ORIGINAL RESEARCH

What matters most to patients when choosing treatment for mild–moderate asthma? Results from a discrete choice experiment

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ABSTRACT

Background An as-needed combination preventer and reliever regimen was recently introduced as an alternative to conventional daily preventer treatment for mild asthma. In a subgroup analysis of the PRACTICAL study, a pragmatic randomised controlled trial of budesonide–formoterol reliever therapy versus maintenance budesonide plus terbutaline reliever therapy in adults with mild asthma, we recently reported that about two-thirds preferred as-needed combination preventer and reliever therapy. The aim of this study was to determine the relative importance of attributes associated with these two asthma therapies in this subgroup of participants who indicated their preferred treatment in the PRACTICAL study.

Methods At their final study visit, a subgroup of participants indicated their preferred treatment and completed a discrete choice experiment using the Potentially All Pairwise RanKings of all possible Alternatives method and 1000minds software. Treatment attributes and their levels were selected from measurable study outcomes, and included: treatment regimen, shortness of breath, steroid dose and likelihood of asthma flare-up.

Results The final analysis dataset included 288 participants, 64% of whom preferred as-needed combination preventer and reliever. Of the attributes, no shortness of breath and lowest risk of asthma flare-up were ranked highest and second highest, respectively. However, the relative importance of the other two attributes varied by preferred therapy: treatment regimen was ranked higher by participants who preferred as-needed treatment than by participants who preferred maintenance treatment.

Conclusions Knowledge of patient preferences for treatment attributes together with regimen characteristics can be used in shared decision-making regarding choice of treatment for patients with mild–moderate asthma.

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Key message

What is the key question?

► What are the most important features or 'attributes' of asthma treatments to patients when choosing between a new combination symptom-driven inhaled corticosteroid-reliever regimen and a conventional maintenance inhaled corticosteroid regimen with separate as-needed short-acting beta$_2$-agonist?

What is the bottom line?

► In this discrete choice experiment, the most important attribute of asthma treatment was the amount of shortness of breath, whereas the relative importance of other attributes varied depending on whether the patient preferred symptom-driven or maintenance-inhaled corticosteroids.

Why read on?

► Knowledge of patient preferences for asthma treatment together with regimen characteristics may aid clinical decision-making.

INTRODUCTION

Symptom-driven inhaled corticosteroid (ICS)-formoterol represents a new paradigm in the treatment of mild asthma. This regimen has been shown to be safe and efficacious in four randomised controlled trials (RCTs)[1–4] and was included in the 2019 update of the Global Initiative for Asthma (GINA) strategy framework[5 6] as the preferred option at step 1 and as an alternative to low-dose maintenance ICS at step 2.

We have previously reported the results of a survey of patients with mild–moderate asthma who were completing an RCT comparing budesonide–formoterol reliever versus maintenance budesonide plus terbutaline reliever,[4] asking them to choose between combination preventer and reliever therapy as-needed or twice-daily preventer with reliever as needed. About two-thirds of patients overall stated that they preferred a combination preventer and reliever as needed.[7] However, the strength of patient preferences and the tradeoffs they might be willing to make to obtain this therapy are not known. Such knowledge of patient preferences could be incorporated into shared decision-making by patients and their doctors.

Discrete choice experiments (DCEs),[8] a methodology from the social sciences for identifying

participants' stated preferences, are increasingly used to quantify patient preferences with respect to the relative importance of the factors underpinning demand for various health services.[9] DCEs involve participants repeatedly choosing between alternative hypothetical configurations of the service under consideration in terms of its key features or 'attributes'. Participants' choices are analysed to estimate preference weights (often referred to as 'part-worth utilities' in the DCE literature) that represent the relative importance to participants of the service's attributes.[10]

The objective of this study was to conduct a DCE to determine the relative strength of patient preferences for different aspects of asthma treatment, in the context of their preferred treatment regimen: symptom-driven ICS-formoterol or maintenance ICS plus short-acting beta$_2$-agonist (SABA) as needed, in a subgroup of patients with mild–moderate asthma completing the PRACTICAL study, a real-world RCT of these two treatments.[4]

METHODS

Description of the PRACTICAL study

The PRACTICAL study was a 52-week open-label parallel group, multicentre, phase III RCT undertaken across New Zealand. The methods and results are reported elsewhere.[4 11] Adults with mild–moderate asthma who were taking SABA for symptom relief either with or without low-to-medium dose ICS were eligible for inclusion. Use of additional controller medications, such as montelukast, was an exclusion criterion; full inclusion and exclusion criteria for the PRACTICAL study are provided in online supplementary table S1. Participants were randomised 1:1 to either: budesonide–formoterol Turbuhaler (Symbicort), 200/6 μg, one inhalation as needed for symptom relief; or budesonide Turbuhaler (Pulmicort), 200 μg, one inhalation two times a day with terbutaline Turbuhaler (Bricanyl), 250 μg, two inhalations as needed for symptom relief.

Participants

The DCE was conducted with a subset of participants from the PRACTICAL study. Participants who were due their final visit on or after 26 March 2018 at 6 of the 15 sites were eligible. Participants who had withdrawn from the study prior to this date but would have otherwise been eligible were contacted and asked if they would be willing to complete the DCE. Sample size was dictated by the number of potentially eligible participants (n=407).

Stated preference for treatment option

At the final study visit, consenting patients completed a survey on a computer at the study site, with an investigator present in the same room in case of technical issues. At the start of the survey, participants were shown a description of the two randomised treatments in the PRACTICAL study (online supplementary figure S1), and a sheet explaining how to complete the DCE and the rationale for doing it (online supplementary figure S2). Investigators were instructed not to assist participants and to refer them to the explanation sheets if they had any questions. The survey content and results have been reported previously.[7] The final question of the survey asked participants to state which of the two treatment plans they preferred. This choice determined which of two configurations of the DCE the participant completed: the 'as-needed-preference DCE' or the 'maintenance-preference DCE'. Participants completed the DCE immediately after the survey, on the same computer.

Selection of attributes and levels

The attributes included in the DCE, and the levels for each attribute (table 1), represented key features of the two treatment options. They were specified based on a review of the literature, expert consensus and in consultation with participants who had completed the PRACTICAL study before the DCE eligibility date. Eleven participants who had completed the PRACTICAL study attended one of three focus groups to explore the most important features of asthma and its management, with particular focus on factors that had been measured within the PRACTICAL study and how these could be translated into attributes and levels that would be meaningful to participants. The same 11 participants pilot tested the DCE to check understanding, relevance of selected attributed and levels and time taken to complete the DCE, with particular care taken to check their agreement with the inherent ranking of attribute levels. Cognitive debriefing was used to enhance feedback. Based on this feedback, iterative changes to the wording of the DCE were made

Table 1 Attributes and levels

Attribute	Participant's stated ranking of levels, in as-needed-preference DCE	Participant's stated ranking of levels, in maintenance-preference DCE
Type of asthma treatment	A preventer inhaler taken twice a day every day, with a reliever inhaler taken as needed	A combined preventer and reliever inhaler, taken as needed
	A combined preventer and reliever inhaler, taken as needed	A preventer inhaler taken twice a day every day, with a reliever inhaler taken as needed
Attribute	**Inherent ranking of levels, in as-needed-preference DCE**	**Inherent ranking of levels, in maintenance-preference DCE**
The dose of your steroid inhaler	Medium	Medium
	Low	Low
	Very low	Very low
Likelihood of a flare-up in your asthma severe enough that you need to see a doctor	20 out of 100 people in a year (20%)	20 out of 100 people in a year (20%)
	10 out of 100 people in a year (10%)	10 out of 100 people in a year (10%)
	5 out of 100 people in a year (5%)	5 out of 100 people in a year (5%)
In an average week you will be short of breath because of asthma	A moderate amount or more	A moderate amount or more
	A little	A little
	Not at all	Not at all

Each attribute's levels are presented within the table in increasing order of preference (ie, the lowest ranked level is listed first).
DCE, discrete choice experiment.

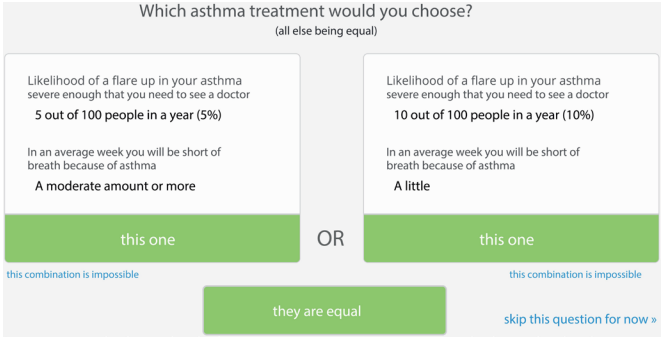

Figure 1 Example of a tradeoff question from the 1000minds software.

during the pilot phase to improve understanding. None of the pilot participants found the DCE to be difficult to understand or unduly burdensome.

Wording was refined during pilot testing, and understanding was checked. Further details are given in the online supplementary.

Discrete choice experiment

The DCE was based on the PAPRIKA method[12]—an acronym for *P*otentially *A*ll *P*airwise *RanK*ings of all possible *A*lternatives—as implemented by 1000minds software (www.1000minds.com). This method and software have been used in a wide range of health applications.[13–17]

All DCE methodologies involve the participants being asked to choose between two or more hypothetical options which are defined by different combinations of the attributes' levels included in the DCE. In the present context, the PAPRIKA method[12] involved each participant being asked a series of 'tradeoff questions', where each question invited them to choose their preferred asthma treatment from a pair of hypothetical treatments defined on just two attributes at a time. Each choice required the participant to confront a tradeoff between the two attributes included for the pair of treatments, where the two other attributes were assumed to be the same for both treatments. An example of a tradeoff question appears in figure 1.

Such questions (always involving a tradeoff between the attributes, two at a time) are repeated with different pairs of hypothetical treatments. Each time the participant answers a question—that is, ranked a pair of treatments (including potentially ranking them equally)—all other pairs of treatments that could be pairwise ranked by applying the logical property of 'transitivity' are identified and eliminated by the software. For example, as an illustration of transitivity, if a person prefers treatment *X* to treatment *Y* and *Y* to *Z*, then—by transitivity—*X* is also preferred to *Z* (and so is not asked about by the software). Also, each time a person answers a question, the method adapts the selection of the next question based on all of their preceding answers (always one whose answer was not implied by earlier answers); thus, PAPRIKA is a type of *adaptive* DCE. This adaptivity combined with the above-mentioned elimination procedure based on transitivity minimises the number of questions the participant is asked while ensuring they have pairwise ranked all possible treatments defined on two attributes at a time, either explicitly or implicitly (by transitivity).

Finally, from the participant's explicit pairwise rankings (ie, answers to the tradeoff questions), the software uses linear programming techniques to derive weights ('part-worth utilities') for the levels on each attribute.[12]

The values for the highest levels across the four attributes sum to 1, so each of these values represents the attribute's relative weight overall. The lowest level of each attribute gets a value of zero. The values assigned to the middle level of an attribute represents the combined effect of the level's middle position on the particular attribute as well as the attribute's relative weight (as above). This representation of weights is equivalent to the more traditional approach where normalised attribute weights and single-attribute value scores are used; we used non-normalised representation because it simplifies the presentation of results. Further details on the PAPRIKA method—in particular, the method by which the weights were derived are provided in the online supplementary appendix.

PAPRIKA's application of the transitivity property requires that each attribute's levels have an inherent ranking in terms of people's preferences,[12] that is, a ranking that would be universally accepted. For example, with respect to the attribute 'likelihood of a flare up', a 5% risk would be assumed to be universally preferred (higher ranked) relative to a 10% risk. In contrast, the two levels for the attribute 'treatment regimen' (ie, the two randomised treatments in the PRACTICAL study) do not have an inherent ranking because each person's ranking would depend on which therapy they preferred. Therefore, it was necessary to implement two separate DCEs, identical except that the ranking of the two levels for the 'treatment regimen' attribute were reversed. After each participant had indicated their preferred therapy, they were presented with the appropriate DCE for them. For participants who had stated they preferred the as-needed therapy this regimen was ranked above the maintenance regimen in their DCE, and vice versa.

The final specification for each DCE's attributes and levels is presented in table 1.

Data quality checks

The consistency of each participant's choices was tested by repeating two previously answered tradeoff questions at the end of the DCE. The time each participant took to answer each question was also recorded by the 1000minds software. Participants who answered both repeated questions inconsistently and/or answered their questions implausibly quickly (less than 4 seconds per question) were excluded from the final analysis.

Data analysis

Preference weights were calculated for each participant and were also averaged across all participants. Continuous variables are described by mean and SD or median and IQR. Categorical variables are described by counts and proportions as percentages.

RESULTS

Participants

Participant flow is shown in online supplementary figure S3. Of the 407 eligible patients, 306 recorded their preferred treatment and 296 (73%) started a DCE. Eight participants' DCEs were excluded: one because it was incomplete, and seven because the participant answered both repeated questions inconsistently. No participant answered their questions implausibly quickly. This gave a total of 288 DCEs in the final dataset. Overall, 185 participants (64%) preferred a combined preventer and reliever inhaler as needed and so completed the as-needed-preference DCE; 103 participants (36%) preferred a preventer inhaler taken two times a day every day, with a reliever inhaler taken as needed, and so completed the maintenance-preference DCE.

Table 2 Participant characteristics by their preferred treatment therapy*, which determined which of the two discrete choice experiments (DCEs) they completed

Characteristic	Preferred therapy, chosen before the DCE	
	As-needed combination preventer and reliever, n=185	Twice-daily maintenance treatment, n=103
Randomised treatment		
Budesonide–formoterol, n (%)	125 (68)	14 (14)
Maintenance budesonide, n (%)	60 (32)	89 (86)
Baseline variables		
Age (year)	44.2 (15.3)	47.6 (17.8)
Female sex, n (%)	104 (56)	59 (57)
Ethnicity, n (%)		
Asian	8 (4)	8 (8)
NZ European	145 (78)	88 (85)
Māori	18 (10)	3 (3)
Other	3 (2)	2 (2)
Pacific	11 (6)	2 (2)
Smoking status, n (%)		
Current smokers	11 (6)	1 (1)
Ex-smokers	47 (25)	29 (28)
Never smokers	127 (69)	73 (71)
Pack years (among ever smokers)	5.5 (4.7) n=58	5.2 (5.4) n=30
Age at diagnosis (year)	19.1 (18.4)	24.1 (20.9)
Self-reported ICS use in 12 weeks prior to randomisation, n. (%)†	122 (66)	79 (77)
Self-reported ICS adherence (%)	54.3 (36.7) n=122	61.7 (33.5) n=79
Self-reported ICS use ever, n (%)	158 (85)	90 (87)
End-of-study variables		
Final visit ACQ-5‡	0.82 (0.70)	0.64 (0.69)
Final visit on treatment FEV_1 % of predicted value§	89.9 (15.0)	88.7 (15.6)
Final visit median Fe_{NO}, ppb (IQR)	22 (15–38)	23 (15–40)
Participants experiencing ≥1 exacerbation or severe exacerbation during the study, n (%)	25 (14)	19 (18)
Number of severe exacerbations during the study, n (%)		
0	160 (86)	84 (82)
1	18 (10)	17 (17)
2	6 (3)	2 (2)
3	1 (1)	0
Early withdrawal, n (%)	8 (4)	11 (11)

Values are expressed as means (SD), unless otherwise stated.
*Participants were asked 'Which of the following asthma treatment plans would you prefer?' with the options of either 'A preventer inhaler taken twice a day every day, with a reliever inhaler taken as needed' or 'A combined preventer and reliever inhaler taken as needed'. Depending on their answer they were directed to the as-needed-preference DCE or the maintenance-preference DCE.
†Patient-reported adherence to inhaled corticosteroid (ICS) in the 4 weeks prior to enrolment (% prescribed dose).
‡The Asthma Control Questionnaire-5 (ACQ-5) consists of five questions that assess asthma symptoms in the previous week, each of which is scored on a 7-point scale that ranges from 0 (no impairment) to 6 (maximum impairment), and averaged, in which a 0.5-unit change represents the minimal clinically important difference.
§Participants received no instruction to withhold their bronchodilator before measurement of FEV_1.[33]
ppb, parts per billion; SABA, short-acting $beta_2$-agonist.

Participant characteristics are reported in table 2. As previously reported,[7] study randomised treatment differed between the two groups, with participants more likely to express a preference for the randomised treatment they took during the study, particularly for those randomised to budesonide–formoterol as needed.

DCE results

For the DCEs, the median number of tradeoff questions answered by each participant was 13, with a mean time of 18.6 s per answer.

Mean preference weights for the attributes and levels and attribute ranking for the two DCEs are reported in table 3.

For both DCEs, the highest ranking was given to 'shortness of breath in an average week' ('not at all'), with a weight of 0.33 (0.12) in the as-needed-preference DCE and 0.34 (0.12) in the maintenance-preference DCE. The second highest rank in both DCEs was for the lowest 'likelihood of an asthma flare-up', that is, 5 out of 100 people (5%) having a flare-up in a year.

For the as-needed-preference DCE, this 'likelihood of asthma flare up' had a similar mean weight as an as-needed 'treatment regimen': 0.25 (0.09) and 0.24 (0.11) respectively. 'Dose of steroid' was the lowest ranked attribute, with a weight of 0.17 (0.11) for 'very low' dose. For the maintenance-preference DCE, the level of 5 out of 100 people for 'likelihood of asthma flare up' was ranked second, with a weight of 0.30 (0.12). 'Very low' dose of steroid was ranked third and the maintenance 'treatment regimen' ranked fourth; however, they had similar weights: 0.19 (0.10) and 0.18 (0.12), respectively. For both DCEs, there was evidence of variability in preferences for each attribute as indicated by the SD. Mean preference weights within each DCE were similar irrespective of randomised treatment (online supplementary tables S4 and S5).

DISCUSSION

In patients with mild–moderate asthma completing a pragmatic open-label study of two treatments, this study has shown for an average week being short of breath 'not at all' had the greatest influence on patient preferences for an asthma treatment, out of the treatment attributes and levels included in a DCE. However, the influence on patient preferences for levels of the other three attributes included in our DCEs differed depending on whether participants, prior to starting the DCE, stated that they preferred a combined preventer and reliever inhaler taken as needed, or a preventer inhaler taken two times a day every day with a reliever inhaler taken as needed. Though a lower likelihood of an asthma flare-up was ranked second in both DCEs, for those who preferred combined treatment taken as needed, this regimen and a lower likelihood of an asthma flare-up had similar preference weights, indicating that they were of similar importance. A very low 'dose of steroid' was the lowest ranked attribute, indicating that it was the least important. In contrast, for participants who preferred maintenance treatment two times a day, this regimen and very low 'dose of steroid' were of similar weight and the least important attributes.

For both DCEs, the mean preference weights were similar irrespective of the patients' randomised treatment group (the treatment group that they were randomised to, not necessarily the one that they preferred), suggesting that strength of preference for the attribute levels associated with a particular regimen was not determined by prior experience of that regimen during the RCT (online supplementary tables S4 and S5). This finding contrasts with the preference for the specific regimen,

Table 3 Mean preference weights and ranking for the attributes and levels in each discrete choice experiment (DCE)

Attribute	Level	Mean weight (SD)	Attribute rank
As-needed-preference DCE, n=185			
Treatment regimen	A preventer inhaler taken two times a day every day, with a reliever inhaler taken as needed	0	
	A combined preventer and reliever inhaler, taken as needed	**0.24** (0.11)	3
Dose of steroid	Medium	0	
	Low	0.10 (0.08)	
	Very low	**0.17** (0.11)	4
Likelihood of asthma flare-up severe enough to need to see your doctor	20 out of 100 people in a year (20%)	0	
	10 out of 100 people in a year (10%)	0.14 (0.07)	
	5 out of 100 people in a year (5%)	**0.25** (0.09)	2
Shortness of breath in an average week	A moderate amount or more	0	
	A little	0.20 (0.09)	
	Not at all	**0.33** (0.12)	1
Maintenance-preference DCE, n=103			
Treatment regimen	A combined preventer and reliever inhaler, taken as needed	0	
	A preventer inhaler taken twice a day every day, with a reliever inhaler taken as needed	**0.18** (0.12)	4
Dose of steroid	Medium	0	
	Low	0.11 (0.08)	
	Very low	**0.19** (0.10)	3
Likelihood of asthma flare-up severe enough to need to see your doctor	20 out of 100 people in a year (20%)	0	
	10 out of 100 people in a year (10%)	0.16 (0.08)	
	5 out of 100 people in a year (5%)	**0.30** (0.12)	2
Shortness of breath in an average week	A moderate amount or more	0	
	A little	0.19 (0.09)	
	Not at all	**0.34** (0.12)	1

Bold values represent the relative weights of the attributes overall (ie, these bold values sum to 1, subject to rounding).

which we have previously reported was strongly determined by the randomised treatments received by the participants[7]: 90% of patients randomised to budesonide–formoterol preferred as-needed treatment, and 60% of those randomised to maintenance budesonide-preferred maintenance treatment.

Our results are consistent with other DCEs completed by patients with asthma using different DCE methods, which found attributes that represent more shortness of breath or higher symptom frequency are the most important attributes.[18 19] Similar to other DCE studies,[20 21] reduced risk of asthma exacerbations and flare-ups were also important, ranking second in this population with mild–moderate asthma. Other DCEs report conflicting results with respect to the importance of ICS dose.[19 22] No previous DCEs included an as-needed asthma regimen as an attribute, but previous studies found that patients prefer regimens with fewer inhalers[21–23] or that are convenient to use and have a lower dosing frequency.[20]

Patient preferences for different attributes of asthma treatment may help determine which regimen is most suitable for them. The PRACTICAL study[4] reported no difference between the treatment regimens in asthma symptoms as assessed by the group mean Asthma Control Questionnaire-5. However, the SYmbicort Given as-needed in Mild Asthma (SYGMA) 1 and 2[1 2] and Novel Symbicort Turbuhaler Asthma Reliever Therapy (START)[3] studies reported a slightly higher level of asthma symptoms with as-needed budesonide–formoterol compared with maintenance budesonide. Although in all three studies, this was well below the minimal clinically important difference. Though either regimen may be suitable for a patient who wishes to avoid breathlessness, the results of these four studies considered together suggest that maintenance budesonide may be more appropriate for patients who have a strong preference to avoid symptoms. The lower rate of severe exacerbations with as-needed budesonide–formoterol compared with maintenance budesonide in the PRACTICAL and Novel START studies[3 4] and similar rates between the two regimens in the SYGMA studies[1 2] suggests that as-needed budesonide–formoterol may be more appropriate for those at risk of exacerbations, or who are concerned about exacerbations. Exposure to ICS was significantly lower in the as-needed budesonide–formoterol group in all four studies. Therefore, as-needed budesonide–formoterol may be more appropriate for patients who wish to limit their exposure to ICS. Understanding patient preferences and priorities for asthma treatment is important when discussing management options with patients, particularly as as-needed budesonide–formoterol enters clinical practice.

As with any DCE, hypothetical bias and different interpretations of the attributes and levels between participants may have affected the results.[24] We attempted to mitigate this risk by only including attributes and levels that were realistic and relatable. Shortness of breath was the only symptom included in the DCE, whereas asthma also causes wheeze, cough and night waking. During pilot testing, the attribute 'dose of steroid' and its associated levels were interpreted as reflecting different levels of exposure to ICS, rather than specific levels of risk of side effects. Prior to completing the DCE, participants were aware of both treatment regimens—from personal experience in the case of their own randomised treatment, and from information provided at the start of the PRACTICAL study and at the last visit for the other treatment. To limit cognitive burden and the number of questions in the DCE, we opted to include only four attributes which were considered to be the important influencers of choice, but other attributes such as side effects or asthma-related healthcare costs[19] may also be relevant. However, for both DCEs, the levels of all four attributes influenced participants' choices.

Other potential limitations include the fact that participants were asked to choose between hypothetical asthma treatments defined on levels of just two attributes at a time. Therefore, participants were not making each choice based on the full set of four attributes, and so our results may be susceptible to bias as participants may have been choosing based on assumptions about the other two attributes.[25 26] However, the use of partial profiles can help mitigate effects of attribute dominance and reduces the complexity of choices for the participant.[27] In

addition, the maintenance regimen offered in the DCE-specified twice-daily treatment, as studied in PRACTICAL; however, several ICS formulations are approved for once-daily use, and specifying twice-daily treatment for the regimen attribute may have biased preferences towards the as-needed regimen. Reading ability was not specifically evaluated, but prior to starting the DCE, participants had already completed the consent form and the preferences survey, as well as questionnaires at each visit of the RCT itself.

As the categorical attribute of regimen preference did not have an inherent ranking (ie, that was universally accepted), we developed two almost identical DCEs in order to use the PAPRIKA method and obtain preference weights for each individual participant. As this study was conducted in participants completing an RCT, the sample may not be representative of the general mild–moderate asthma population, who would be eligible for as-needed treatment, but may have different preferences and priorities. Previous population-based studies conducted in patients with asthma have found patients prefer regimens that are less intrusive[28] and to increase their reliever inhalers over their preventer inhalers even in response to worsening asthma symptoms.[29]

A DCE was not completed by 112 eligible participants (28%). On review of their characteristics (online supplementary table S6), there was a higher early withdrawal rate and their preferences may be different from those who completed a DCE. There were 19 participants who withdrew early and completed a DCE. Of these, those who completed the maintenance-preference DCE had a higher preference weight for the lowest likelihood of an asthma flare-up, whereas those who completed the as-needed-preference DCE had a higher weight for dose of steroid compared with the whole group (online supplementary table S7).

This study is the first to investigate patient preferences for two specific asthma therapies using DCE methodology. Previous DCEs have explored patient preferences for attributes of asthma treatment,[20–22 30 31] but this is the first DCE to have compared a regular versus an as-needed preventer therapy. This is highly relevant as symptom-driven ICS formoterol is a new treatment which was included in the 2019 GINA update at steps 1 and 2, and has been approved by regulators in multiple countries. Understanding patient preferences and priorities for their asthma treatment is important when discussing management options with patients. Previous qualitative studies have shown that patients can have a strong attachment to their SABA reliever inhalers,[32] which may have implications when switching to a new reliever medication. However, in a survey of patient preferences for, and experiences of, as-needed budesonide–formoterol also conducted in this subgroup of participants,[7] we found that 92% of those who were randomised to as-needed budesonide–formoterol were confident in using it as a reliever inhaler by the end of the study. This finding suggests that after an opportunity to try low-dose budesonide–formoterol as reliever therapy, most patients will find it an acceptable strategy. However, we cannot assume that the results of this analysis, conducted among clinical trial participants, are generalisable to the wider population of people with asthma. The priority now is to explore attitudes and barriers to budesonide–formoterol reliever therapy in the general asthma population and the perspective of prescribers to this new approach to reliever therapy.

Strengths of our study include that we have incorporated investigation of patient preferences for attributes of asthma regimens into an RCT. This study was independent of the pharmaceutical industry and was independently funded. That we asked participants to state their preference for one of the two regimens prior to commencing the DCE means that preference weights for attribute levels are directly related to their preferred treatment regimen.

In conclusion, we investigated the relative importance to patients of different levels of four attributes of symptom-driven combination preventer and reliever or of maintenance preventer with symptom-driven reliever regimens, and related those preferences back to data measured in an RCT. Our results suggest that no shortness of breath and low likelihood of asthma flare-up were the two most important attributes. However, the patient's preferred regimen influenced their preference for likelihood of a flare-up, steroid dose and treatment regimen. Knowledge of patient preferences for treatment attributes together with knowledge of regimen characteristics could be used in discussion with patients to determine the most appropriate regimen for them, based on their preferences for regimen, shortness of breath, likelihood of an asthma flare-up and steroid dose.

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Contributors CB, PH, RJH, RB, HKR and JF conceived the idea and designed the study. CB, JKH and JS collected the data. MH monitored the study and undertook data management. CB, JF and MW undertook data analysis. All authors had access to analyses of study data. CB and PH wrote the first draft of the manuscript, and all authors contributed to and approved the final version.

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Competing interests CB reports personal fees from AstraZeneca and Novartis. PH co-owns and cocreated the 1000minds software used in this study, which was created for the purpose of supporting elements of the methodology explained herein and which is made available to many academics (to date, more than 2000 researchers and students worldwide), including for the present study for free. RJH reports grants from AstraZeneca and Boehringer Ingelheim; and personal fees from Menarini. JKH reports personal fees from AstraZeneca. RB reports grants from Genentech, AstraZeneca, GlaxoSmithKline; and personal fees from AstraZeneca and Theravance. HKR reports grants from AstraZeneca and Novartis; personal fees from AstraZeneca, GlaxoSmithKline, Merck, Novartis, Teva, Mundipharma, and Boehringer Ingelheim; and is chair of the Global Initiative for Asthma scientific committee. JF reports grants from AstraZeneca, GlaxoSmithkline, and Genentech; and personal fees and non-financial support from AstraZeneca and Boehringer Ingleheim.

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Data availability statement Data are available upon reasonable request. Deidentified individual participant DCE data from the PRACTICAL trial will be shared beginning two years after article publication with no end date. These data will be available to researchers who provide a methodologically sound proposal for the

purposes of achieving specific aims outlined in that proposal. Proposals should be directed to Richard Beasley via email: richard.beasley@mrinz.ac.nz and will be reviewed by the PRACTICAL study management committee. Requests to access data to undertake hypothesis-driven research will not be unreasonably withheld. To gain access, data requesters will need to sign a data access agreement and to confirm that data will only be used for the agreed purpose for which access was granted.

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