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Patient preferences for symptom-driven or regular preventer treatment in mild to moderate asthma – findings from the PRACTICAL study, a randomised clinical trial

Christina Baggott, Helen K. Reddel, Jo Hardy, Jenny Sparks, Mark Holliday, Andrew Corin, Barney Montgomery, Jim Reid, Davitt Sheahan, Robert J. Hancox, Mark Weatherall, Richard Beasley, James Fingleton

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Title

Patient preferences for symptom-driven or regular preventer treatment in mild to moderate asthma – findings from the PRACTICAL study, a randomised clinical trial.

Authors

[1]Christina Baggott, [2]Helen K Reddel, [1]Jo Hardy, [1]Jenny Sparks, [1]Mark Holliday, [3]Andrew Corin, [4]Barney Montgomery, [5]Jim Reid, [6]Davitt Sheahan, [4,5]Robert J Hancox, [6]Mark Weatherall, [1,7]Richard Beasley, [1,7]James Fingleton on behalf of the PRACTICAL study team

Author's affiliations

[1]Medical Research Institute of New Zealand, Wellington, New Zealand

[2]Woolcock Institute of Medical Research, University of Sydney, Sydney, Australia

[3]Clinical Horizons, Tauranga, New Zealand

[4]Optimal Clinical Trials Ltd, Auckland, New Zealand

[5]RMC Research Ltd, Dunedin, New Zealand

[6]Papamoa Pines Medical Centre, Tauranga, New Zealand

[4]Waikato Hospital, Hamilton, New Zealand

[5]University of Otago, Dunedin, New Zealand

[6]University of Otago Wellington, Wellington, New Zealand

[7]Capital and Coast District Health Board, Wellington, New Zealand

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Corresponding author

Christina Baggott

Medical Research Institute of New Zealand, Wellington Regional Hospital, Newtown, Wellington, 6021, New Zealand

Christina.baggott@mrinz.ac.nz

Take home message: (250 characters)

In a clinical trial of patients with mild-moderate asthma comparing as-needed budesonide-formoterol with maintenance budesonide plus as needed terbutaline, as-needed budesonide-formoterol was preferred by 90% of patients randomised to this treatment.

Abstract

Symptom-driven low-dose inhaled corticosteroid-formoterol is safe and effective in mild asthma and has been recommended as one of the preferred treatment regimens at steps 1 and 2 in the 2019 update of the Global Initiative for Asthma (GINA). However there are no data on patient preferences for this regimen.

A subgroup of participants in the PRACTICAL study (ACTRN12616000377437), a randomised control trial comparing symptom-driven budesonide-formoterol with maintenance budesonide plus as-needed terbutaline, completed a survey on treatment preferences, satisfaction, beliefs and experience at their final study visit.

306 of 407 eligible participants (75%) completed the survey. Regimen preference was strongly associated with randomised treatment as were preferences for and beliefs about preventer inhaler use. Combination preventer and reliever as needed therapy was preferred by 135/150 (90%, 95% CI 85.2 to 94.8) who were randomised to as-needed budesonide-formoterol, and by 63/156 (40%, 95% CI 32.7 to 48.1) who were randomised to maintenance budesonide. By contrast, twice daily preventer inhaler with a reliever inhaler as required was preferred by 15/150 (10%) of those randomised to as-needed budesonide-formoterol and 93/156 (60%) of those randomised to maintenance budesonide. Satisfaction with all study inhalers was high. Of patients randomised to as-needed budesonide-formoterol (n=138), 92% were confident using it as a reliever at the end of the study.

Although most participants preferred the regimen to which they had been randomised, this association was much stronger for those randomised to budesonide-formoterol as needed, indicating that most patients preferred as-needed corticosteroid-formoterol therapy if they had experienced it.

Word count 248

Introduction

Treatment options in mild asthma have expanded, following results from four randomised controlled trials (RCTs) into the safety and efficacy of symptom-driven low-dose budesonide-formoterol.[1–4] The 2019 update of the Global Initiative for Asthma (GINA) strategy for asthma management and prevention endorsed symptom-driven low dose inhaled corticosteroids (ICS) in combination with formoterol, a fast-onset long-acting beta2 agonist (LABA), for mild asthma. GINA now recommends that, for adults and adolescents with mild asthma, as-needed ICS-formoterol is preferred to short-acting beta2 agonist (SABA) reliever therapy alone (Step 1), and is an alternative to maintenance low dose ICS plus as-needed SABA (Step 2).[5,6]

From a medical perspective, symptom-driven ICS-formoterol is an attractive regimen for mild asthma as it has the potential to circumvent the problem of SABA overuse and ICS underuse during periods of asthma worsening.[7,8] Despite having apparently mild asthma, patients are at risk of severe exacerbations,[9] which are often associated with poor adherence to ICS.[10] There is evidence that patients prefer regimens that are less intrusive[11], prefer to increase their reliever medications over their preventer medications[12], have concerns about the necessity of using preventer inhalers regularly[13] and want to have control over how they use their asthma medications.[14] A potential advantage of symptom-driven ICS-formoterol is that it may align more closely with patients' preferences and current patterns of use in the real world. However, as it is a novel management strategy, there are no data as to whether a symptom-driven ICS-formoterol regimen is acceptable to patients, or of patients' experiences of using symptom-driven ICS-formoterol to control asthma.

The PRACTICAL study, was an open label study of low dose as-needed budesonide-formoterol for symptom relief or twice daily maintenance budesonide plus as-needed terbutaline for symptom relief.[4] Within this study a subgroup of participants completed a survey at their final study visit, exploring their preferences, beliefs, satisfaction, patterns of use and experience with respect to the study inhaler regimens.

Methods

Description of PRACTICAL study.

The methods and results for the PRACTICAL study are reported in detail elsewhere.[4,15] The PRACTICAL study was a 52 week open label parallel group, multi-centre, phase III randomised control trial undertaken at sites across New Zealand (ACTRN 12616000377437). Adults aged 18 – 75 with a self-reported doctor diagnosis of asthma who were taking either SABA alone or together with

maintenance ICS, and so were eligible for step 2 treatment of the GINA 2014 strategy,[16] were recruited. Participants were randomised to budesonide-formoterol Turbuhaler (Symbicort™) 200/6mcg one inhalation for relief of symptoms as required, or budesonide Turbuhaler (Pulmicort™) 200mcg, 1 inhalation twice a day plus terbutaline (Bricanyl™) 250mcg 2 inhalations as required for relief of symptoms. Neither participants nor investigators were blinded to treatment allocations and no placebo inhalers were used. Both the survey and PRACTICAL study had ethical approval from the Northern B Health and Disability Ethics Committee, reference 15/NTB/178.

Participants

This was a sub-study nested within the PRACTICAL study. Participants at six of the 15 sites in New Zealand who were due their final study visit on or after 26th March 2018 were eligible to complete the survey. Participants who had withdrawn from the study prior to this date but would have otherwise been eligible were contacted and invited to complete the survey retrospectively.

Survey design

The survey design was informed by the study aims and review of the literature; which identified patterns of behaviour with respect to asthma management, poor adherence, beliefs about medicines and preferences for asthma medications as important themes to be explored. Where relevant, we incorporated existing questions.[7,17,18] The full survey is supplied in the supplement. During the survey, participants were asked their preferred choice of future inhaler regimen: this was a dichotomous choice between "*a combined preventer and reliever inhaler taken as needed*" or "*a preventer inhaler taken twice a day every day, with a reliever inhaler taken as needed*". The questions in the rest of the survey represented the following themes (Tables 2 to 7): preferences for preventer inhaler use; beliefs around use of preventer inhalers; satisfaction with the study inhalers; patterns of reliever inhaler use; and, for those randomised to as-needed budesonide-formoterol, their experience of this regimen. Responses were recorded using 5 point Likert scales. The survey was piloted on 11 people with mild asthma to test ease of understanding, relevance of questions, and cognitive burden. Cognitive debriefing techniques were used to enhance feedback on the survey. During pilot testing iterative changes were made to improve the understanding of the survey.

Survey delivery

The survey was undertaken at the final study visit, or if the participant had withdrawn before 26th March 2018 they were invited to return to undertake the survey. Prior to starting the survey all participants provided separate written informed consent and read an information sheet, explaining

the terms ‘preventer’, ‘reliever’ and ‘combination’, and incorporating the relevant part of the original Participant Information Statement to describe the two inhaler regimens that were being investigated in the PRACTICAL study (Figure S1 and legend Table 3). The survey data were collected and managed using REDCap electronic data capture tools hosted at the Medical Research Institute of New Zealand.[19,20] The participants self-completed the survey online in the same room as an investigator; if they had a query they were referred to the information sheet or asked to answer the question to the best of their ability.

Outcomes

The primary outcome was the proportion of participants stating a preference for each regimen in response to the question “which of the following asthma treatment plans would you prefer? A combined preventer and reliever inhaler taken as needed or a preventer inhaler taken twice a day every day, with a reliever inhaler taken as needed?”

Secondary outcomes included participants’ preferences for and beliefs around preventer inhaler use, satisfaction with study inhalers, patterns of study reliever inhaler use, and experience of using symptom-driven budesonide-formoterol.

Statistical analysis

Continuous variables are described by mean (SD) or median (IQR), categorical variables including the primary outcome by frequencies and proportions, expressed as a percentage. The association between regimen preference and randomised treatment was analysed by logistic regression and an interaction term tested if stated preference differed by ICS use prior to randomisation and study randomised treatment. Likert scale secondary outcome variables were analysed by ordinal logistic regression to estimate the association with randomised treatment and an interaction term tested if response differed by ICS use prior to randomisation and study randomised treatment. For descriptive purposes agree/strongly agree responses were aggregated. No corrections were made for multiple analyses and the secondary analyses should be considered exploratory.

SAS version 9.4 (SAS Institute Inc., Cary, USA) was used for all analyses.

Results

407 participants were eligible to undertake the survey. Participant flow is shown in Figure S2; 307/407 (75%) participants started the survey and 306 completed it. Participants who started the survey were older, had higher self-reported pre-study ICS adherence and were less likely to have withdrawn early than those who did not (Table 1). Baseline characteristics of those who started the

survey by randomised treatment are given in the supplement (Table S2). Similar proportions of participants from each randomisation arm completed the survey. Of those who started the survey, 20 (6.5%) had withdrawn from the RCT before completion; these 'early-withdrawers' represented 26% of the 76 participants who were withdrawn. Reasons for early withdrawal and for not undertaking the survey are given in Figure S2.

Primary outcome

Most participants stated a preference for the treatment regimen to which they had been randomised. Of those randomised to budesonide-formoterol as needed 135/150 (90%, 95%CI 85.2 to 94.8) preferred combination preventer and reliever as needed and 15/150 (10%) preferred twice daily preventer inhaler with a reliever inhaler as required. By contrast, of those randomised to maintenance budesonide plus as-needed terbutaline 63/156 (40%, 95%CI 32.7 to 48.1) preferred combination preventer and reliever as needed, and 93/156 (60%) preferred twice daily preventer inhaler with a reliever inhaler as required. Overall, a combined preventer and reliever inhaler taken as needed was the preferred regimen in 198/306 (65%; 95% CI 59.4 to 70.1) and a preventer inhaler taken twice a day with a reliever inhaler as needed was the preferred regimen in 108/306 (35%). Participant characteristics by randomised treatment and preferred regimen are given in Table 2. Regimen preference in the 20 participants who withdrew from the study early and completed the survey are given in Table S3; the as-needed combination regimen was preferred by 3/7 (43%) of early-withdrawers randomised to as-needed budesonide-formoterol.

The odds ratio for association between randomised treatment and preference for a combined preventer and reliever inhaler was 13.3 (95% CI 7.1 to 24.7), p<0.001 (Table 3). The odds ratio after adjustment for whether the participant was taking maintenance ICS or not prior to randomisation was 13.6 (95% CI 7.3 to 25.5), p<0.001, suggesting that ICS use prior to randomisation did not change the association between randomised treatment and regimen preference.

Secondary outcomes

Numbers and proportions of participants who agreed/strongly agreed (Tables 4, 5 and 7) or who were satisfied/very satisfied (Table 6) are summarised by randomised treatment and regimen preference.

Preferences around preventer inhaler type and use (Table 4)

Participants randomised to as-needed therapy were more likely to prefer not to take an inhaler every day, express a preference for being able to adjust dosing, and for all asthma medications to be combined into a single inhaler (Table 4). Again, there was strong evidence of variation in response by

randomisation arm, and these effects were not modified by ICS use prior to randomisation. The proportions of participants who agreed/strongly agreed to these questions were similar for participants who had expressed a preference for as-needed treatment between both randomised treatment arms.

Beliefs around asthma and preventer inhaler use (Table 5)

Participants randomised to budesonide-formoterol as needed were more likely to believe that a daily preventer was not necessary when they were feeling well, to have concerns about taking too much medication when they were feeling well, to consider it normal to get asthma symptoms and to have confidence in being able to intervene when asthma symptoms were worsening. There was no evidence of effect modification from use of ICS prior to randomisation. While more participants randomised to budesonide-formoterol as needed were willing to accept more asthma symptoms to avoid taking a daily preventer, numbers expressing agreement with this statement were low.

Satisfaction with study inhalers (Table 6)

Satisfaction with each study inhaler in all three domains (inhaler effectiveness, frequency of use, and speed of action [reliever inhaler only]) was high. For each of the three domains, participants were more likely to be satisfied/very satisfied if they had been randomised to as-needed budesonide-formoterol. There was no evidence of effect modification from use of ICS prior to randomisation.

Patterns of reliever inhaler use during the study (Table 7)

For this set of statements there was weak, or no association with randomised treatment. Most participants agreed they always carried their reliever inhaler with them and took their reliever inhaler as soon as they got mild symptoms. However in both randomised groups around one third waited until asthma was having an impact on what they were doing and almost 20% tried to avoid taking their reliever inhalers as much as possible. Approximately 30% admitted difficulty in recognising asthma symptoms. Responses to questions regarding timing of reliever inhaler use and numbers of participants who experienced an exacerbation are given in table S4.

Experience of using budesonide-formoterol as symptom-driven preventer and reliever (Table 8)

Amongst participants randomised to as-needed budesonide-formoterol, 32/151 (21%) agreed/strongly agreed they would have preferred to take a regular preventer inhaler to stop them getting asthma symptoms and 102/151 (68%) disagreed/strongly disagreed. Over one-third (55/150, 37%) agreed/strongly agreed they were apprehensive about not taking their usual reliever inhaler any more. 111/150 (74%) reported that they had felt confident in using budesonide-formoterol as a

reliever inhaler at the start of the study and 138/150 (92%) reported that they felt confident with using budesonide-formoterol as reliever inhaler by the end of the study. Approximately one third felt the onset of budesonide-formoterol was faster than their previous reliever inhalers, one third were uncertain and one third felt onset was slower than their previous reliever. In all 66/150 (44%) felt the duration of relief from budesonide-formoterol was longer than their previous reliever inhalers.

Discussion

This study has shown that the regimen that participants preferred, and their response to questions on preferences for and beliefs around preventer inhalers were strongly associated with their randomised treatment. Most participants preferred their randomised treatment, however a higher proportion of participants randomised to as-needed budesonide-formoterol than maintenance budesonide preferred their randomised treatment (90% versus 60%), and use of ICS prior to randomisation did not affect preference. This suggests that patients are likely to prefer to use budesonide-formoterol as needed if they have experienced this regimen. Although most patients randomised to regular budesonide maintenance preferred this treatment, patients may have been better able to make an informed choice after experiencing both regimens, and the regimen participants preferred may have reflected their satisfaction with their randomised treatment. Overall, our findings are consistent with evidence from other studies that show patients want quick symptom relief[21] and a flexible, easy to use asthma regimen over which they are in control.[13,14,22]

While most participants were satisfied with their study inhalers, participants randomised to budesonide-formoterol inhaler reported higher degrees of satisfaction in all three domains investigated (inhaler effectiveness, frequency of use, and speed of onset of the reliever inhaler) than those randomised to maintenance budesonide plus as-needed terbutaline.

This study complements findings from the SYGMA 1 & 2, Novel START and PRACTICAL studies[1–4] that symptom-driven budesonide-formoterol is a safe and effective alternative in mild to moderate asthma and suggests the new GINA recommendation for symptom-driven ICS-formoterol at steps 1 and 2[5] may be preferred by many patients over the alternative, maintenance ICS with a separate as-needed SABA reliever.

Most participants randomised to symptom-driven budesonide-formoterol rated their experiences of using this regimen favourably. While some participants reported they had been apprehensive about switching reliever, nearly all participants (92%) said that they were confident in using budesonide-

formoterol as a reliever by the end of the study. Hence, if a patient expresses reservations about this regimen, it may be worth suggesting they may wish to try it for a period of time, as after a 12 month trial of the budesonide-formoterol reliever therapy 90% of patients expressed a preference for this regimen.

It might be assumed that in order for budesonide-formoterol reliever therapy to be safe and effective, patients would need to take the inhaler in response to symptoms and not delay or avoid using it. We found that some patients admitted having difficulty recognising if a symptom was due to asthma or avoided or delayed taking their reliever inhalers. It is reassuring that they were in the minority with similar numbers in both treatment arms and that this pattern of response was not linked with a higher exacerbation rate (Table S4). However, identification of symptoms and appropriate use of reliever inhalers should be considered when starting a patient on either therapeutic regimen, and they should be provided with education about when to use inhalers.

We pre-specified that we would examine the effect of ICS use prior to randomisation on preferences as we considered this was the characteristic most likely to have an effect. In fact, ICS use prior to randomisation did not affect response to any of the questions in the survey. We opted not to test interaction with other co-variates due to risk of type 1 error inflation. Because the overwhelming majority (90%) of participants who were randomised to as-needed budesonide-formoterol preferred this treatment, randomised treatment was likely to dominate other characteristics. However, the participants in both treatment groups who did not prefer their randomised treatment are of interest. Review of their characteristics (Table 2) suggests that they had worse asthma symptom control at the end of the study than those who preferred their randomised treatment. There were too few asthma exacerbations to assess the effect of experiencing an exacerbation during the study on regimen preference. It may be that regimen preference may be related to the individual's experience of using that regimen, particularly for those randomised to maintenance budesonide, in addition health beliefs or factors specific to the individual may have an influence.

While we have shown that, among adult RCT participants with mild asthma, symptom-driven preventer reliever therapy was preferred to twice daily preventer therapy with a reliever as required, we did not compare this with other regimens such as once daily preventer therapy plus as-needed SABA or single maintenance and reliever therapy (SMART). We did not ask participants their preferred regimen at the start of the trial so we cannot comment if their preferences changed. Participants randomised to maintenance budesonide did not have the opportunity to experience both regimens, whereas 88% of those randomised to budesonide-formoterol as needed had used maintenance ICS during their lifetime. Therefore the preferred treatment particularly of those

randomised to maintenance budesonide may reflect their satisfaction with their current regimen rather than a preference for maintenance treatment over as-needed treatment.

We asked participants to answer some questions on reliever and preventer inhaler use to reflect what they did or felt during the study, so the results for these questions will be vulnerable to recall bias. The key question about preferred regimen was asked after the participant had answered multiple questions about their beliefs, attitudes and experiences about asthma and treatment, so reflection on these issues may have influenced regimen preference. In addition mood or prior expectation of undertaking the survey may have influenced response. As the survey was completed in the same room as an investigator it is possible that they may also be affected by social desirability bias. To limit cognitive burden we did not include any consistency check questions. We opted not to exclude any questions for central tendency of response (where the middle option is chosen above all others) or straight lining (where the same option is repeatedly chosen) therefore we did not undertake any checks for these. Secondary endpoints were not adjusted for multiplicity of analyses and should not be used to infer definitive outcomes.

Other limitations of the current study are that 100 eligible participants did not complete the survey. Comparison of their baseline demographics suggests that they may have been different from those who did. Participants who withdraw early from an RCT are more likely to have been non-responders,[23] and, as suggested by the treatment preferred by the small proportion of withdrawers who completed the survey (Table S4), it is possible that the responses of other early-withdrawers could have been quite different from those that did complete the survey. This may affect the representativeness of our results; however there was a similar non-completion rate between the two treatment arms. In addition the preferences of patients with mild asthma in the general population may be different from those who are willing to take part in an RCT for a year.

The strengths of this study are that it was investigator conceived, designed and implemented. It was independently funded with no involvement of pharmaceutical industry at any point. It was nested within the context of a RCT and is the first study to report on patient preference for and experiences of using as-needed budesonide-formoterol in mild asthma. The survey was implemented before the results of the SYGMA 1 and 2 studies[1,2] and the Novel START study[3] had been published. Therefore we feel it is unlikely that participants would have been influenced by the results of these studies.

Our study highlights how investigation of patient preferences can be incorporated into RCTs. This may help us to understand the differences between effectiveness and efficacy seen when a treatment moves from a RCT into clinical practice,[24] in which factors such as patient preferences and experience of a treatment are likely to play a role. Information on how different attributes of

treatment regimens influence patient preferences, which can be determined from conjoint analysis methods such as discrete choice experiments, would provide additional understanding. Deeper understanding of patient preferences will also be obtained from qualitative interviews. As ICS-formoterol as needed is incorporated into clinical practice, patient preferences for and experiences of using this regimen should be examined to determine if they are congruent with the patterns observed in this population of patients completing this RCT.

In conclusion, participants' future preference for inhaler regimen was strongly influenced by their randomised treatment; particularly if they had been randomised to budesonide-formoterol as needed with 90% preferring this regimen to maintenance budesonide plus as-needed reliever. This suggests that in clinical practice decision-making by a clinician and a patient about treatment of mild asthma could include the option of a trial of as-needed ICS-formoterol.

Role of the funding source

The PRACTICAL study and the survey were funded through a programme grant (15/573) provided by the Health Research Council of New Zealand to the study sponsor, the Medical Research Institute of New Zealand (MRINZ). MRINZ had overall responsibility for the study conduct, monitoring and data management. The funder had no role in the design, data collection, data analysis or interpretation, or writing of the manuscript. All authors had full access to the data analysis report, assisted in the writing of the manuscript and approved the final version.

Data sharing statement

De-identified individual participant preference data collected during 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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The study was funded through a programme grant (15/573) provided by the Health Research Council of New Zealand to the study sponsor, the Medical Research Institute of New Zealand. MRINZ had overall responsibility for the study conduct, monitoring, and data management. The randomised medications were purchased commercially. We thank the participants for their time and involvement and the PRACTICAL study team (listed in the supplement).

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Table 1: Participant characteristics

Characteristic	Survey not started (n=100)	Survey started (n=307)*
Randomised treatment		
Budesonide-formoterol – no. (%)	52 (52)	151 (49)
Maintenance budesonide – no. (%)	48 (48)	156 (51)
Baseline characteristics		
Age – yr	30.1 (10.6)	45.9 (16.2)
Female sex – no. (%)	50 (50)	172 (56)
Ethnicity – no. (%)		
Asian	10 (10)	17 (6)
NZ European	67 (67)	247 (81)
Maori	11 (11)	24 (8)
Other	4 (4)	5 (2)
Pacific	8 (8)	14 (5)
Smoking status – no. (%)		
Current smokers	9 (9)	14 (5)
Ex-smokers	28 (28)	77 (26)
Never smokers	63 (63)	214 (70)
Pack years (among ever smokers)	3.5 (3.6)	5.4 (5.0)
Age at diagnosis – yr		
Mean	11.2 (10.7)	21.1 (19.3)
Median	7 (4-15.5)	14 (5-33)
Self-reported ICS use in the 12 weeks prior to randomisation – no. (%)	66 (66)	215 (70)
Self-reported ICS adherence – (%)¥	40.5(32.8) (n=66)	57.0 (35.9) (n=215)
Self-reported ICS use ever – no. (%)	71 (71)	264 (86)
Self-reported frequency of SABA use in 4 weeks prior to randomisation		
Mean (SD)	4.0 (4.0)	4.0 (5.2)
Median (IQR)	3 (1 to 5)	2 (1 to 5)
Min to max	0 to 88	0 to 28
Participants with ≥1 lifetime hospital admissions for asthma — no. (%)	18 (18)	40 (13)
Participants with ≥1 severe exacerbation in the 12 months prior to study entry – no. (%)	14 (14)	28 (9)
GINA level of asthma symptom control at randomisation no.(%)		
Well controlled	10 (10)	76 (25)
Part controlled	50 (50)	151 (49)
Uncontrolled	40 (40)	80 (26)
End of study characteristics**		
Final visit ACQ-5†	0.97 (0.88) (n=56)	0.78 (0.72) (n=307)
Final visit on treatment FEV1 % of predicted value‡	88.3 (15.9) (n=54)	89.2 (14.8) (n=307)
Final visit median FeNO – ppb (IQR)	40.5 (28-58) (n=54)	23 (15-40) (n=307)
Participants experiencing ≥1 exacerbation or severe exacerbation during the study – no. (%)	15 (15)	47 (15.3)

Number of severe exacerbations during the study – no. (%)		
0	86 (86)	273 (89)
1	12 (12)	27 (9)
2	2 (2)	7 (2)
Early withdrawal – no. (%)	56 (56)	20 (7)

Values are expressed as means (SD) unless otherwise indicated. FeNO denotes fraction of exhaled nitric oxide, FEV1 forced expiratory volume in 1 second, IQR interquartile range, ppb parts per billion, and SABA short-acting β2-agonist.

*307 participants started the survey and 306 completed it.

¥ Patient-reported adherence to ICSs 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 specific instruction to withhold use of their bronchodilator before measurement of FEV1.[25]

** End of study characteristics were collected at the final study visit (either on completion of the study or on early withdrawal). The preferences survey was optional so not all participants who attended a final study visit completed the survey. The higher rate of missing data in those who did not start the survey is due to participants who withdrew early without a final study visit or were lost to follow up in this group. Participant flow is presented in Figure S2.

Table 2: Participant characteristics by randomised treatment and regimen preference

Randomised treatment	**Budesonide-formoterol as needed**		**Maintenance budesonide plus as-needed terbutaline**	
Preferred treatment	Combined preventer and reliever inhaler taken as needed	Preventer inhaler taken twice a day with a reliever inhaler as needed	Combined preventer and reliever inhaler taken as needed	Preventer inhaler taken twice a day with a reliever inhaler as needed
Baseline characteristics				
Number	135	15	63	93
Age – yr	45.6 (14.5)	44.1 (23.2)	41.8 (16.1)	47.7 (17.1)
Female sex – no. (%)	78 (58)	10 (67)	33 (52)	50 (54)
Age at diagnosis – yr				
Mean (SD)	19.7 (17.9)	23.9 (26.9)	18.7 (18.7)	24.1 (20.1)
Median (IQR)	14 (4-31.5)	7 (4-42)	12 (5-25.5)	18 (6-40)
Self-reported frequency of SABA use in 4 weeks prior to randomisation				
Mean	3.9 (5.1)	4.4 (5.9)	4.2 (4.9)	3.9 (5.5)
Median	2 (1-5)	2 (0.5-5)	2 (1-5)	2 (1-4)
Self-reported ICS use in the 12 weeks prior to randomisation– no. (%)	93 (69)	11 (73)	39 (62)	72 (77)
Self-reported ICS use ever – no. (%)	119 (88)	14 (93)	51 (81)	80 (86)
Self-reported ICS adherence – (%)¥	53.1 (36.7)	67.5 (33.3)	53.3 (38.2)	62.6 (33.7)
Participants with ≥1 lifetime hospital admissions for asthma— no. (%)	20 (15)	2 (13)	8 (13)	10 (11)
Participants with ≥1 severe exacerbation in the 12 months prior to study entry no.%	12 (9)	1 (7)	7 (11)	8 (9)
Ever smoker no.(%)	42 (31)	4 (27)	20 (32)	26 (28)
Pack years (among ever smokers)	5.2 (4.3)	5.8 (7.8)	6.5 (5.9)	5.2 (5.2)
GINA level of asthma symptom control at randomisation no.(%)				
Well controlled	28 (21)	7 (47)	12 (19)	29 (31)
Part controlled	68 (50)	4 (27)	35 (56)	44 (47)

Uncontrolled	39 (29)	4 (27)	16 (25)	20 (22)
End of study characteristics				
Final visit ACQ-5†	0.84 (0.64)	1.00 (0.76)	0.82 (0.84)	0.62 (0.73)
Final visit median FeNO – ppb (IQR)	22 (15 to 38.5)	22 (15 to 47.5)	22 (13 to 36.5)	23 (15 to 40)
Final visit on treatment FEV1 % of predicted value‡	89.5 (14.8)	92.6 (17.6)	89.7 (14.4)	88.0 (14.9)
Participants who experienced ≥1 exacerbation or severe exacerbation during the study – no. (%)	16 (12)	1 (7)	12 (19)	18 (19)
Early withdrawal – no. (%)	3 (2)	4 (27)	6 (10)	7(8)

Values are expressed as means (SD) unless otherwise indicated. FeNO denotes fraction of exhaled nitric oxide, FEV1 forced expiratory volume in 1 second, IQR interquartile range, ppb parts per billion, and SABA short-acting β2-agonist.

¥ Patient-reported adherence to 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 specific instruction to withhold use of their bronchodilator before measurement of FEV1.[25]

Table 3: Regimen preference

Randomised treatment	**Preferred treatment, n (%)**			
	*Combined preventer and reliever inhaler taken as needed	±Preventer inhaler taken twice a day with a ¥reliever inhaler as needed	Odds ratio & 95% CI preference for combined vs regular treatment	P
Budesonide-formoterol n=150	135 (90)	15 (10)		
Maintenance budesonide n=156	63 (40)	93 (60)		
Total n=306	198 (65)	108 (35)	13.3 (7.1 to 24.7)	<0.001
After adjustment for ICS use prior to randomisation			13.6 (7.3 to 25.5)	<0.001

Descriptions given to participants prior to starting the survey were as follows (see Appendix for full details):

* Combined preventer and reliever inhaler: In the study, you may have been using Symbicort (red) as a combined preventer and reliever when you had asthma symptoms.

± Preventer inhaler: contains a corticosteroid to reduce inflammation. This type of inhaler is normally used regularly twice a day to prevent asthma symptoms and reduce the risk of flare-ups. In the study you may have been using Pulmicort (brown) inhaler twice a day as your preventer. Other preventer inhalers you may have taken before the study are Beclazone (brown) or Flixotide (orange).

¥ Reliever inhaler: used when you are getting symptoms of asthma such as breathlessness, wheeze, tight-chested or cough. You may have been on a Ventolin or Respigen inhaler as your reliever before the study. In the study you would have used either Bricanyl (blue) or Symbicort (red) inhaler as your reliever inhaler.

Table 4: Preferences around preventer inhaler use

Participants who agree or strongly agree with the following statement, n (%)								
Randomised treatment	Budesonide-formoterol* n=151		Maintenance budesonide n=156		Budesonide formoterol overall	Maintenance budesonide overall	±Odds ratio & 95% CI	P
Preferred treatment	As needed preference n=135	Maintenance preference n=15	As needed preference n=63	Maintenance preference n=93	n=151	n=156		
I would prefer not to take a preventer inhaler every day if I don't have asthma symptoms	110 (82)	4 (27)	48 (76)	34 (37)	115 (76)	82 (53)	2.98 (1.93 to 4.59)	<0.001
I would prefer to take a preventer inhaler every day to try and avoid as many symptoms as possible¥[7]	51 (38)	13 (87)	27 (43)	80 (86)	64 (42)	107 (69)	3.01 (1.96 to 4.60)	<0.001
I would prefer to adjust the amount of my preventer inhaler to the changes in my asthma taking less when feeling well and more when feeling worse[7]	101 (75)	4 (27)	41 (65)	31 (33)	106 (70)	72 (46)	2.62 (1.71 to 4.0)	<0.001
I would prefer all my asthma medications to be combined into one inhaler	120 (89)	5 (33)	52 (83)	17 (18)	126 (83)	69 (44)	6.29 (3.99 to 9.93)	<0.001

±Odds ratio greater than one indicates survey respondents were more likely to agree with the statement if randomised to as needed budesonide-formoterol than if randomised to maintenance budesonide plus as-needed terbutaline.

* One participant randomised to as needed budesonide-formoterol did not complete the survey. If they agreed/strongly agreed with a statement then the sum of the as needed preference and maintenance preference columns will be one less than the overall.

¥Direction of response was in the opposite direction to all other questions, this was reversed for analysis.

Table 5: Beliefs around preventer inhaler use

Participants who agree or strongly agree with the following statement, n (%)								
Randomised treatment	Budesonide-formoterol*		Maintenance budesonide		Budesonide formoterol overall	Maintenance budesonide overall	Odds ratio & 95% CI	P
Preferred treatment	As needed preference n=135	Maintenance preference n=15	As needed preference n=63	Maintenance preference n=93	n=151	n=156		
I am confident I know my asthma well enough to intervene early to try and prevent worsening symptoms.[17]	120 (89)	11 (73)	51 (81)	74 (80)	132 (87)	125 (80)	1.89 (1.21 to 2.94)	0.005
I consider it normal for me to get symptoms of asthma.	97 (72)	10 (67)	43 (68)	56 (60)	107 (71)	99 (63)	1.59 (1.03 to 2.48)	0.039
When I feel well, I believe there is no need to take a preventer inhaler every day.[7]	90 (67)	4 (27)	32 (51)	18 (19)	95 (63)	50 (32)	3.94 (2.57 to 6.04)	<0.001
I am willing to accept having asthma symptoms more often if it means I don't have to take a preventer inhaler every day	41 (30)	1 (7)	15 (24)	6 (6)	42 (28)	21 (13)	2.58 (1.69 to 3.94)	<0.001
I am concerned about taking too much medication when I am well.[7]	69 (51)	3 (20)	27 (43)	23 (25)	73 (48)	50 (32)	1.85 (1.23 to 2.78)	0.003

±Odds ratio greater than one indicates survey respondents were more likely to agree with the statement if randomised to as needed budesonide-formoterol randomised treatment than if randomised to maintenance budesonide.

* One participant randomised to as needed budesonide-formoterol did not complete the survey. If they agreed/strongly agreed with a statement then the sum of the as needed preference and maintenance preference columns will be one less than the overall.

Table 6: Satisfaction with study inhalers

Participants who were satisfied or very satisfied with the following domains, n (%)											
Inhaler	Budesonide-formoterol* inhaler n=151		Terbutaline inhaler n=147¥		Budesonide inhaler n=156		Budesonide-formoterol inhaler overall	Terbutaline inhaler overall	Budesonide inhaler overall	Odds ratio & 95% CI budesonide formoterol vs terbutaline	Odds ratio & 95% CI budesonide formoterol vs budesonide
Preferred treatment	As needed preference n=135	Maintenance preference n=15	As needed preference n=59	Maintenance preference n=88	As needed preference n=63	Maintenance preference n=93	n=151	n=147¥	n=156		
Inhaler effectiveness[18]	129 (96)	10 (67)	51 (86)	76 (86)	51 (81)	84 (90)	140 (93)	127 (86)	135 (87)	2.74 (1.74 to 4.29) p<0.001	2.37 (1.53 to 3.68) p<0.001
Frequency of inhaler use[18]	125 (93)	8 (53)	48 (81)	76 (86)	41(65)	81 (87)	134 (89)	124 (84)	122 (78)	1.90 (1.21 to 2.97) p=0.005	2.26 (1.46 to 3.51) p<0.001
Reliever inhaler speed of action[18]α	118 (87)	10 (67)	46 (78)	69 (78)	---	---	129 (85)	115 (78)	---	1.56 (1.01 to 2.41) p=0.044	---

±Odds ratio greater than one indicates survey respondents were more likely to agree with the statement if randomised to as needed budesonide-formoterol randomised treatment than if randomised to maintenance budesonide.

¥Participants randomised to maintenance budesonide only saw questions on the terbutaline inhaler if they answered yes to using the inhaler during the study. Nine patients answered no.

α Question only asked regarding budesonide-formoterol and terbutaline inhalers

* One participant randomised to as needed budesonide-formoterol did not complete the survey. If they agreed/strongly agreed with a statement then the sum of the as needed preference and maintenance preference columns will be one less than the overall.

Table 7: Patterns of reliever use during the study

Participants who agree or strongly agree with the following statement, n (%)								
Randomised treatment	Budesonide-formoterol*		Maintenance budesonide		Budesonide formoterol overall	Maintenance budesonide overall	Odds ratio & 95% CI	P
Preferred treatment	As needed preference n=135	Maintenance preference n=15	As needed preference n=63	Maintenance preference n=93	n=151	n=156		
I always carried my reliever inhaler with me	107 (79)	9 (60)	44 (70)	58 (62)	117 (77)	102 (65)	1.67 (1.10 to 2.53)	0.016
Sometimes I found it difficult to know if a symptom was due to asthma or not	41 (30)	3 (20)	20 (32)	29 (31)	43 (28)	49 (31)	1.03 (0.68 to 1.57)	0.89
I took my reliever as soon as I got mild asthma symptoms	91 (67)	8 (53)	42 (67)	59 (63)	100 (66)	101 (65)	1.25 (0.81 to 1.94)	0.31
I waited until asthma symptoms were having an impact on what I was doing before I took my reliever inhaler	48 (36)	6 (40)	26 (41)	32 (34)	54 (36)	58 (37)	1.01 (0.66 to 1.53)	0.98
I tried to wait as long as possible before I took my reliever inhaler	22 (16)	4 (27)	10 (16)	15 (16)	26 (17)	25 (16)	1.36 (0.87 to 2.15)	0.18
I tried to avoid taking my reliever inhaler as much as possible	23 (17)	3 (20)	11 (17)	16 (17)	27 (18)	27 (17)	0.97 (0.62 to 1.51)	0.88
There were times when I felt I should have taken the reliever inhaler but didn't	53 (39)	8 (53)	19 (30)	25 (27)	61 (40)	44 (28)	1.67 (1.10 to 2.54)	0.017
I usually took my reliever before or during exercise	65 (48)	5 (33)	27 (43)	31 (33)	71 (47)	58 (37)	1.61 (1.07 to 2.43)	0.024

* One participant randomised to as needed budesonide-formoterol did not complete the survey. If they agreed/strongly agreed with a statement then the sum of the as needed preference and maintenance preference columns will be one less than the overall.

Table 8: Experience of using budesonide-formoterol as symptom-driven preventer and reliever

	Agree/strongly agree	Uncertain	Disagree/strongly disagree
I would have preferred to take a regular preventer inhaler to stop me getting asthma symptoms n=151 no.(%)	32 (21)	17 (11)	102 (68)
I was apprehensive about not taking the reliever inhaler I was on before the study any more n=150 no.(%)	55 (37)	20 (13)	75 (50)
	Confident/very confident	Uncertain	Unconfident/very unconfident
Confidence in using budesonide-formoterol as a reliever inhaler at the start of the study n=150	111 (74)	28 (19)	11 (7)
Confidence in using budesonide-formoterol as a reliever inhaler at the end of the study n=150 no.(%)	138 (92)	5 (3)	7 (5)
	A bit/ a lot faster	About the same	A bit/a lot slower
Compared to the reliever inhaler I was on before the study, I felt that when I took the budesonide-formoterol inhaler, it worked: no.(%)	58 (39)	43 (29)	49 (33)
	A bit/a lot longer	About the same	A bit/a lot shorter
Compared to the reliever inhaler I was on before the study, I felt the length of time the budesonide-formoterol inhaler worked for after I took a puff was: no.(%)	66 (44)	60 (40)	24 (16)

Patient preferences for symptom-driven or regular preventer treatment in mild to moderate asthma – findings from the PRACTICAL study, a randomised clinical trial.

Supplementary Appendix

PRACTICAL Study Team

Clinical Horizons (Tauranga, New Zealand): Andrew Corin, Liz Dronfield, Colin Helm, Tracy Paterson; Bhuwan Poudel; Coastal Medical Rooms (Kapiti, New Zealand): Malcolm Dyer, Christine Jasinski; Culloden Research (Papamoa, New Zealand): Davitt Sheahan, Pamela Sheahan; Greenhithe Medical Centre (Auckland, New Zealand): Nick Gailer, Jan Van Zuilen; Henderson Medical Centre (Auckland, New Zealand): Andy Basa, Christine Devereaux, Karin Egan, Sneha Haughey, Rodney Marks, Dirk Venter, Hank Zhang; Lakeland Clinical Trials (Rotorua, New Zealand): Karen Trevithick, Mike Williams, Philippa Williams; Medical Research Institute of New Zealand and Lower Hutt After Hours Medical Centre (Wellington, New Zealand): Christina Baggott, Richard Beasley, Irene Braithwaite, Alexandra Eathorne, Stefan Ebmeier, James Fingleton, Daniela Hall, Jo Hardy, Matire Harwood, Mark Holliday, Claire Houghton, Saras Mane, John Martindale, Karen Oldfield, Janine Pilcher, Donah Sabbagh, Philippa Shirtcliffe, Suzanne Snively, Jenny Sparks, Alexandra Vohlidkova, Mathew Williams; Optimal Clinical Trials Ltd (Auckland, New Zealand): Patrick Collins, Summer Hassan, Annika Lam, Claudette Lionnet, Barney Montgomery, Liz Smaill; P3 Clinical Trials (Wellington, New Zealand): Stella Moon, Dean Quinn; RMC Medical Research (Dunedin, New Zealand): Elena Bayly-McCredie, Chris Millar-Coote, Dean Millar-Coote, Jim Reid, Anna Samuel; South Pacific Clinical Trials (Auckland, New Zealand): Nicola Burton, Tina Mullard, Tyronne Tranquilino, Edward Watson; Southern Clinical Trials (Auckland, New Zealand): Jill Bell, Rachel Harris, John Richmond, Sue Smith; Team Medical (Kapiti, New Zealand): Brent Krivan, Cheryl Robertson; University of Otago, Dunedin: Robert J Hancox; University of Otago, Wellington: Mark Weatherall; Waikanae Medical Centre (Kapiti, New Zealand): Sue Glensor, Dermot O'Connor, Anne-Christine Porrachia; Woolcock Institute of Medical Research (Sydney, Australia): Helen K Reddel

Figure S1:

Explanation of Terms in the Survey

Reliever inhaler: used when you are getting symptoms of asthma such as breathlessness, wheeze, tight-chested or cough. You may have been on a Ventolin or Respigen inhaler as your reliever before the study. In the study you would have used either Bricanyl (blue) or Symbicort (red) inhaler as your reliever inhaler.

Preventer inhaler: contains a corticosteroid to reduce inflammation. This type of inhaler is normally used regularly twice a day to prevent asthma symptoms and reduce the risk of flare-ups. In the study you may have been using Pulmicort (brown) inhaler twice a day as your preventer. Other preventer inhalers you may have taken before the study are Beclazone (brown) or Flixotide (orange).

Combined preventer and reliever inhaler: In the study, you may have been using Symbicort (red) as a combined preventer and reliever when you had asthma symptoms.

The different inhaler regimens in the study:

Regimen	**What inhalers are given and why?**	**When would I take the inhaler(s)?**	
Symbicort	Symbicort inhaler Combined preventer and reliever This contains: - a beta- agonist to quickly open up the airways - a steroid to reduce airway inflammation	When I have symptoms	
Pulmicort and Bricanyl	Bricanyl inhaler Reliever inhaler This contains a beta- agonist to quickly open up the airways	When I have symptoms	
	Pulmicort inhaler Preventer inhaler This contains a steroid to reduce airway inflammation	Morning and night	

Figure S2: Flow of participants through the PRACTICAL study and the survey

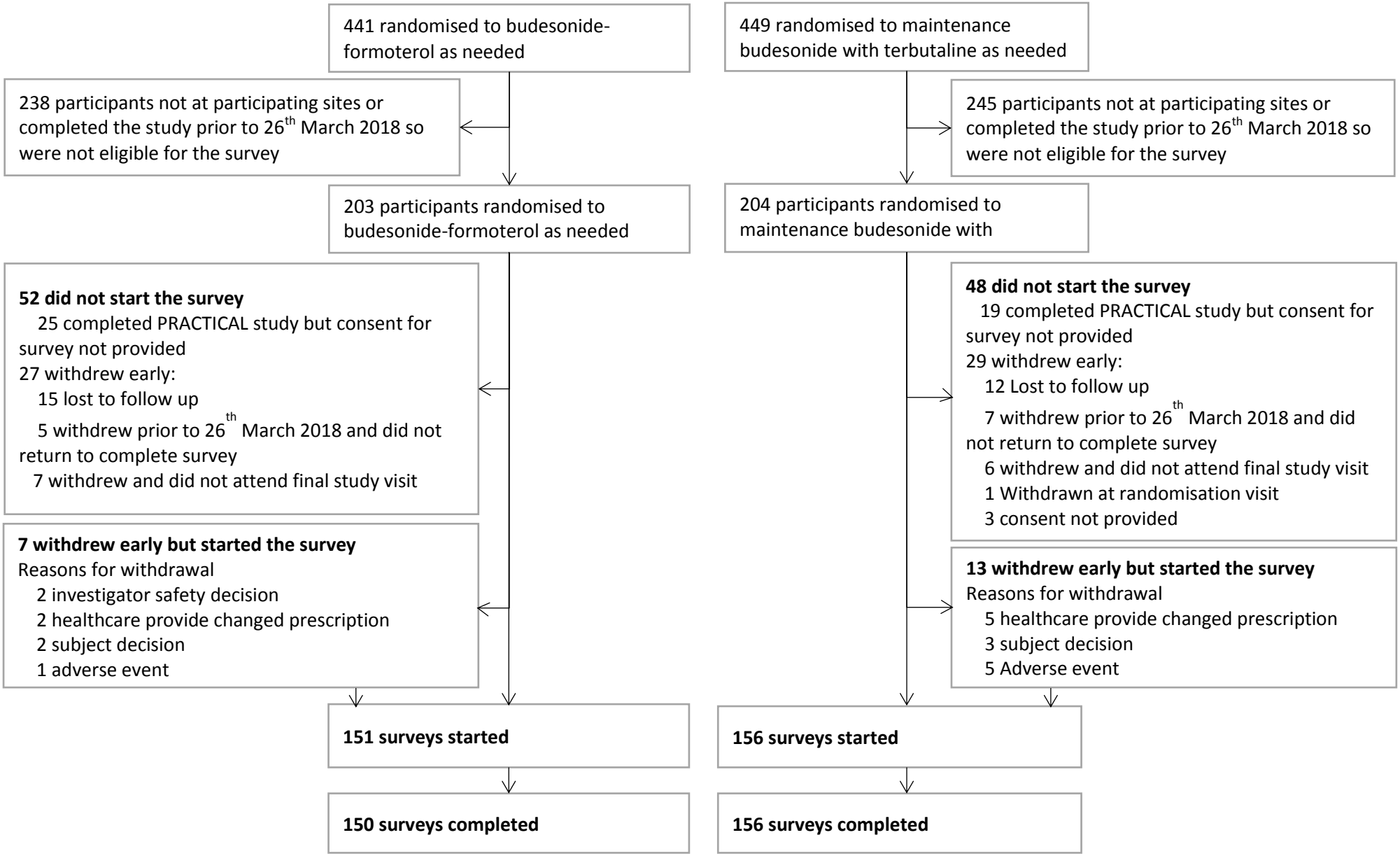

Table S1: Complete survey

Below is the complete survey, with themes. Where a question has been taken from prior publications the reference is supplied.

Question themes: preferences around preventer inhaler use (theme 1) and beliefs about preventer inhaler use (theme 2). Themes are numbered in the left column (not shown to participants)

Question Theme	Following are some questions about your asthma and asthma treatment. Please put a tick in the box which is closest to how you feel.	Strongly Disagree	Disagree	Uncertain	Agree	Strongly Agree
2	When I feel well, I believe there is no need to take a preventer inhaler every day.[1]					
2	I am willing to accept having asthma symptoms more often if it means I don't have to take a preventer inhaler every day.					
1	I would prefer not to take a preventer inhaler every day if I don't have asthma symptoms.					
2	I am concerned about taking too much medication when I am well.[1]					
1	I would prefer to adjust the amount of my preventer inhaler to the changes in my asthma, taking less when feeling well and more when feeling worse.[1]					
1	I would prefer to take a preventer inhaler every day to try and avoid as many symptoms as possible.[1] *					
1	I would prefer all my asthma medications to be combined into one inhaler.					
2	I am confident I know my asthma well enough to intervene early to try and prevent worsening symptoms.[2]					
2	I consider it normal for me to get symptoms of asthma.					

* Question [q6_gp1]: the direction of response is opposite to the questions above. If a participant agreed they are indicating they would prefer regular treatment, whereas for the other questions above agreement indicates a preference for symptom driven treatment.

Question themes: Patterns of study reliever inhaler use (theme 3) and experience of using budesonide-formoterol reliever regimen theme (theme 5). Themes are numbered in the left column

Question Theme	Please put a tick in the box which corresponds best to what you felt or did during the study.	Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
3	During the study sometimes I found it difficult to know if a symptom was due to asthma or not					
3	During the study I took my reliever as soon as I got mild asthma symptoms					
3	During the study I waited until asthma symptoms were having an impact on what I was doing before I took my reliever inhaler					
3	During the study I tried to wait as long as possible before I took my reliever inhaler					
3	During the study I tried to avoid taking my reliever inhaler as much as possible					
3	During the study there were times when I felt I should have taken the reliever inhaler but didn't					
5	During the study I would have preferred to take a regular preventer inhaler to stop me getting asthma symptoms¥					
3	I usually took my reliever before or during exercise exercised					
3	I always carried my reliever inhaler with me					

¥ Question asked to budesonide-formoterol arm only

Question theme: Satisfaction with study inhalers (theme 4).

Question Theme	Thinking about how satisfied you were with the budesonide-formoterol inhaler you were on for the study please put a tick in the box which is closest to how you feel.[3]	Very dissatisfied	Dissatisfied	Uncertain	Satisfied	Very satisfied
4	Effectiveness (how well it worked for me)					
4	How fast it acted					
4	How often I needed to take it					

Question Theme	Thinking about how satisfied you were with the budesonide inhaler you were on for the study please put a tick in the box which is closest to how you feel.[3]	Very dissatisfied	Dissatisfied	Uncertain	Satisfied	Very satisfied
4	Effectiveness (how well it worked for me)					
4	How often I needed to take it					

Did you use the Bricanyl inhaler during the study? (following questions on Bricanyl not shown if no selected)

i. Yes/No

Thinking about how satisfied you were with the Bricanyl inhaler you were on for the study please put a tick in the box which is closest to how you feel.

Question Theme	Thinking about how satisfied you were with the terbutaline inhaler you were on for the study please put a tick in the box which is closest to how you feel.[3]	Very dissatisfied	Dissatisfied	Uncertain	Satisfied	Very satisfied
4	Effectiveness (how well it worked for me)					
4	How fast it acted					
4	How often I needed to take it					

Question theme: Experience of using the budesonide-formoterol reliever regimen (theme 5)

Budesonide-formoterol arm only:

Question Theme	Thinking about using budesonide-formoterol as a reliever during the study, please put a tick in the box which you feels best corresponds to how you feel.	Very unconfident	Unconfident	Uncertain	Confident	Very confident
5	How confident were you in using budesonide formoterol as a reliever inhaler at the start of the study?					
5	How confident were you in using budesonide-formoterol as a reliever inhaler at the end of the study?					
5	I was apprehensive about not taking the reliever inhaler I was on before the study (e.g. Ventolin) any more	Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
5	Compared to the reliever inhaler I was on before the study, I felt that when I took a puff of the budesonide-formoterol inhaler, it worked:	A lot slower	A bit slower	About the same	A bit faster	A lot faster
5	Compared to the reliever inhaler I was on before the study, I felt the length of time the budesonide-formoterol inhaler worked for after I took a puff was:	A lot shorter	A bit shorter	About the same	A bit longer	A lot longer

Question theme: overall regimen preference (theme 6).

Regimen preference

Which of the following asthma treatment plans would you prefer?

1. A preventer inhaler taken twice a day every day, with a reliever inhaler taken as needed
2. A combined preventer and reliever inhaler taken as needed.

Table S2: characteristics of participants who started the survey by randomised treatment

	Budesonide-formoterol as needed N=151	Maintenance budesonide N=156
Baseline characteristics		
Age – yr	45.4 (15.5)	45.3 (16.9)
Female sex – no. (%)	89 (59)	83 (53)
Age at diagnosis – yr		
Mean (SD)	20.2 (18.8)	21.9 (19.7)
Median (IQR)	14 (4-31.5)	18 (6-40)
Self-reported frequency of SABA use in 4 weeks prior to randomisation		
Mean (SD)	4.0 (5.2)	4.0 (5.3)
Median (IQR)	2 (1-5)	2 (1-4)
Min to max	0-28	0-28
Self-reported ICS in the 12 weeks prior to randomisation – no. (%)	104 (69)	111 (71)
Self-reported ICS use ever – no. (%)	133 (88)	131 (84)
Self-reported ICS adherence – (%)¥	54.6 (36.5)	59.3 (35.4)
Participants with ≥1 lifetime hospital admissions for asthma — no. (%)	22 (15)	18 (12)
Participants with ≥1 severe exacerbation in the 12 months prior to study entry no.(%)	13 (9)	15 (10)
Ever smoker no.(%)	47 (31)	46 (30)
Pack years (among ever smokers)	5.2 (4.6)	5.7 (5.5)
GINA level of asthma symptom control at randomisation no.(%)		
Well controlled	39 (19)	47 (23)
Part controlled	101 (50)	100 (49)
Uncontrolled	63 (31)	57 (28)
End of study characteristics		
Final visit ACQ-5†	0.86 (0.65)	0.70 (0.78)
Final visit median FeNO – ppb (IQR)	22 (15-41)	23 (14-39)
Final visit on treatment FEV1 % of predicted value‡	89.75 (15.04)	88.66 (14.65)
Participants who experienced ≥1 exacerbation or severe exacerbation during the study – no. (%)	17 (11)	30 (19)
Early withdrawal – no. (%)	7 (5)	13 (8)

Values are expressed as means (SD) unless otherwise indicated. FeNO denotes fraction of exhaled nitric oxide, FEV1 forced expiratory volume in 1 second, IQR interquartile range, ppb parts per billion, and SABA short-acting β2-agonist.

¥ Patient-reported adherence to ICSs 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 specific instruction to withhold use of their bronchodilator before measurement of FEV1.[25]

Table S3: Randomised treatment and regimen preference in the participants who completed the survey after early withdrawal from (n=20) or completion of (n=286) the PRACTICAL study.

Randomised treatment	**Preferred treatment, n (%)**	
	Combined preventer and reliever inhaler taken as needed	Preventer inhaler taken twice a day with a reliever inhaler as needed
Early withdrawal n=20		
Budesonide-formoterol as needed n=7	3 (43)	4 (57)
Maintenance budesonide n=13	6 (46)	7 (54)
Completed the PRACTICAL study n=286		
Budesonide-formoterol as needed n=143	132 (92)	11 (8)
Maintenance budesonide n=143	57 (40)	86 (60)

Table S4: Number and percentage of participants who experienced at least one exacerbation or severe exacerbation and response to questions on patterns of reliever inhaler use

	Overall N=307		**Budesonide-formoterol as needed N=151**		**Maintenance budesonide N=156**	
≥1 exacerbation/severe exacerbation	Yes	No	Yes	No	Yes	No
I took my reliever as soon as I got mild asthma symptoms						
Strongly disagree/ disagree/uncertain	10 (3)	96 (31)	3 (2)	48 (32)	7 (5)	48 (31)
Agree/strongly agree	37 (12)	164 (53)	14 (9)	86 (57)	23 (15)	78 (50)
I waited until asthma symptoms were having an impact on what I was doing before I took my reliever inhaler						
Strongly disagree/ disagree/uncertain	34 (11)	161 (52)	12 (8)	85 (56)	22 (14)	76 (49)
Agree/strongly agree	13 (4)	99 (32)	5 (3)	49 (33)	8 (5)	50 (32)
I tried to wait as long as possible before I took my reliever inhaler						
Strongly disagree/ disagree/uncertain	39 (13)	217 (71)	14 (9)	111 (74)	25 (16)	106 (68)
Agree/strongly agree	8 (3)	43 (14)	3 (2)	23 (15)	5 (3)	20 (13)
I tried to avoid taking my reliever inhaler as much as possible						
Strongly disagree/ disagree/uncertain	37 (12)	216 (70)	13 (9)	111 (74)	24 (15)	105 (67)
Agree/strongly agree	10 (3)	44 (14)	4 (3)	23 (15)	6 (4)	21 (13)
There were times when I felt I should have taken the reliever inhaler but didn't						
Strongly disagree/ disagree/uncertain	24 (8)	178 (58)	7 (5)	83 (55)	17 (11)	95 (61)
Agree/strongly agree	23 (7)	82 (27)	10 (7)	51 (34)	13 (8)	31 (20)

References

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3 Blaiss MS, Kaliner MA, Baena-Cagnani CE, *et al.* Barriers to asthma treatment in the United States: results from the global asthma physician and patient survey. *World Allergy Organ J* 2009;**2**:303–13. doi:10.1097/WOX.0b013e3181c81ea4