



## Early View

Original article

# **“What matters to people with severe asthma? Exploring add-on asthma medication and outcomes of importance”**

Vanessa L. Clark, Peter G. Gibson, Vanessa M. McDonald

Please cite this article as: Clark VL, Gibson PG, McDonald VM. “What matters to people with severe asthma? Exploring add-on asthma medication and outcomes of importance”. *ERJ Open Res* 2020; in press (<https://doi.org/10.1183/23120541.00497-2020>).

This manuscript has recently been accepted for publication in the *ERJ Open Research*. It is published here in its accepted form prior to copyediting and typesetting by our production team. After these production processes are complete and the authors have approved the resulting proofs, the article will move to the latest issue of the ERJOR online.

Copyright ©ERS 2020. This article is open access and distributed under the terms of the Creative Commons Attribution Non-Commercial Licence 4.0.

**Title:** *“What matters to people with severe asthma? Exploring add-on asthma medication and outcomes of importance”*

Dr. Vanessa L Clark, Ph.D.

National Health and Medical Research Council Centre for Research Excellence in Severe Asthma and The Priority Research Centre for Healthy Lungs. The University of Newcastle, NSW, Australia; School of Nursing and Midwifery, The University of Newcastle, NSW, Australia

Professor Peter G Gibson, D.Med.

National Health and Medical Research Council Centre for Research Excellence in Severe Asthma and The Priority Research Centre for Healthy Lungs. The University of Newcastle, NSW, Australia; Department of Respiratory and Sleep Medicine, John Hunter Hospital, Hunter Medical Research Institute, NSW, Australia

Professor. Vanessa M McDonald, Ph.D.

National Health and Medical Research Council Centre for Research Excellence in Severe Asthma and The Priority Research Centre for Healthy Lungs. The University of Newcastle, NSW, Australia; School of Nursing and Midwifery, The University of Newcastle, NSW, Australia; Department of Respiratory and Sleep Medicine, John Hunter Hospital, Hunter Medical Research Institute, NSW, Australia

**Funding Source:** Centre of Research Excellence in Severe Asthma

**Word count:** 3000

**Corresponding Author:** Professor Vanessa McDonald

[Vanessa.McDonald@newcastle.edu.au](mailto:Vanessa.McDonald@newcastle.edu.au)

**Take Home Message:** Improving quality-of-life is an important treatment outcome. Shared decision-making discussions between clinicians and patients that centre around efficacy and side-effect profile incorporates patient preferences for add-on therapy in severe asthma.

## **ABSTRACT:**

**Introduction:** There is an increasing number of new therapies for severe asthma, however what outcomes people with severe asthma would like improved and what aspects they prioritise in new medications remain unknown. This study aimed to understand what outcomes are important to patients when prescribed new treatments and to determine the characteristics of importance to patients in their choice of asthma treatments.

**Methods:** Participants with severe asthma (n=50) completed a cross-sectional survey that ranked 17 potential hypothetical outcomes of treatment using a seven point Likert scale, as well as selecting their top five overall outcomes. Participants also completed hypothetical scenarios trading off medication characteristics for four hypothetical add-on asthma treatments.

**Results:** Participants (58% male), had a mean (SD) age of 62.2 (13.5) years. Their top three prioritised outcomes were: to improve overall quality-of-life (selected by 83% of people), reduce number and severity of asthma attacks (72.3%), and being able to participate in physical activity (59.6%) When trading off medication characteristics the majority of patients with severe asthma chose the hypothetical medication with the best treatment efficacy (68%). However, a subgroup of patients prioritised the medications side effect profile and mode of delivery to select their preferred medication.

**Conclusion:** People with severe asthma value improved quality-of-life as an important outcome of treatment. Shared decision-making discussions between clinicians and patients that centre around medication efficacy and side effect profile can incorporate patient preferences for add-on therapy in severe asthma.

**Keywords:** Severe Asthma; asthma medications; monoclonal antibody therapies

## **Abbreviations:**

mAb – monoclonal antibody

ACQ- Asthma control questionnaire

HRQoL – Health related quality-of-life

OCS- Oral corticosteroids

**Introduction:**

Severe asthma is a complex chronic disease, with a burdensome symptom profile and is associated with frequent asthma attacks, increased healthcare use, significant comorbidity and an increased mortality risk [1-4]. Recent advances have resulted in an increasing number of efficacious add-on treatment options for people with severe asthma [5-10]. Accordingly, patients and health professionals now have increased options for treatments, which also requires them to choose between different therapeutic options. Whilst these treatment decisions should be guided by the health care professional in terms of appropriate asthma phenotyping and predictors of response, there may be times where one individual might respond to a number of different treatments; therefore understanding the patient's perspective may lead to rational prescribing that considers the holistic needs of patients.

The treatments currently available for asthma differ in the outcomes they target which is likely to be an important factor in drug choice. Clinical trials have focused on outcomes that have been recommended by regulatory bodies, such as lung function, oral corticosteroid (OCS) use, asthma control and asthma exacerbations [6-8]. Whilst these outcomes have been identified as important from a clinician's perspective [11], the outcomes of most importance to patients with severe asthma remain unknown. Prior research examining symptom control in asthma identified cough and breathlessness as key symptoms which people with asthma wish to prioritise [12], however other outcomes that may be important to people with severe asthma remain unexplored.

Understanding what aspects of treatment patients consider a priority is important in guiding shared decision-making between patient and clinician discussions [13,14]. Gelhorn et al. evaluated treatment preferences for mAb therapies in severe asthma and illustrated that clinicians and patient preferences align in regards to favouring less frequent dosing and faster time to treatment efficacy [15]. However, preferences in terms of the impact of side-effect profiles, or treatment efficacy have not been examined, nor has the relative priority of

different medication attributes. Therefore, we aimed to understand what outcomes patients would like their add-on asthma treatments to improve, and to determine whether patients have an overall preference for different medication attributes when asthma treatment efficacy, side-effect profile and mode of administration each are hypothetically traded off against each other. We hypothesised that patients would prioritise quality-of-life as their most important outcome and prefer the medication that provided the greatest efficacy.

## **Materials and Methods**

### **Study Design**

After obtaining ethical approval (Hunter New England Human Research Ethics:16/05/8/5.02) and written informed consent, participants with severe asthma were recruited to a cross-sectional survey.

### **Setting**

Recruitment occurred from the research database and clinics of the Department of Sleep and Respiratory Medicine (May 2018-March 2019) at a tertiary referral hospital in Australia.

### **Inclusion**

Adult ( $\geq 18$  years) participants ( $n=50$ ), with a prior confirmed doctor diagnosis of severe persistent asthma were recruited. Severe asthma was defined based on the American Thoracic Society/ European Respiratory Society taskforce [16] as being on high-dose treatment with inhaled corticosteroid and long-acting  $\beta_2$ -agonist, or required mAb therapy for severe asthma.

### **Assessments**

Demographic characteristics, self-reported disease related characteristics and a paper-based survey (see supplement) about medication and outcome preferences were collected during a face-to-face assessment with a researcher (VLC).

## **Questionnaire**

### **Survey Design**

The design of the survey was informed by the study aims and a review of the severe asthma patient experience literature [17-19]. As no suitable instrument existed, the survey was developed by the research team (PGG and VM McD- expert severe asthma multidisciplinary clinicians and VLC –behavioural scientist). The survey had two components: The first assessed “outcomes of importance” using 17 statements related to outcomes that people with severe asthma would like treated as part of their severe asthma management (Figure 1). The statements were derived from the literature regarding living with severe asthma [17-19]. The second component was based on “treatment aspect preferences”, which included the presentation of hypothetical scenarios in which the participant was asked to consider multiple attributes within the scenario, and decide which medication best met their needs. The scenarios were designed based on the best-worst scaling survey method [20] considering the Likelihood of Action component of the Health Belief Model [21,22]. This model is based on understanding balance of the perceived benefit of preventative action (benefit to asthma symptoms) weighted against the perceived barriers (potential side-effects, burden or receiving the treatment). The scenarios addressed the aspects of a medication that been identified in the literature as important in decision making in regards to treatment [23-25].

#### **Component 1: Outcomes of importance to patients**

##### *Individual outcomes of importance*

Participants ranked 17 statements (Figure 1) related to severe asthma outcomes (examples, reductions in acute attacks or OCS use) on a seven-point Likert scale (0-not important to me to 6-very important to me).

##### *Overall outcomes of importance*

After participants rated the 17 outcomes, they nominated the five outcomes that were most important to them, with one being most important. Participants were also asked a free text question asking if there were any additional outcomes they would like addressed.

## **Component 2: Treatment aspect preferences**

### *Considerations for making a medication choice*

Participants answered an open-ended question “are there any other factors of which you think are important to consider when choosing between two or more medications?”

### *Ranking the aspects of treatment*

Participants ranked in order of one to four (one being the most important), what treatment aspects they thought were the most important to them in terms of their asthma management (e.g. asthma treatment efficacy, logistics (how your medication is administered), side-effect or the personal cost of your medication).

### *Hypothetical scenarios*

Participants ranked four different medications in order of most preferred to least preferred in four separate scenarios. In the first scenario “asthma treatment efficacy” participants were presented with a series of statements related to their asthma management (table 1), e.g., ‘if I have this treatment I am likely to have fewer bad attacks’. Each statement was given an expected impact for each medication, e.g. for Medication A ‘On average, my bad asthma attacks would reduce by just over one third’; for Medication B ‘On average, my bad asthma attacks would reduce by about half’ (see Figure 4A for all medication properties). The four hypothetical medications were modelled on treatment effects observed in the large scale randomised controlled trials for severe asthma add-on therapies currently available in Australia (omalizumab, mepolizumab, benralizumab and azithromycin). The medications were displayed to the participants as medication A, B, C and D. They included three injectable medications (omalizumab =A, mepolizumab =B, benralizumab =C), and one oral



tablet (azithromycin =D). Participants were asked to consider all the statements and medication properties within each scenario and select the medication that best met their preferences, that is, their most preferred treatment choice. After each scenario participants were also asked a free-text question “Why did you choose this medication?”

This process was repeated for the second scenario “logistics” (how the medication is received, how frequently) and third scenario “side-effects profile”. In the fourth scenario these three aspects of treatment (“asthma treatment efficacy”, “logistics” and “side-effects”) were combined and participants were asked to consider all aspects of treatment collectively. This enabled the participant to weigh the benefits of the four hypothetical medications compared to each other, trading off the benefits of treatment against the perceived barriers.

## **Analysis**

Data were analysed using IBM SPSS statistics v25. Free-text responses were analysed using content analysis. Subgroups were compared using analysis of variance, significance levels were set at  $p < 0.05$ . Dichotomous subgroups compared age ( $\geq 65$  and above versus  $\leq 64$ ), gender (male versus female), asthma control (controlled, ACQ  $< 1.5$  versus poor control, ACQ  $\geq 1.5$ ), asthma attack prone ( $> 2$  asthma attacks in the past year versus  $\leq 2$  asthma attacks in the past year), prescription of mAb therapy (prescribed versus not prescribed), duration of mAb therapy ( $\geq 6$  months versus  $< 6$  months), maintenance prednisone prescription (prescribed versus not prescribed). Preference data were reported using proportions. There was sufficient power to detect group differences of a large effect size ( $d = 0.8$ ), at 80% power, for a two-tailed significance test with  $p < 0.05$ .

## **Results**

Demographic details are displayed in Table 2. Participants were predominately male, had poorly controlled asthma, with 92% ( $n=46$ ) of respondents reporting at least one asthma attack in the past year, 38% of the sample were prescribed maintenance (daily) oral

corticosteroids and 88% of participants had been prescribed at least one course of oral corticosteroids for greater than three days within the past year (Table 2).

### **Component 1: Outcomes of importance to patients**

#### *Individual outcomes of importance*

The outcome “I want to improve my overall quality-of-life” was the highest rated (Figure 1), with most participants (86%, n=43) scoring this at the highest possible score, followed by “...reduce the number and severity of attacks”, and “...take less oral steroids”. The outcomes “I want to be less breathlessness” and “...be able to do more physical activity” (Figure 1) were also rated highly.

#### *Overall outcomes of importance*

Figure 2 shows the proportion of people who nominated each outcome anywhere in their top five responses. Improving overall quality-of-life was the most frequently selected outcome, with 83% of participants choosing it in their top five. Reducing the number and severity of attacks was also an important priority among patients’ top five responses (72.3%) (Figure 2). Being able to participate in physical activity was considered the third most important outcome (Figure 2), followed by a reduction in oral corticosteroids. Reducing OCS was a concern for patients who were taking them on a daily basis, but this group only made up 44.4% of participants who selected this outcome as a priority, the remainder 56.4% of people were only taking OCS as needed. In the free text responses, 32% of participants reiterated that they would like an improvement in quality of life, 16% reiterated that they wanted a reduction in oral corticosteroids. Additionally, 14% of people wanted to be able to participate in physical activity, and 12% mentioned they wanted stable asthma and less wheeze.

#### *Subgroup comparison of individual outcomes of importance*

Subgroup analyses assessed whether the outcomes of importance differed by age, gender, prescription or duration of mAb therapy, prescription of maintenance OCS, asthma control or history of frequent asthma attacks.

Outcomes of importance scores did not differ by age ( $\geq 65$  years (52%) compared to  $< 65$  years). Females however, rated wanting to improve their overall quality-of-life higher, uniformly rating this item at the highest score (6, SD), compared to males (mean=5.70, SD=0.60),  $p=0.03$ . Additionally, females rated wanting to improve their workplace attendance and productivity higher than males, mean (SD) 5.30 (1.56) versus 3.57 (2.71),  $p=0.01$ , respectively. Wanting to be more social was also rated more important to females than males, mean (SD) 4.90 (1.21) versus 3.90 (1.90) respectively,  $p=0.04$ , as was wanting to be less tired mean (SD) 5.70 (0.57) versus 4.70 (4.60),  $p=0.01$ .

Wanting to be less breathless, was rated as more important in those who had inadequate asthma control (ACQ  $\geq 1.5$ ;  $n=31$ , 62%), with a mean rating of 5.84, (0.45) compared to those with adequate control 5.32 (1.29),  $p=0.04$ .

Asthma attack prone participants ( $>2$  exacerbations in the past year;  $n=31$ , 62%), significantly rated improved quality-of-life higher, mean (SD) 5.97 (0.18) than those without frequent attacks 5.58 (0.69),  $p=0.004$ , although this was ranked highly in both groups. There was also significantly higher rating of "I want to improve my workplace productivity and attendance" in those who were prone to asthma attacks, mean (SD) 5.00 (1.97) compared to those who were not 3.05 (2.74),  $p=0.01$ , although the majority were not currently employed.

There were no significant differences in outcome ratings for the subgroup analyses for participants prescribed a mAb therapy to those that were not; the duration of mAb therapy prescription; and those who were on maintenance OCS (daily) compared to those who were not.

## **Component 2: Treatment aspect preferences**

*Considerations for making a medication choice*

The self-reported aspects of treatment that patients considered important when choosing between medications are shown in Figure 3. Overwhelmingly, the medication's side-effect profile was considered the main driver of choice, followed by the medication's beneficial effects on symptoms (Figure 3). Logistics (such as how you receive the medication, and how frequently) followed by doctors' advice were the next highest-rated considerations (Figure 3).

#### *Ranking the aspects of treatment*

When asked to rank the most important aspects of treatment, the majority of respondents (92%) stated it was related to asthma characteristics, e.g., "how the medication improves their asthma" (improvement in symptoms, reduction in OCS, improvement in asthma-related quality-of-life). Side-effect profile was the second most preferred characteristic (64% of respondents). Logistics, how the medication is administered (tablet, injection), was considered third most important by 56% of respondents, and cost (presented as cost to the patient) was the least important by 58% of respondents.

#### *Hypothetical scenarios*

The main properties of each hypothetical medication are shown in Figure 4A. When asked to choose a medication based on "asthma treatment efficacy", the most preferred treatment was medication C (based on benralizumab; 94%; Figure 4B). The second scenario, assessing logistic related characteristics, medication D (based on azithromycin; a tablet), was the most preferred treatment chosen by 82%; Figure 4B. Medication D was also most preferred in terms of side-effects profile (n=56%; Figure 4B).

When asked to consider asthma treatment efficacy, logistics and side-effect profile collectively in the fourth scenario, the majority (68%) selected medication C as their most preferred treatment (based on benralizumab), with 26% choosing medication D (based on azithromycin; Figure 4B). Participants provided a reason as to why they chose a particular medication. Of those that selected medication C (based on benralizumab; n=34), the major choice drivers were the effect on asthma attacks "number or severity of asthma attacks"

(41.2%), followed by the greatest reduction OCS use (35.3%), overall quality-of-life improvement (32.4%) the best side-effect profile (29.4%). Of the people who chose medication D (based on azithromycin; n=13), the majority (76.9%) selected this option because it was a tablet, 30.8% felt it provided the best balance in terms of asthma treatment efficacy, logistic characteristics and side-effects, and just over half of the participants felt it had the best side-effect profile (53.8%).

## **Discussion**

We report the results of a survey examining patient preferences relating to add-on asthma medications; providing new knowledge to assist with person-centred severe asthma care. People with severe asthma rated all the outcomes shown as important, however the highest ranked treatment priorities were improvement in quality-of-life, reducing the number and severity of asthma attacks, increasing physically activity, OCS reduction and being less breathless. Using hypothetical scenarios we assessed 'trade-offs' made by patients in the decision-making providing an improved understanding of the outcomes and aspects of treatment that are important to patients with severe asthma, including medication efficacy versus side-effects. These data will inform the delivery of shared-decision making among patients and clinicians.

Quality-of-life was considered the most important outcome that people wanted to improve. Impairments in quality-of-life have been consistently illustrated among people with severe asthma, and has largely remained unchanged over the past decade [17,18,26,27]. The majority of patients in this study were already prescribed a mAb therapy, nonetheless, this did not reduce their endorsement of wanting better quality-of-life or fewer attacks, indicating that while these medications are known to improve these asthma outcomes, patients still see room for further improvement.

The experience of asthma attacks and OCS use are known to contribute significantly to the burden experienced by people with severe asthma [18,28]. Clinical trials of azithromycin and

mAb therapies [8,29,30] have demonstrated efficacy in reducing asthma attacks, however both attacks and OCS continue to play a central role in uncontrolled severe asthma [31]. This study demonstrates that even with the introduction of add-on medications for severe asthma, there remains a residual burden with patients wanting to reduce asthma attacks and OCS use as a priority, regardless of whether they are taking OCS on daily basis or as needed.

#### *Medication characteristic preferences*

Shared decision-making between patients and clinicians leads to improvements in chronic disease management and increases the likelihood of treatment adherence [14]. As more severe asthma treatment options become available, understanding what characteristics patients consider a priority in terms of treatment outcomes is increasingly important and may assist clinician's decision-making. However, knowing how to convey relevant information about the benefits, disadvantages and points of difference of these treatments remains a challenge. This present study revealed that patients place high-value on medication efficacy, specifically on the treatments ability to reduce the number and severity of asthma attacks, reduce OCS use, and improve quality-of-life. Whilst "asthma treatment efficacy" was considered the most important factor for decision-making, approximately one-quarter of patients selected a medication that was not consistent with this preference when the hypothetical scenarios were presented collectively. These participants traded off asthma treatment efficacy in favour of how the medication is administered and the side-effect profile, and their preferred medication was a tablet, medication D, based on azithromycin, (Figure 1A). This indicates that for a subgroup of patients, a medication's performance in improving asthma related outcomes alone is not enough information for them to make a fully informed choice regarding their treatment options. Additionally, cost was not considered a priority however this is likely to vary depending on cost to the patient within different health care systems. In Australia, several add-on asthma medications for severe asthma are subsidised under the pharmaceutical benefits scheme, so out of pocket expenses to people with certain

severe asthma phenotypes are minimal. We acknowledge that results may differ within different countries with varied health care systems. In this study the majority of participants were currently prescribed a mAb therapy, suggesting that their preferences are based on their real-life experiences for participants within a severe asthma clinic. Identifying patient preferences or priorities in relation to their real world experience of current or future severe asthma add-on treatments is essential to the foundation of real world shared-decision making.

There are several limitations to the current study. Although the survey tool was not a validated instrument, it enabled an understanding of what treatment aspects people with severe asthma consider important in terms of their medications, and the outcomes they would like to improve. Whilst it was the aim of the study to understand what people with severe asthma want from add-on asthma treatments, whether they be current, past or future treatments, the survey sample consisted largely of patients who were prescribed a mAb therapy. There was however no difference between those prescribed mAb therapy versus those that were not in the respective sub-analysis. We acknowledged that we were underpowered in this particular analysis, therefore we are unable to determine the impact that current, past or future add-on asthma treatments have on these outcomes of importance. Nevertheless understanding patients' preferences and priorities are important aspects of shared-decision making regardless of their current or future treatment experience. Further, this survey was conducted on a relatively small sample size who were recruited from one respiratory clinic. Experiences with mAb therapy prior to enrolment were not recorded and adherence to current treatment was not investigated, however patients receive monitoring with the administration of the mAb therapies, so we can be confident of adequate adherence at least with the mAbs. This is an important observation however, as it highlights that despite receiving these treatments, patients with severe asthma continue to suffer a symptom and quality of life burden. This is consistent with data from a large survey of

people with severe asthma. This residual burden needs to be addressed in future asthma research and practice.

The medications used in the “medication characteristic preferences section” were presented to elicit what aspects of a medication patients consider important when making a medication choice. Presenting a clear winner, in terms of treatment efficacy from a patient’s perspective enabled us to determine what was the most important outcome when all treatment aspects were traded off together. Further, whilst the medication side effects listed were based on those that were common across all medications, for readability, an exhaustive list of medication attributes and side effects were not included. More extensive work examining which side effects would be weighted more heavily in decision making would be of benefit in this population. Additionally, the hypothetical medication scenarios were based only on those mAbs available for prescription at the time of the study. Given this, there were no scenarios which represented “Dupilumab” or “Reslizumab”.

These factors may limit the generalisability of the findings. Further, it is a limitation of the current study that consumers did not review the list of priorities during the development of the survey, however the survey items were derived from prior qualitative research in the population of interest (2-4). We acknowledge that we did not provide an exhaustive list of potential outcomes of importance, however we believe the inclusion of open-ended questions about additional outcomes will have overcome this limitation.

## **Conclusions**

This study highlights what aspects of treatment and outcomes people with severe asthma regard as important. Some of these outcomes, such as breathlessness, inability to exercise and impaired sleep are not current targets of severe asthma treatments, infrequently measured in the clinical trials, or assessed in routine asthma management. Given these outcomes are of high importance to patients, and are of high clinical relevance [32,33], future research focusing on the development of interventions that improve these outcomes (both



pharmacological and non-pharmacological) are needed. Further, patients consider asthma treatment efficacy as a priority when deciding what medication to take, but also want to know the burden of the medication side-effects to enable them to evaluate the overall improvements to their quality-of-life. Together these data can inform patient-centred development of new severe asthma treatments and patient centred models-of-care.

**Table 1:** Example of the first hypothetical scenario. Participants were provided the following instructions: “There are different medicines that may work for you to help treat your severe asthma. We would like to understand what is most important to you in terms of your asthma medicines. To help us understand this, I’m going to ask you present you with a series of scenarios, in which you can choose one of four different medications. There are no right or wrong answers here, we just want to get an understanding of what you want from your severe asthma medicine”.

“Below we have provided some information about each of these treatments. We would like you to consider each of the medications and tell us which medication most meets your preferences”.

<b>Asthma Outcomes</b>	<b>Medication A</b>	<b>Medication B</b>	<b>Medication C</b>	<b>Medication D</b>
I am likely to have fewer bad attacks	On average, my bad asthma attacks would reduce by just over one third	On average, my bad asthma attacks would reduce by about half.	On average, my bad asthma attacks would reduce by more than half	On average, my bad asthma attacks would reduce by just under half
I am likely to have an improvement in the control of my asthma (for example, have less symptoms)	😊	😊	😊	😊
I am likely to achieve an improvement in how my asthma symptoms affects my daily life (such as having to avoid social situations, completing my daily tasks of living).	😊😊	😊😊	😊😊😊	😊
I am likely to reduce my oral steroids (prednisone)	On average my steroid dose would reduce by just under half	On average my steroid dose would reduce by half	On average my steroid dose would reduce by up to three quarters	Steroid reduction not known
<b>Thinking about the above information, which medication would you choose? (Rank 1 (this is the one I want!) to 4 (this is the one I would prefer least))</b>				
<b>What was the main reason you chose that medication?</b>				

**Table 2:** Patient demographics

Patient Demographics	(n =50)
Age, mean (SD)	62.20 (13.47)
Male, n (%)	30 (57.69)
Living arrangement, n (%)	
Living alone	9 (20.93)
Living with spouse/family	34 (79.07)
Employment status, n (%)	
Retired	26 (57.78)
Not working for medical reasons	7 (15.56)
Working (full or part-time)	12 (26.67)
Age of asthma diagnosis, years, mean (SD)	23.60 (21.45)
ACQ score, mean (SD)	2.01 (1.27)
Exacerbations past year, median (IQR)	3.00 (2, 5)
Maintenance OCS prescription, n (%)	19 (38%)
OCS daily dose (mg), median (IQR)	7.00 (5.00, 25.00)
ICS daily dose, Beclomethasone equivalent units, median (IQR)	2000 (1000, 2000)
Add-on severe asthma medication*, n (%)	41 (82)
Azithromycin	11 <sup>+</sup> (22)
Mepolizumab	27 (54)
Omalizumab	10 (20)
Benralizumab	3 (6)
Tezepilumab*	1 (2)
No add-on therapy	9 (18)
Months of monoclonal antibody therapy, median (IQR)	7 (3, 24)

SD: standard deviation; IQR: interquartile range. OCS: oral corticosteroid; ICS inhaled corticosteroid; \*One participant was on a clinical trial of tezepilumab in the survey group; <sup>+</sup>azithromycin was an add-on therapy to the monoclonal medications in all but one participant. ACQ: asthma control questionnaire.

**Figure 1:** Outcomes of importance for people with severe asthma. Ranking on a 0 (this is not important to me) to 6 (this is very important to me) point Likert scale. Data expressed as mean and standard deviation.

**Figure 2:** Proportion of the preferences (%) nominated by participants when asked to select their top five.

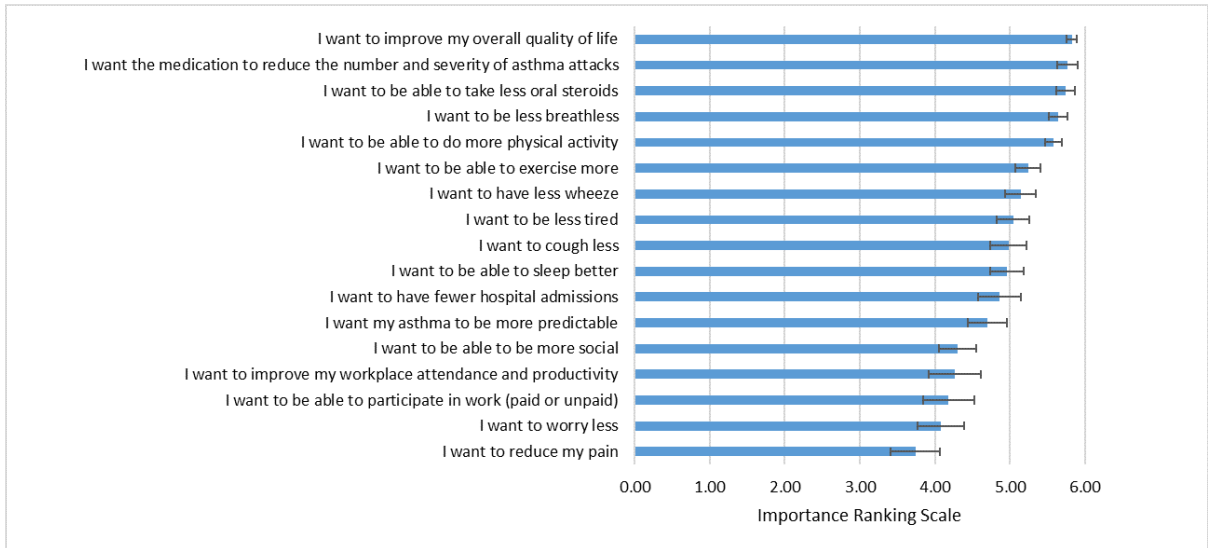
**Figure 3:** Self-reported factors used to decide when given a choice of medication

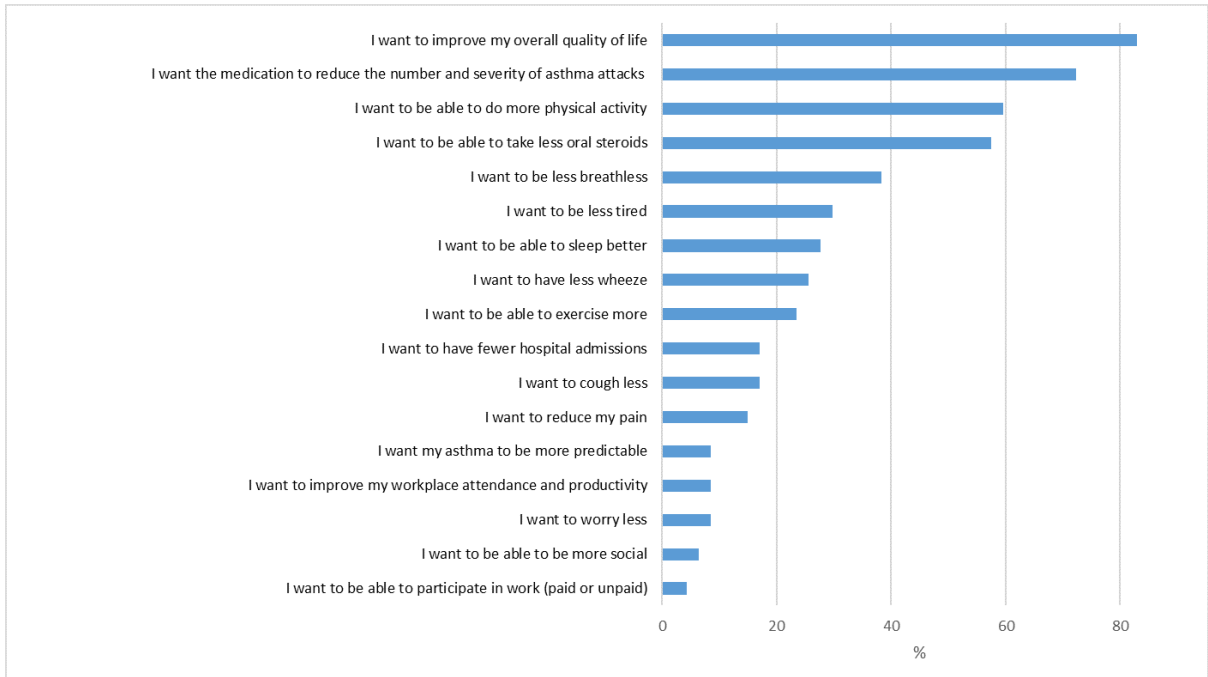
**Figure 4:** A) Overview of the features of the hypothetical medications \*several of the side-effects were "not a known side-effect". B) Proportion of preference for each medication (%), based on the effect of the medication on asthma treatment efficacy "outcomes" (exacerbations, steroid reduction), the logistics of the medication (tablet, injection, frequency of dose), potential side-effects of the medication and all these factors overall

## References

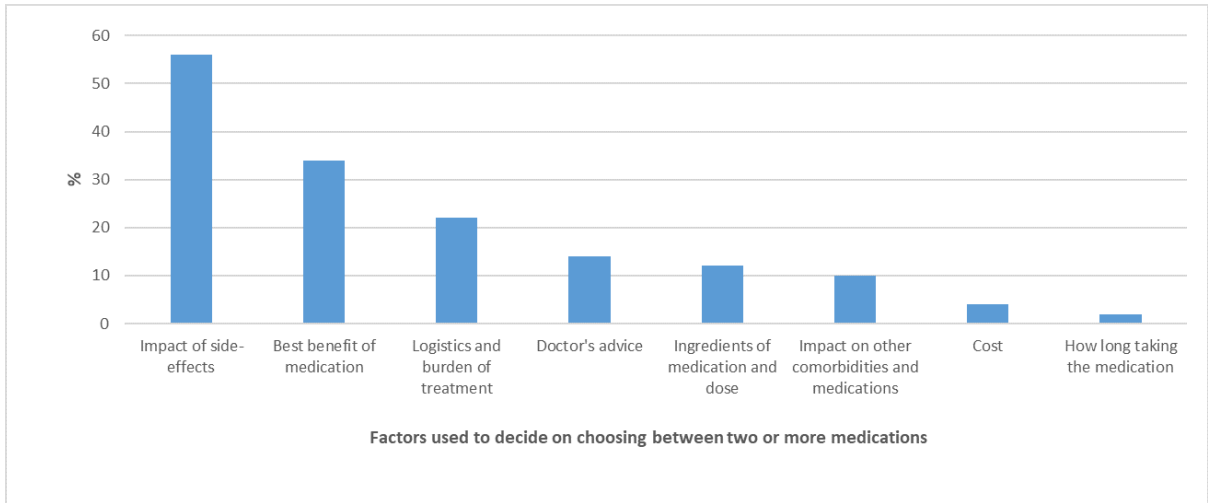
1. Pavord ID, Beasley R, Agusti A, Anderson GP, Bel E, Brusselle G, Cullinan P, Custovic A, Ducharme FM, Fahy JV, Frey U, Gibson P, Heaney LG, Holt PG, Humbert M, Lloyd CM, Marks G, Martinez FD, Sly PD, von Mutius E, Wenzel S, Zar HJ, Bush A. After asthma: redefining airways diseases. *The Lancet* 2018; 391(10118): 350-400.
2. McDonald VM, Gibson PG. Exacerbations of severe asthma. *Clinical & Experimental Allergy* 2012; 42(5): 670-677.
3. McDonald V, Kennington E, Hyland M. Understanding the experience of people living with severe asthma. In: Chung K, Gibson P, eds. *Severe Asthma (ERS Monograph)*. European Respiratory Society, Sheffield, 2019.
4. McDonald VM, Hiles SA, Godbout K, Harvey ES, Marks GB, Hew M, Peters M, Bardin PG, Reynolds PN, Upham JW, Baraket M, Bhikoo Z, Bowden J, Brockway B, Chung LP, Cochrane B, Foxley G, Garrett J, Jayaram L, Jenkins C, Katelaris C, Katsoulotos G, Koh MS, Kritikos V, Lambert M, Langton D, Lara Rivero A, Middleton PG, Nanguzgambo A, Radhakrishna N, Reddel H, Rimmer J, Southcott AM, Sutherland M, Thien F, Wark PAB, Yang IA, Yap E, Gibson PG. Treatable traits can be identified in a severe asthma registry and predict future exacerbations. *Respirology* 2019; 24(1): 37-47.
5. Upham J, LP C. Optimising treatment for severe asthma. *Medical Journal of Australia* 2018; 209(2): S22-S27.
6. Bleeker ER, FitzGerald JM, Chanez P, Papi A, Weinstein SF, Barker P, Sproule S, Gilmartin G, Aurivillius M, Werkstrom V, Goldman M. Efficacy and safety of benralizumab for patients with severe asthma uncontrolled with high-dosage inhaled corticosteroids and long-acting beta2-agonists (SIROCCO): a randomised, multicentre, placebo-controlled phase 3 trial. *Lancet (London, England)* 2016; 388(10056): 2115-2127.
7. Castro M, Zangrilli J, Wechsler ME, Bateman ED, Brusselle GG, Bardin P, Murphy K, Maspero JF, O'Brien C, Korn S. Reslizumab for inadequately controlled asthma with elevated blood eosinophil counts: results from two multicentre, parallel, double-blind, randomised, placebo-controlled, phase 3 trials. *The Lancet Respiratory medicine* 2015; 3(5): 355-366.
8. Pavord ID, Korn S, Howarth P, Bleeker ER, Buhl R, Keene ON, Ortega H, Chanez P. Mepolizumab for severe eosinophilic asthma (DREAM): a multicentre, double-blind, placebo-controlled trial. *The Lancet* 2012; 380(9842): 651-659.
9. Clark VL, Gibson PG, Genn G, Hiles SA, Pavord ID, McDonald VM. Multidimensional assessment of severe asthma: A systematic review and meta-analysis. *Respirology* 2017; 22(7): 1262-1275.
10. Hiles SA, McDonald VM, Guilhermino M, Brusselle GG, Gibson PG. Does maintenance azithromycin reduce asthma exacerbations? An individual participant data meta-analysis. *European Respiratory Journal* 2019; 1901381.
11. Greening AP, Stempel D, Bateman ED, Virchow JC. Managing asthma patients: which outcomes matter? *European Respiratory Review* 2008; 17(108): 53-61.
12. Osman LM, McKenzie L, Cairns J, Friend JAR, Godden DJ, Legge JS, Douglas JG. Patient weighting of importance of asthma symptoms. *Thorax* 2001; 56(2): 138-142.
13. Barry MJ, Edgman-Levitan S. Shared decision making — The pinnacle patient-centered care. *The New England Journal of Medicine* 2012; 366(9): 780-781.
14. Wilson SR, Strub P, Buist AS, Knowles SB, Lavori PW, Lapidus J, Vollmer WM, Better Outcomes of Asthma Treatment Study G. Shared treatment decision making improves adherence and outcomes in poorly controlled asthma. *American journal of respiratory and critical care medicine* 2010; 181(6): 566-577.
15. Gelhorn HL, Balantac Z, Ambrose CS, Chung YN, Stone B. Patient and physician preferences for attributes of biologic medications for severe asthma. *Patient Prefer Adherence* 2019; 13: 1253-1268.
16. Chung KF, Wenzel SE, Brozek JL, Bush A, Castro M, Sterk PJ, Adcock IM, Bateman ED, Bel EH, Bleeker ER, Boulet L-P, Brightling C, Chanez P, Dahlen S-E, Djukanovic R, Frey U, Gaga M, Gibson P,

- Hamid Q, Jajour NN, Mauad T, Sorkness RL, Teague WG. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *European Respiratory Journal* 2014; 43(2): 343-373.
17. 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. *The Journal of asthma : official journal of the Association for the Care of Asthma* 2019; 56(3): 311-322.
  18. Foster JM, McDonald VM, Guo M, Reddel HK. "I have lost in every facet of my life": the hidden burden of severe asthma. *The European respiratory journal* 2017; 50(3).
  19. Jones KA, Gibson PG, Yorke J, Niven R, Smith A, McDonald VM. Attack, flare-up, or exacerbation? The terminology preferences of patients with severe asthma. *Journal of Asthma* 2019; 1-10.
  20. Cheung KL, Wijnen BFM, Hollin IL, Janssen EM, Bridges JF, Evers SMAA, Hiligsmann M. Using Best-Worst Scaling to Investigate Preferences in Health Care. *Pharmacoeconomics* 2016; 34(12): 1195-1209.
  21. Becker MH. The Health Belief Model and Sick Role Behavior. *Health Education Monographs* 1974; 2(4): 409-419.
  22. Janz NK, Becker MH. The Health Belief Model: A Decade Later. *Health Education Quarterly* 1984; 11(1): 1-47.
  23. Chapman S, Dale P, Svedater H, Stynes G, Vyas N, Price D, Horne R. Modelling the effect of beliefs about asthma medication and treatment intrusiveness on adherence and preference for once-daily vs. twice-daily medication. *NPJ Prim Care Respir Med* 2017; 27(1): 61-61.
  24. Svedater H, Leather D, Robinson T, Doll H, Nafees B, Bradshaw L. Evaluation and quantification of treatment preferences for patients with asthma or COPD using discrete choice experiment surveys. *Respiratory Medicine* 2017; 132: 76-83.
  25. King MT, Hall J, Lancsar E, Fiebig D, Hossain I, Louviere J, Reddel HK, Jenkins CR. Patient preferences for managing asthma: results from a discrete choice experiment. *Health economics* 2007; 16(7): 703-717.
  26. Stubbs M, Clark V, McDonald V. Living well with severe asthma. *Breathe* 2019; 15(2).
  27. Katsaounou P, Odemyr M, Spranger O, Hyland ME, Kroegel C, Conde LG, Gore R, Menzella F, Domingo Ribas C, Morais-Almeida M, Gasser M, Kasujee I. Still Fighting for Breath: a patient survey of the challenges and impact of severe asthma. *ERJ Open Research* 2018; 4(4): 00076-02018.
  28. 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. *Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation* 2015; 24(3): 631-639.
  29. Niebauer K, Dewilde S, Fox-Rushby J, Revicki DA. Impact of omalizumab on quality-of-life outcomes in patients with moderate-to-severe allergic asthma. *Annals of allergy, asthma & immunology : official publication of the American College of Allergy, Asthma, & Immunology* 2006; 96(2): 316-326.
  30. Busse W, Corren J, Lanier BQ, McAlary M, Fowler-Taylor A, Cioppa GD, van As A, Gupta N. Omalizumab, anti-IgE recombinant humanized monoclonal antibody, for the treatment of severe allergic asthma. *The Journal of allergy and clinical immunology* 2001; 108(2): 184-190.
  31. Ramsahai JM, Wark PA. Appropriate use of oral corticosteroids for severe asthma. *The Medical journal of Australia* 2018; 209(S2): S18-s21.
  32. Frostad A, Soyseth V, Andersen A, Gulsvik A. Respiratory symptoms as predictors of all-cause mortality in an urban community: a 30-year follow-up. *Journal of internal medicine* 2006; 259(5): 520-529.
  33. Cordova-Rivera L, Gibson PG, Gardiner PA, McDonald VM. A Systematic Review of Associations of Physical Activity and Sedentary Time with Asthma Outcomes. *The Journal of Allergy and Clinical Immunology: In Practice* 2018; 6(6): 1968-1981.e1962.





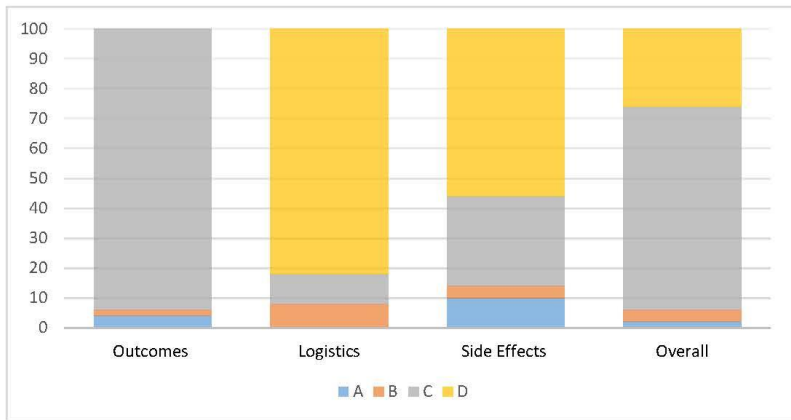




A)

- |              |   |   |
|--------------|---|---|
| Medication A | } | <ul style="list-style-type: none"> <li>• Reduces asthma attacks by one third</li> <li>• Improves asthma control a little</li> <li>• Improves health related quality of life a fair bit</li> <li>• Reduces steroid dose by under half</li> <li>• An injection, every four weeks</li> <li>• Commonly associated with a headache, sore throat, weight increase, nausea and rash</li> </ul> |
| Medication B | } | <ul style="list-style-type: none"> <li>• Reduces asthma attacks by half</li> <li>• Improves asthma control a little</li> <li>• Improves health related quality of life a fair bit</li> <li>• Reduces steroid dose by half</li> <li>• An injection every four weeks</li> <li>• Commonly associated with headache, and fatigue</li> </ul>   |
| Medication C | } | <ul style="list-style-type: none"> <li>• Reduces asthma attacks by more than half</li> <li>• Improves asthma control a little</li> <li>• Improves health related quality of life a lot</li> <li>• Reduces steroid dose by three quarters</li> <li>• An injection every eight weeks</li> <li>• Commonly associated with headache, sore throat</li> </ul>                                 |
| Medication D | } | <ul style="list-style-type: none"> <li>• Reduces asthma attacks by just under half</li> <li>• Improves asthma control a little</li> <li>• Improves health related quality of life a little</li> <li>• Steroid reduction is unknown</li> <li>• Oral tablet</li> <li>• Commonly associated with diarrhoea</li> </ul>  |

B)



# Novel Asthma Medication Study

Patient ID: \_\_\_\_\_  
Date \_\_\_\_\_

## Clinical scenarios

**“There are different medicines that may work for you to help treat your severe asthma. We would like to understand what is most important to you in terms of your asthma medicines. To help us understand this, I’m going to ask you present you with a series of scenarios, in which you can choose one of four different medications. There are no right or wrong answers here, we just want to get an understanding of what you want from your severe asthma medicine”.**

# Novel Asthma Medication Study

Patient ID: \_\_\_\_\_

Date \_\_\_\_\_

## 1. Outcomes

### 1.1 Outcome properties

“Below we have provided some information about each of these treatments. We would like you to consider each of the medications and tell us which medication most meets your preferences”.

Asthma Outcomes	Medication A	Medication B	Medication C	Medication D
I am likely to have fewer bad attacks	On average, my bad asthma attacks would reduce by just over one third	On average, my bad asthma attacks would reduce by about half.	On average, my bad asthma attacks would reduce by more than half	On average, my bad asthma attacks would reduce by just under half
I am likely to have an improvement in the control of my asthma (for example, have less symptoms)	😊	😊	😊	😊
I am likely to achieve an improvement in how my asthma symptoms affects my daily life (such as having to avoid social situations, completing my daily tasks of living).	😊😊	😊😊	😊😊😊	😊
I am likely to reduce my oral steroids (prednisone)	On average my steroid dose would reduce by just under half	On average my steroid dose would reduce by half	On average my steroid dose would reduce by up to three quarters	Steroid reduction not known
<b>Thinking about the above information, which medication would you choose? (Rank 1 (this is the one I want!) to 4 (this is the one I would prefer least))</b>				
<b>What was the main reason you chose that medication?</b>				

**Key:** 😊 improves a little 😊😊 improves a fair bit 😊😊😊 improves a lot

# Novel Asthma Medication Study

Patient ID: \_\_\_\_\_

Date \_\_\_\_\_

## 1.2 Logistics

“Some of the new asthma medications are given via injection, instead of the traditional inhaler device. Thinking about the logistics below please tell us which medication most meets your preferences.”.

Logistics	Medication A	Medication B	Medication C	Medication D
Mode of delivery (how you take your medicine)	Subcutaneous injection (in your tummy)	Subcutaneous Injection (in your tummy)	Subcutaneous injection (in your tummy)	Oral tablet
Time commitment (how long it takes to receive your medicine)	Every 4 weeks, remain in the hospital or doctor’s office for 2 hours post the first injection, then 30 thereafter for observation	Every 4 weeks, remain in the hospital or doctor’s office for 1 hour post the first injection, then 30 thereafter for observation	Every 4 weeks for the first 3 doses, followed by once every 8 weeks thereafter. Remain for 1 hour post injection for observation, then 30 thereafter for observation	< 1 minute
Location of treatment (where you take it)	Severe asthma clinic for first 3 doses and then your GP for follow-up doses.	Severe asthma clinic for first 3 doses and then your GP for follow-up doses.	Severe asthma clinic for first 3 doses and then your GP for follow-up doses.	Home
Availability of treatment (where you get it from)	Pharmacy	Pharmacy	Pharmacy	Pharmacy
<b>Thinking about these things, which medication would you choose? (Rank 1 (this is the one I want!) to 4 (this is the one I would prefer least))</b>				
<b>What was the main reason you chose that medication?</b>				

# Novel Asthma Medication Study

Patient ID: \_\_\_\_\_

Date \_\_\_\_\_

## 1.3 Side effects

*“Thinking about some common medication side effects of the proposed medications, tell us which medication you would prefer”*

Side effect	Medication A	Medication B	Medication C	Medication D
Headache	Common	Common	Common	Less common
Sore throat	Common	Less common	Common	Rare
Allergic reaction (severe reaction)	Rare	Rare	Rare	Rare
Injection site pain	Common	Common	Common	None
Weight increase	Common	Not a known side effect	Not a known side effect	Not a known side effect
Nausea	Common	Less common	Not a known side effect	Rare
Diarrhoea	Less common	Less common	Not a known side effect	Common
Fatigue	Less common	Common	Not a known side effect	Less common
Rash	Common	Less common	Less common	Less common
<b>Thinking about these things, which medication would you choose? (Rank 1 (this is the one I want!) to 4 (this is the one I would prefer least))</b>				
<b>What was the main reason you chose that medication?</b>				

## 2. Overall: Now thinking about all the aspects of the medications, which one would you be most likely to choose?

Asthma Outcomes	Medication A	Medication B	Medication C	Medication D
I am likely to have fewer bad attacks	On average my bad asthma attacks would reduce by just over one third	On average my bad asthma attacks would reduce by about half	On average my bad asthma attacks would reduce by more than half	On average my bad asthma attacks would reduce by just under half
I am likely to have an improvement in asthma control (for example, have less symptoms)	☺	☺	☺	☺
I am likely to achieve an improvement in how my asthma symptoms impact my daily life (such as having to avoid social situations, completing your daily tasks of living).	☺☺	☺☺	☺☺☺	☺
I am likely to reduce my oral steroids (prednisone)	On average my steroid dose would reduce by just under half	On average my steroid dose would reduce by half	On average my steroid dose would reduce by up to three quarters	Steroid reduction not known
<b>Logistics</b>				
Mode of delivery	Subcutaneous injection (in your tummy)	Subcutaneous Injection (in your tummy)	Subcutaneous injection (in your tummy)	Oral tablet
Time commitment	Every 4 weeks, remain in the hospital or doctor's office for 2 hours post the first injection, then 30 thereafter for observation	Every 4 weeks, remain in the hospital or doctor's office for 1 hour post the first injection, then 30 thereafter for observation	Every 4 weeks for the first 3 doses, followed by once every 8 weeks thereafter. Remain for 1 hour post injection, then 30 thereafter for observation	< 1 minute
Location of treatment (where you take it)	Severe asthma clinic for first 3 doses and then continue or go to GP	Severe asthma clinic for first 3 doses and then continue or go to GP	Severe asthma clinic for first 3 doses and then continue or go to GP	Home
Availability of treatment (where you get it from)	Pharmacy	Pharmacy	Pharmacy	Pharmacy
<b>Side effects</b>				
Headache	Common	Common	Common	Less common
Sore throat	Common	Less common	Common	Rare
Allergic reaction (severe reaction)	Rare	Rare	Rare	Rare
Injection site pain	Common	Common	Common	None
Weight increase	Common	Not a known side effect	Not a known side effect	Not a known side effect
Nausea	Common	Less common	Not a known side effect	Rare
Diarrhoea	Less common	Less common	Not a known side effect	Common
Fatigue	Less common	Common	Not a known side effect	Less common
Rash	Common	Less common	Less common	Less common
<b>Thinking about all these things, which medication would you choose? (rank 1 – 4)</b>				
<b>What was the main reason you chose that medication?</b>				

# Novel Asthma Medication Study

Patient ID: \_\_\_\_\_

Date \_\_\_\_\_

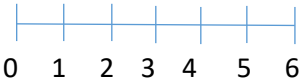
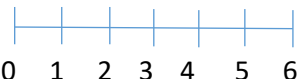
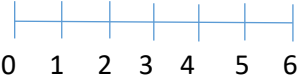
### 3. Cost

“There are direct costs (like paying for a medication) and indirect costs (like the cost of petrol or public transport to attend a medical appointment) associated with managing a chronic illness, such as severe asthma”.

“Thinking about direct and indirect costs how much does cost influence your decision-making in what medication you would prefer to take?”

“In the box below, please indicate how burdensome each cost is to you using the key below from 0 (no burden) to 3 (very burdensome).”

Once you have done that, please rank them in order in relation to each other from 1 (most important) to 3 (least important)”.

	Rank the burden (0-6) of each outcome using the key below	Now order from 1-3 in order of most important (1) to least important (3)
1. The cost to get to the appointment (public transport, petrol, tolls, parking)		
2. The cost of the appointment (GP fees, specialist fees)		
3. The cost of the medicine at the pharmacy		

**Scale 0 = “I don’t care/this cost does not apply to me” to 6 “this would be very burdensome”**



# Novel Asthma Medication Study

Patient ID: \_\_\_\_\_

Date \_\_\_\_\_

## 4. Ranking the domains

“Overall, thinking about the factors that go into making a decision about which medications you were prefer to take please rate the following factors in terms of their importance from 1 (most important) to 4 (least important)”.

	Now order from 1-4 in order of most important (1) to least important (4)
1. <b>Asthma outcomes</b> , such as improvement in your asthma symptoms; improvement in how your asthma impacts your life; and/or the ability of the new medication to allow you to reduce the oral steroids you take.	
2. How you <b>take your medication</b> (administered in the Dr’s office/clinic versus self-administered at home), injection versus tablet	
3. The <b>side effects</b> of the medication, for example, are fewer side effects is more likely to make you choose the medication	
4. The <b>cost</b> associated with taking the medication (direct and indirect costs)	
Why was _____ the most important to you?	

# Novel Asthma Medication Study

Patient ID: \_\_\_\_\_

Date \_\_\_\_\_

## 5. Patient outcomes

**“To see if a medication is working for you to improve your asthma, we want to understand what would most likely change or improve when you start using the new medicine”.**

**“Sometimes the Doctors and Nurses will measure how well your lungs are working, or measure your blood to see how you are responding to a new medication, but we want to know what are the important improvements to your life as a result of taking a new medication”**

**“In answering the following questions, think about what areas of improvement would be most important to you. Are any areas more important than others?”**

**“In the box, please indicate how important each outcome is to you using the key below, from 0 (not very important/don’t care) to 6 (very important).”**

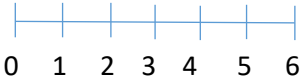
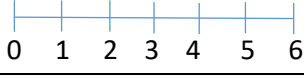
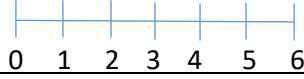
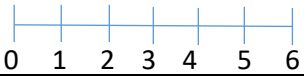
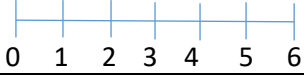
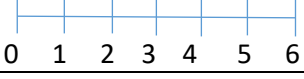
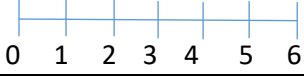
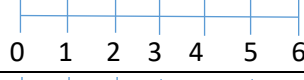
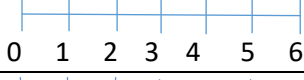
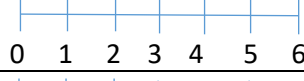
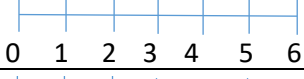
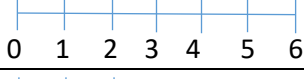
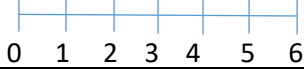
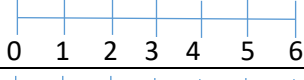
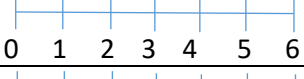
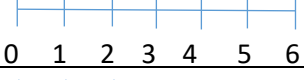
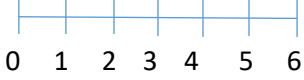
**“Once you have done that, please rank the top five things you consider the most important, start at 1 for the most important overall.”**

**Scale 0 = “I don’t care, this doesn’t worry me” to 6 = “this is very important to me”.**

# Novel Asthma Medication Study

Patient ID: \_\_\_\_\_

Date \_\_\_\_\_

	<p>Rank the importance (0-6) of each outcome using the key below</p> <p>Scale: 0 = "I don't care, this doesn't worry me" to 6 = "this is very important to me".</p>	<p>Now nominate the top five things that you consider the most important, starting at 1 for the most important thing</p>
1. I want the medication to reduce the number and severity of asthma attacks I have.		
2. I want to improve my overall quality of life.		
3. I want to have fewer hospital admissions.		
4. I want to improve my workplace attendance and productivity.		
5. I want to be able to do more physical activity.		
6. I want to be able to sleep better.		
7. I want to be able to be more social.		
8. I want to be able to exercise more.		
9. I want to be able to take less oral steroids.		
10. I want to have less wheeze.		
11. I want to cough less.		
12. I want to be less breathless.		
13. I want to be less tired.		
14. I want to reduce my pain.		
15. I want to worry less.		
16. I want my asthma to be more predictable.		
17. I want to be able to participate in work (paid or unpaid).		

# Novel Asthma Medication Study

Patient ID: \_\_\_\_\_

Date \_\_\_\_\_

**Are there any other outcomes that are important to you that you would like a medication to address?** \_\_\_\_\_

---

---

---

---

---

---

## Final thoughts

**Are there any other factors of which you think are important to consider when choosing between two or more medication choices?**

---

---

---

---

---

---

---

---

---

---

---