terms of biologicals used and in terms of responders and non-responders. Other interesting comparisons would be to compare the perceptions of (the burden of) treatment between patients and healthcare

Table 3. Main takeaway message for healthcare practice.

Themes	Findings
Burden of disease and treatment	Provide timely, accurate diagnosis and supportive communication; include patient's perspective on everyday life in care provision and in self-management support strategies.
Biologicals	Help to manage patients' expectations; give attention to severe asthma patients not eligible for treatment with biologicals

professionals. This might bring to light more concrete information on how to further improve self-management and communication. Comparing the experiences of patients across healthcare systems would also be interesting. For example, our respondents did not mention the relative high costs of biologicals (5), which could be an effect of the Dutch healthcare system in which biologicals are insured without out-of-pocket costs for eligible patients. Another limitation of this study is that, although we have strived to discuss patients' experiences over time through our life-history interviews, we only collected data on one point in time. For future research it is important to gauge if and how patients' experiences of biologicals develop over time using a repeated longitudinal design.

Conclusions

Severe asthma poses a significant burden of disease and treatment on patients, families and healthcare systems. By performing this study, important lessons have been learned based on everyday experiences of patients living with severe asthma and receiving treatment with biologicals. These lessons can have implications for daily healthcare practice, see Table 3.

Lessons reported in this study include the importance of timely and accurate diagnosis of (severe) asthma, the availability of supportive communication with health care providers, the relevance of patients' perspective on everyday life with self-management strategies, and attention to the invisibility of severe asthma patients not eligible for treatment with biologicals. Most importantly, severe asthma generally still seems to be a rather 'invisible disease', and more attention could be paid to the burden of disease and treatment experienced by patients. It is important for clinicians, scientists, politicians and healthcare insurance companies to join forces to help all severe asthma patients deal with this 'hidden burden' of severe asthma.

Notes

1. See: https://www.eur.nl/library/collecties/collectie-patientervaringen
2. Benralizumab is administered using a syringe, once every 8 weeks, with a loading dose in week 4, about 8-6x times a year – a much smaller frequency than the daily medication patients with severe asthma are accustomed to. Tests by, amongst others, the pharmaceutical company show it to be a rather successful add-on treatment; 74% of patients report no exacerbations of severe asthma in their second year of taking it. Overall, biologicals' greatest clinical benefit lies in reducing severe asthma exacerbations, with modest effects on day-to-day symptoms and quality of life (1), thus diminishing the need for the use of oral corticosteroids, and prednisone, of which side-effects are relatively strong both physically (osteoporosis, cataract, blood pressure drops) and mentally (anxiety, irritability, depression).
3. All quotes are translated from Dutch by the first author and edited for readability.

Acknowledgements

We are thankful to the respondents for participating in this study and sharing their experiences with us and for the authors of the ego-documents for writing down their experiences. We thank Coleta Platenkamp for her help in the selection process of the patient narratives. We would also like to acknowledge the support of the physicians who aided us in recruiting our respondents and to thank Sean O'Quinn, Wendy Beekman-Hendriks, Michiel Ferns and Andrea Sellink for their comments on earlier versions of our findings. Bryan Bong provided language editing.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

Funding

This study is financially supported by AstraZeneca BV, The Hague (D3250R00063, 22–05-2019). This study has been executed by researchers from Erasmus School of Health Policy & Management through an addendum to the existing agreement between the institute of Medical Technology Assessment (iMTA) and AstraZeneca. The agreement and addendum ensure, amongst others, the independence of the researchers in the design, execution and reporting of the results of this study. AstraZeneca provided assistance for the selection of participating hospitals and gave input on the manuscript, however the researchers remained fully independent in their decision to adopt or reject the input.

ORCID

M. B. de Graaff http://orcid.org/0000-0001-9840-8626
S. A. Bendien http://orcid.org/0000-0003-2069-9181
H. M. van de Bovenkamp http://orcid.org/0000-0002-6412-2707

References

1. Chung KF, Wenzel SE, Brozek JL, Bush A, Castro M, Sterk PJ, Adcock IM, Bateman ED, Bel EH, Bleecker ER, 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.
2. Muhrer JC. Update on diagnosis and management of severe asthma. J Nurse Practitioners. 2018;14(7):520–525. doi:10.1016/j.nurpra.2018.04.003.
3. Wenzel SE, Brillhart S, Nowack K. An invisible disease: severe asthma is more than just "bad asthma. Eur Respir J. 2017;50(3):1701109. doi:10.1183/13993003.01109-2017.
4. Busse WW. Biological treatments for severe asthma: where do we stand?Curr Opin Allergy Clin Immunol. 2018;18(6):509–518. doi:10.1097/ACI.0000000000000487.
5. Patel SS, Casale TB, Cardet JC. Biological therapies for eosinophilic asthma. Expert Opin Biol Ther. 2018;18(7):747–754. doi:10.1080/14712598.2018.1492540.
6. Bleecker ER, FitzGerald JM, Chanez P, Papi A, Weinstein SF, Barker P, Sproule S, Gilmartin G, Aurivillius M, Werkström V, et al. Efficacy and safety of benralizumab for patients with severe asthma uncontrolled with high-dosage inhaled corticosteroids and long-acting β2-agonists (SIROCCO): a randomised, multicentre, placebo-controlled phase 3 trial. Lancet. 2016;388(10056):2115–2127. doi:10.1016/S0140-6736(16)31324-1.
7. Finn A, Gross G, van Bavel J, Lee T, Windom H, Everhard F, Fowler-Taylor A, Liu J, Gupta N. Omalizumab improves asthma-related quality of life in patients with severe allergic asthma. J Allergy Clin Immunol. 2003;111 (2):278–284. doi:10.1067/mai.2003.54.
8. Eassey D, Reddel HK, Foster JM, Kirkpatrick S, Locock L, Ryan K, Smith L . "…I've said I wish I was dead, you'd be better off without me": a systematic review of people's experiences of living with severe asthma". J Asthma. 2019;56(3):311–322. doi:10.1080/02770903.2018.1452034.
9. May CR, Eton DT, Boehmer K, Gallacher K, Hunt K, MacDonald S, Mair FS, May CM, Montori VM, Richardson A, et al. Rethinking the patient: using Burden of Treatment Theory to understand the changing dynamics of illness. BMC Health Serv Res. 2014;14:281–292. doi:10.1186/1472-6963-14-281.
10. Porsbjerg C, Menzies-Gow A. Co-morbidities in severe asthma: clinical impact and management. Respirology. 2017;22(4):651–661. doi:10.1111/resp.13026.
11. Franco R, Nascimento HF, Cruz AA, Santos AC, Souza-Machado C, Ponte EV, Souza-Machado A, Rodrigues LC, Barreto ML. The economic impact of severe asthma to low-income families. Allergy. 2009;64(3):478–483. doi:10.1111/j.1398-9995.2009.01981.x.
12. Hyland ME, Whalley B, Jones RC, Masoli M. A qualitative study of the impact of severe asthma and its treatment showing that treatment burden is neglected in existing asthma assessment scales. Qual Life Res. 2015;24(3):631–639. doi:10.1007/s11136-014-0801-x.
13. 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.
14. Apps LD, Chantrell S, Majd S, Eglinton E, Singh SJ, Murphy AC, Bradding P, Green RH, Hudson N, Evans RA, et al. Patient perceptions of living with severe asthma: challenges to effective management. J Allergy Clin Immunol Pract. 2019;7(8):2613–2621.e1. doi:10.1016/j.jaip.2019.04.026.
15. Eassey D, Reddel HK, Ryan K, Smith L. The impact of severe asthma on patients' autonomy: a qualitative study. Health Expect. 2019;22(3):528–536. doi:10.1111/hex.12879.
16. Kuipers H. Ademtocht - Losgelaten in een wereld zonder lucht. Hoogwoud: Uitgeverij Kirjaboek; 2013.
17. Nikolaus H. Astma - Een patiëntenboek. Haarlem: De Toorts; 1994.
18. Parry G. Ik en mijn dokters (Mon asthme et mes médecins' editions des Seuil). Utrecht (Paris): Het Spectrum; 1959.
19. Talsma A. Leven(s)lang!' Ademen door een rietje en eten uit een slang. Barneveld: Uitgeverij Boekenbent; 2015.
20. Thomas M. Ademloos verlangen……' Dagboek van een achttienjarige met ernstig astma. Badhoevedorp: Kaft Media; 2013.
21. Veelen-van de Reep A. Astma: Karma en Uitdaging. Posterholt: Centrum Rosa Alba; 2004.
22. Vissers M. Kleine Koning en de Wonderpil. Noord-Scharwoude: Uitgeverij Kirjaboek; 2006.
23. Vereniging Nederland-Davos. *Davoser Witboek*. Online at: https://nederland-davos.nl/witboek-magazine/. ; 2018.
24. Vereniging Nederland-Davos. *Gezichten achter ernstig astma*. Vereniging Nederland-Davos & Sanofi Genzyme; 2019.
25. Linde C. Life stories: the creation of coherence. Oxford: Oxford University Press; 1993.
26. Goldman R, Hunt MK, Allen JD, Hauser S, Emmons K, Maeda M, Sorensen G. The life history interview method: applications to intervention development. Health Educ Behav. 2003;30(5):564–581. doi:10.1177/1090198103254393.
27. Charmaz K. Constructing grounded theory – a practical guide through qualitative analysis. London: Sage; 2006.
28. Tavory I, Timmermans S. Abductive analysis – theorizing qualitative research. University of Chicago Press; 2014.
29. Yonas MA, Marsland AL, Emeremni CA, Moore CG, Holguin F, Wenzel S. Depressive symptomatology, quality of life and disease control among individuals with well-characterized severe asthma. J Asthma. 2013;50(8):884–890. doi:10.3109/02770903.2013.810750.

30. Haw J, Cunningham S, O'Doherty KC. Epistemic tensions between people living with asthma and healthcare professionals in clinical encounters. Soc Sci Med. 2018;208:34–40. doi:10.1016/j.socscimed.2018.04.054.
31. Apter AJ, Wan F, Reisine S, Bender B, Rand C, Bogen DK, Bennett IM, Bryant-Stephens T, Roy J, Gonzalez R, et al. The association of health literacy with adherence and outcomes in moderate-severe asthma. J Allergy Clin Immunol. 2013;132(2):321–327. doi:10.1016/j.jaci.2013.02.014.
32. Ross CJM, Williams BA, Low G, Vethanayagam D. Perceptions about self-management among people with severe asthma. J Asthma. 2010;47(3):330–336. doi:10.3109/02770901003611462.
33. Menzies-Gow A, Canonica G-W, Winders TA, Correia de Sousa J, Upham JW, Fink-Wagner A-H. A charter to improve patient care in severe asthma. Adv Ther. 2018;35(10):1485–1496. doi:10.1007/s12325-018-0777-y.
34. Katsaounou P, Odemyr M, Spranger O, Hyland ME, Kroegel C, Conde LG, Gore R, Menzella F, Domingo Ribas C, Morais-Almeida M, et al. Still fighting for breath: a patient survey of the challenges and impact of severe asthma. ERJ Open Res. 2018;4(4):00076-2018–2018. doi:10.1183/23120541.00076-2018.
35. Bidad N, Barnes N, Griffiths C, Horne R. Understanding patients' perceptions of asthma control: a qualitative study. Eur Respir J. 2018;51(6):1701346. doi:10.1183/13993003.01346-2017.