OptimAIR: Towards right care in asthma through point-of-care phenotyping, guideline-based assessment and management optimalisation using the AsthmaOptimiser in primary care

PROTOCOL TITLE: OptimAIR: Towards right care in asthma through point-of-care phenotyping, guideline-based assessment and management optimalisation using the AsthmaOptimiser in primary care

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Version 2	*6 December 2024*	- More background information Oracle score in introduction - Assessment of exacerbation history in short visit - ACQ-6 and CAAT added to appendices
Version 3	*21 January 2025*	- Amount of patients and sites
Version 4	*17 February*	- Added 'or equivalent' regarding the used FeNO device - Added section 9.4: biases and limitations - Mentioning loss to follow up in sample size

TABLE OF CONTENTS

1. INTRODUCTION AND RATIONALE....10
2. OBJECTIVES AND ENDPOINTS....12
3. STUDY DESIGN....13
4. STUDY POPULATION....15
4.1 Population (base)....15
4.2 Inclusion criteria....15
4.3 Exclusion criteria....15
4.4 Sample size calculation....15
5. AsthmaOptimiser and other procedures....16
5.1 AsthmaOptimiser....16
5.2 ALDS....16
5.3 FeNO....17
5.4 Blood Eosinophil counts (bEOS counts)....18
5.5 Chronic Airways Assessment Test....18
5.6 Oxford Asthma Attack Risk Scale....18
5.7 eCRF....18
5.8 Patient report....18
5.9 Healthcare provider report....19
5.10 GPRI Respiratory Registry....19
6. METHODS....20
6.1 Study parameters/endpoints....20
6.1.1 Main study endpoint....20
6.1.2 Secondary study endpoints....20
6.1.3 Exploratory study endpoints....20
6.2 Study procedures....21
6.3 Withdrawal of individual patients....22
6.4 Replacement of individual patients after withdrawal....22
7. SAFETY REPORTING....23
7.1 Temporary halt for reasons of subject safety....23
7.2 AEs and SAEs....23
7.2.1 Adverse events (AEs)....23
7.2.2 Serious adverse events (SAEs)....23
8. STATISTICAL ANALYSIS....24
8.1 Primary study parameter....24
8.2 Secondary study parameters....24
8.3 Exploratory study parameters....24
9. ETHICAL CONSIDERATIONS....25
9.1 Regulation statement....25
9.2 Informed consent....25
9.2.1 Informed consent procedure....25
9.2.2 Paper-based consent....25

9.2.3 Electronic Consent 25
9.2.4 Electronic Data Capture System 25
9.3 Benefits and risks assessment, group relatedness.....26
10. ADMINISTRATIVE ASPECTS, MONITORING AND PUBLICATION 27
10.1 Handling and storage of data 27
10.2 Public disclosure and publication policy.....27
11. REFERENCES 28
12. Appendices 30
12.1 Appendix 1. IPCRG conference Dublin 2021. Results CAPTURE study[19].....30
12.2 Appendix 2. Screenshot AsthmaOptimiser 31
12.3 Appendix 3 – ACQ-6 questionnaire 37
12.4 Appendix 4 – CAAT questionnaire.....39
CAAT_AU1.0_eng-on.docx
..39

LIST OF ABBREVIATIONS AND RELEVANT DEFINITIONS

ACQ	Asthma Control Questionnaire
AE	Adverse Event
ALDS	Ambulatory Lung Diagnosis System
bEOS	Blood Eosinophils
CAAT	Chronic Airways Assessment Test
COPD	Chronic obstructive pulmonary disease
ERS	European Respiratory Society
ICC	Intraclass Correlation Coefficient
FeNO	Fraction exhaled nitric oxide
GCP	Good Clinical Practice
GDPR	General Data Protection Regulation
GINA	Global Initiative for Asthma
GPRI	General Practitioners Research Institute
HCP	Healthcare professional
HMA-EMA	Heads of Medicine Agencies – European Medicine Agency
ICF	Informed Consent Form
ICS	Inhaled corticosteroids
METC	Medical research ethics committee (MREC)
ORACLE	Oxford asthma attack risk scale
POC	Point-of-Care
RWD	Real World Data
SABA	Short-Acting Beta Agonists
(S)AE	(Serious) Adverse Event
Sponsor	The sponsor is the party that commissions the organisation or performance of the research, for example a pharmaceutical company, academic hospital, scientific organisation or investigator. A party that provides funding for a study but does not commission it is not regarded as the sponsor but referred to as a subsidising party.
WMO	Medical Research Involving Human Subjects Act; in Dutch: Wet Medisch-wetenschappelijk Onderzoek met Mensen

SUMMARY

Rationale:

Patients with respiratory diseases are mainly treated in primary care, particularly if they have not yet experienced frequent exacerbations. Asthma control remains suboptimal, and symptoms, exacerbations and SABA overuse are common. Around 40% of patients report an ACQ score >1.5 which is a commonly accepted indicator of uncontrolled asthma.[1] Self-perception of disease in patients with asthma appears to be relatively poor, with many patients regarding their asthma as controlled and not serious despite experiencing frequent symptoms and exacerbations. Therefore, there remains a need to assess patients' asthma control, risk, trigger avoidance and inhaler technique, and to ensure that patients are prescribed, and take, appropriate treatments according to the latest (international) guidelines, such as the Global Initiative for Asthma (GINA) guideline.[2]

Innovative e-health solutions, such as the previously developed AsthmaOptimiser, can guide healthcare professionals through asthma consultations and can facilitate healthcare professionals in optimizing asthma treatment. Structured asthma reviews can also help to uncover opportunities for more personalized management actions. Extra attention should be given to those patients at high risk for worse asthma outcomes, like exacerbations. One novel asthma exacerbation risk predictor is the Oxford asthma attack risk scale (ORACLE) score (www.oraclescore.com).[3] This requires collection of biomarkers like FeNO and blood Eosinophils for the calculation. These are not yet assessed routinely in primary care, and further studies to the applicability in primary care are needed.

Many new drug classes are being developed within the respiratory space after decades of limited novel targets in pharmacological treatment. The development programs of these new treatments require large clinical trials and participation of many patients. As patients with respiratory diseases are mainly treated in primary care, the primary care provides a large pool of potential participants for clinical trials that might benefit from participating in studies but migh be unaware of the possibilities to particiate in such studies.[4] Moreover, the society might benefit by assessing efficacy and safety of new interventions. In line with this, GPRI wants to establish the GPRI Respiratory Registry with up-to-date longitudinal data from patients with respiratory diseases to facilitate the recruitment for research and address relevant scientific research questions.

The proposed study will provide insight in the prevalence of (un)controlled asthma and opportunities for management optimalisation, specific disease phenotypes and treatable traits in patients at high risk of exacerbations. In addition, participation in this study might reduce the barrier to participate in further clinical trials.

Objectives and endpoints:

Objectives	**Endpoints**
Primary objective	**Endpoint for the primary objective**
• Assess the level of asthma control and opportunities for management improvement using the AsthmaOptimiser tool in Argentina, Chile and Spain	• Number and distribution of identified opportunities for treatment and management optimisation (based on Global Initiative for Asthma (GINA) guidance (see for example appendix 1))

Secondary objectives:	Endpoints for secondary objectives
• Gain insights into management changes following the use of AsthmaOptimiser and Oxford asthma attack risk scale (ORACLE) score	• Number and type of changes made to inhaled medication • Number of changes of inhaler device made based upon technique optimisation • Number and type of recommendations made to lifestyle changes (eg smoking cessation)
• Determine impact of assessment with AsthmaOptimiser on medium term asthma control	• Change from baseline in CAAT score after 12 weeks • Change from baseline in ACQ-6 score after 12 weeks
Exploratory objectives:	**Endpoints for exploratory objectives**
• Assess the population risk for future exacerbation according to the ORACLE score	• Distribution of ORACLE risk score
• Assess impact OptimAIR participation in engagement with clinical trials	• Number of patients identified based on ICS use, lung function and biomarkers that would be eligible for non-ICS treatment in clinical trials • Willingness to participate in interventional clinical trials when approached through OptimAIR visit • Change in CAAT score in patients eligible and participating in clinical trials versus patients eligible but not participating in clinical trials after 6 months

Study design: A prospective study in asthma evaluating point-of-care phenotyping and guideline-based assessment and management optimalisation using the AsthmaOptimiser in primary care.

Study population: Adult patients with uncontrolled asthma and treated with ICS+LABA.

Study assessment: Each patient will attend a single study visit. This visit can be short or full-length. During the short visit, patient's current asthma control and will be assessed using the ACQ-6 and CAAT, and oscillometry will be performed. In case of controlled asthma and normal lung function, the visit will end after these assessments. In case of uncontrolled asthma and/or abnormal lung function, the patient will continue to the full visit. During the full visit, patient's current asthma control and management will be assessed using the AsthmaOptimiser, including spirometry, complemented by Fraction exhaled nitric oxide (FeNO) measurement, determination of blood eosinophil (bEOS) counts using point-of-care measurements, and post oscillometry. Following the assessment, both patient and their healthcare provider will receive a report with results of the visit, recommended treatment according to the GINA guidance and future risk according to the ORACLE

score. The treating clinicians and, where approved by the ethics committees, patients receive a list of studies being conducted in their region which the patient might be eligible for.

Ethical considerations and extend of the burden: Study specific involvement for patients with asthma is limited to one visit and participation in remote / electronic follow-up. The assessment contains non- and minimally invasive tests, limited to a questionnaire, oscillometry and spirometry and FeNO measurements and a finger stick point-of-care test. These tests might cause a slight inconvenience for the patient but the risks of participating in the study are deemed to be negligible. Patients and healthcare providers will receive a report with result on their visit and recommended treatment in line with GINA guidelines.

1. INTRODUCTION AND RATIONALE

Asthma is a non-communicable lung disease that is characterized by chronic inflammation of the airways, variable and limited expiratory airflow, bronchial hyperresponsiveness and recurrent exacerbations. The Global Initiative for Asthma (GINA) guideline provides clinical treatment guidelines for asthma management and prevention.[2] The population goal of asthma management is to prevent asthma deaths and minimize the burden of asthma on individuals, families, communities, health systems and the environment. For individuals the goal of asthma management is to achieve the patient's best possible long-term outcome in asthma symptom control and risk minimization.[2]

Patients with respiratory diseases are mainly treated in primary care, particularly if they have not yet experienced frequent exacerbations. With regard to asthma, results from the REALISE study (8000 participants) and the SABINA program (over 1 million records) underline that asthma control in Europe remains suboptimal and symptoms, exacerbations and short-acting Beta Agonists (SABA) overuse are common. Around 40% of patients report an Asthma Control Questionnaire (ACQ)-5 score >1.5, which is a commonly accepted indicator of uncontrolled asthma.[1,5–7] Results from the SCAALA programme in Latin America reports similar numbers and that asthma in Latin America tend to be poorly controlled and management needs to be improved.[8] Self-perception of disease in patients with asthma appears to be relatively poor, with many patients regarding their asthma as controlled and not serious despite experiencing frequent symptoms and exacerbations.[5] Therefore, there remains a need to assess patients' asthma control, risk, trigger avoidance and inhaler technique, and to ensure that patients are prescribed, and take, appropriate treatments, according to the latest (international) guidelines, such as the GINA guideline.[5]

Innovative e-health solutions can guide healthcare professionals through asthma consultations and can facilitate healthcare professionals in optimizing asthma treatment. Structured asthma reviews can also help to uncover opportunities for more personalized management actions. In asthma, digital assessment tools have already been developed for use by healthcare professionals to identify patients with potentially severe or uncontrolled asthma who require additional support to optimize disease management.[9–11] Structured questions in these tools can support comprehensive asthma assessments by providing healthcare professionals with personalized, guideline-based strategies to optimize asthma management. ReferID+ is one such digital tool that has shown significant reduction in exacerbations and improvement in asthma control compared to usual care in an 18-month study in the United Kingdom (OASIS study [NCT04941001]).[9] This tool consists of a panel of asthma assessment questions designed to guide structured consultations to ensure critical elements are addressed and asthma treatments are optimized. In the study of 202 patients, the use of the ReferID+ was shown to reduce the number of lung attacks after one year from (1.87[±1.47] to 0.79[±1.21], p<0.001) per year. In the control group without the ReferID+ this remained almost equal from 1.67[±1.46] to 1.46[±1.67], p=0.17). The ACQ score also improved clinically and statistically significantly.[9]

We previously developed the AsthmaOptimiser (www.asthmaoptimiser.com, screenshots in Appendix 2), a digital interface tool adapted from the ReferID+ tool specifically for the Dutch healthcare system. The AsthmaOptimiser is part of the TreatmentOptimiser and a class IIa Medical Device based on the Medical Device Regulation. The AsthmaOptimiser tool creates an overview of

factors and characteristic that may be associated with uncontrolled asthma based on the GINA recommendations.[10] The tool also provides guideline-based management suggestions and includes the Asthma Control Questionnaire (ACQ). The CAPTURE study assessed the implementation of the Asthma Optimiser in the Netherlands.[10] In this study, 220 people with asthma were included by practice nurses from 32 practices. This showed that 60% of the patients still had uncontrolled asthma. The advice given by the AsthmaOptimiser are shown in the figure in appendix I. The feedback from the participating healthcare providers was used to improve the optimizer.

Extra attention should be given to those patients at high risk for worse asthma outcomes like exacerbations. One novel asthma exacerbation risk predictor is the OxfoRd Asthma attack risk sclaLE (ORACLE: www.oraclescore.com.[3] This requires the measurement of biomarkers of type-2 inflammation like Fraction exhaled nitric oxide (FeNO) and blood eosinophil (bEOS) for the calculation of the risk of asthma attacks that may be prevented by more intens ant-inflammatory therapy. Indeed. It has been shown that people with asthma and high type-2 biomarkers have a greater risk of asthma attacks when randomised to placebo, whereas the excess risk is removed by appropriate anti-inflammatory therapy (higher dose ICS or type-2 targeting biologics)[3]. The ORACLE score has been derived from clinical trial data, but its use has not yet been assessed routinely in primary care, and further studies to the applicability in primary care are needed.

Many new drug classes are being developed within the respiratory space after decades of limited novel targets in pharmacological treatment. The development programs of these new treatments require large clinical trials and participation of many patients. As patients with respiratory diseases are mainly treated in primary care, the primary care provides a large pool of potential participants for clinical trials that might benefit from participating in studies but are currently unaware of the possibilities to participate in studies.[4] Moreover, the society might benefit by assessing efficacy and safety of new interventions. In line with this, the General Practitioners Research Institute (GPRI) also wants to establish the GPRI Respiratory Registry with up-to-date longitudinal data from patients with respiratory disease to facilitate the recruitment for research and address relevant scientific research questions. In addition, a Respiratory Registry will also provide the opportunity to easily collect real-world data follow-up data for a longer period without having the necessity of conducting frequent study visits.

The proposed study will provide insight in the prevalence of (un)controlled asthma and opportunities for management optimalisation, specific disease phenotypes and treatable traits, patients at high risk of exacerbations and other patient or disease specific characteristics. In addition, participation in this study might reduce the barrier to participate in further clinical trials.

2. OBJECTIVES AND ENDPOINTS

Objectives	Endpoints
Primary objective	**Endpoint for the primary objective**
• Assess the level of asthma control and opportunities for management improvement using the AsthmaOptimiser tool in Argentina, Chile and Spain	• Number and distribution of identified opportunities for treatment and management optimisation (based on Global Initiative for Asthma (GINA) guidance (see for example appendix 1))
Secondary objectives:	**Endpoints for secondary objectives**
• Gain insights into management changes following the use of AsthmaOptimiser and Oxford asthma attack risk scale (ORACLE) score	• Number and type of changes made to inhaled medication • Number of changes of inhaler device made based upon technique optimisation • Number and type of recommendations made to lifestyle changes (eg smoking cessation)
• Determine impact of assessment with AsthmaOptimiser on medium term asthma control	• Change from baseline in CAAT score after 12 weeks • Change from baseline in ACQ-6 score after 12 weeks
Exploratory objectives:	**Endpoints for exploratory objectives**
• Assess the population risk for future exacerbation according to the ORACLE score	• Distribution of ORACLE risk score
• Assess impact OptimAIR participation in engagement with clinical trials	• Number of patients identified based on ICS use, lung function and biomarkers that would be eligible for non-ICS treatment in clinical trials • Willingness to participate in interventional clinical trials when approached through OptimAIR visit • Change in CAAT score in patients eligible and participating in clinical trials versus patients eligible but not participating in clinical trials after 6 months

3. STUDY DESIGN

The OptimAIR study is a prospective study in asthma evaluating point-of-care phenotyping and guideline-based assessment and management optimalisation using the AsthmaOptimiser.

The OptimAIR study will be conducted in multiple countries. Countries to start with are Argentina, Chile, and Spain. Recruitment will occur in the area surrounding hospital sites participating in clinical trials. The goal is to include 700 patients in the three countries.
Patient recruitment will be done via:

1. Primary care, e.g. general practices or pharmacy sites. The goal is to recruit 15 to 21 sites per country
2. Open recruitment, e.g. patient networks, previous studies or social media
3. Hospitals, other than the participating sites in clinical trials

Each patient will attend a single study visit. This visit can be short or full-length, depending on asthma control and lung function.

Short visit:
During the short visit, patient's current asthma control and status will be assessed using the ACQ-6 and CAAT, and oscillometry will be performed. Based on the outcome of the short visit there are two options:

1. Well controlled asthma, defined as ACQ-6 score ≤ 0.75 and normal oscillometry (ALDS result: "normal lung function"). The visit is finished. The patient will receive follow-up questionnaires via the Respiratory registry after 3 and 6 months.
2. Uncontrolled asthma, defined as ACQ-6 score > 0.75 OR abnormal lungfunction based on the ALDS report. The patient will continue with the full visit.

Full visit:
During the full visit, patient's current asthma control and management will be assessed using the AsthmaOptimiser, including spirometry, complemented by Fraction exhaled nitric oxide (FeNO) measurement, determination of blood eosinophil (bEOS) counts using point-of-care measurements, and post oscillometry. Following the assessment, both patient and their healthcare provider will receive a report with results of the visit, recommended treatment according to the GINA guidance and future risk according to the ORACLE score. Patients and, where approved by the patient, treating clinicians receive a list of studies being conducted in their region which the patient might be eligible for.

Patient follow-up will be conducted after 3 and 6 months using the Respiratory Registry. The patients will receive an online invitation to fill in a digital questionnaire including questions regarding their exacerbations during the past 3 months, potential changes in medication use and the CAAT questionnaire. If patients are not able to fill in the questionnaire digitally, they can request a paper version of the questionnaire. In case patients do not respond to the invitation after 3 months they will get a phone call from the local study team.

The OptimAIR study will consist of a single study visit for each patient and follow-up via the Respiratory registry after 3 and 6 months. The total duration for conducting all study visits will be eight months in each country.

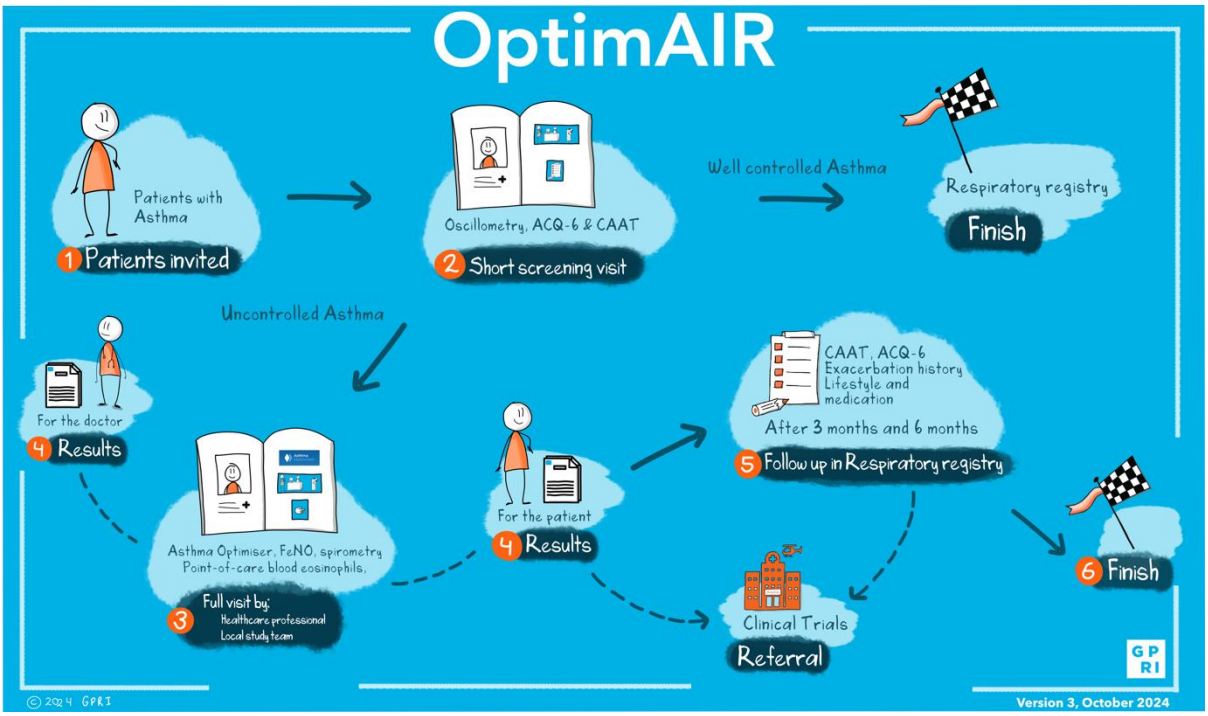

Figure 1. Schematic overview of the OptimAIR study design

4. STUDY POPULATION

4.1 Population (base)

Adult patients with uncontrolled asthma and treated with ICS+LABA.

4.2 Inclusion criteria

In order to be eligible to participate in this study, a patient must meet all of the following criteria:

- Aged 18 years or older
- Documented physician diagnosis of asthma
- Treated with ICS+LABA
- ≥ 1 exacerbation requiring oral or systemic corticosteroids for at least 3 days or hospital admission, or emergency room visit within 12 months prior to the OptimAIR study visit.

4.3 Exclusion criteria

A patient who meets any of the following criteria will be excluded from participation in this study:

- Well controlled asthma, defined as ACQ-6 score ≤ 0.75 and normal oscillometry (ALDS result: "normal lung function")
- Not able to understand the patient information sheet and informed consent form
- Other significant respiratory disease than asthma

4.4 Sample size calculation

The primary objective of the study is to describe the distribution of identified opportunities to optimize treatment and management of asthma.

The CAPTURE study, a previous study using the AsthmaOptimiser has been conducted in the Netherlands. In this study a total of 220 patients with asthma has been evaluated, of which 60% had uncontrolled asthma. This study gave a good distribution of the possible outcomes of the AsthmaOptimiser (Appendix 1).

The CAPTURE study was conducted in all patients with asthma, both controlled and uncontrolled asthma. In the current study only patients with an exacerbation in the previous year will be included, therefore it is uncertain what distribution of identified opportunities to optimize treatment and management from the AsthmaOptimiser will be.

We expect that for one third of the patients the management suggestion will be to consider review by a specialist, which is in line with the observed 34% (45 of 132 patients) in in the group of patients with uncontrolled asthma in the previous study.

To calculate a sample size for estimating a proportion (the distribution of identified opportunities) you need the expected proportion, desired precision and Intralclass Correlation Coefficient (ICC) and cluster size. The expected proportion is 34% as indicated above. The current study will be conducted in three countries, with different healthcare systems and asthma medication use, therefore we expect high variance and therefore a moderate ICC of 0.10. Expected is that within each participating site, on average, 11 patients can be screened (cluster size). Using those numbers in the Statulator sample size calculator for estimating a single proportion [12], the study would require a sample size of 700 patients for estimating a proportion of 34% with 5% absolute precision and 95% confidence. Since the primary endpoint will be assessed after a single study visit, no losses to follow-up are expected and therefore not taken into account in the sample size calculation.

5. AsthmaOptimiser and other procedures

5.1 AsthmaOptimiser

The AsthmaOptimiser (www.asthmaoptimiser.com) is part of the TreatmentOptimiser. The treatmentOptimiser is a digital interface tool and is a class IIa Medical Device based on the Medical Device Regulation (TUEV SUED (CE0123) certification, number G10 102194 0002 Rev. 1). For the OptimAIR study, the AsthmaOptimiser has been translated to be used by healthcare professionals in Argentina, Chile and Spain. The purpose of the AsthmaOptimiser is to conduct structured asthma assessments by the healthcare professional and to identify and address the specific needs of their patients. The AsthmaOptimiser tool creates an overview of factors and characteristics that may be associated with uncontrolled asthma based on the GINA guidelines.[10] The tool also provides guideline-based management suggestions. Screenshots of the AsthmaOptimiser are provided in Appendix 2.
More details regarding the AsthmaOptimiser and its use in previous studies are provided in the Introduction chapter of this protocol.

Variables collected in the AsthmaOptimiser

The following patient characteristics will be collected within the AsthmaOptimiser:

- Age (years)
- Sex (male/female)
- Height (cm)
- Weight (kg)
- Primary physician for Asthma (General practitioner, specialist, unknown)

The following clinical characteristics will be collected within the AsthmaOptimiser to provide GINA-guided management suggestions:

- Exacerbation history
- Symptom control: ACQ-6
- Adherence and attitudes inhalation medication
- Inhaler technique
- Risk factor assessment
- Lung function test

5.2 ALDS

The Ambulatory Lung Diagnosis System (ALDS), manufactured by Lothar Medtec, can be used to perform oscillometry and spirometry (figure 2). The ALDS follows the European Respiratory Society (ERS) technical standards for measurement and reporting of oscillometry and spirometry. Oscillometry is a sensitive measure of the respiratory system resistance, also described as mechanics of breathing. The measurement is obtained by applying small pressure pulses to the airways while the patient breaths normally through the mouthpiece and filter (www.alds.health). The measurement is preformed using approximately 16 seconds of tidal breathing. Three measurements of 16 seconds will be performed, during which the patient will calmly breathe in and out while wearing a nose clip. This requires no specific training or effort from patients. The ALDS has built-in quality control measures and provides feedback if quality is not sufficient.

Spirometry is a sensitive measure of the respiratory flow and volumes. The measurement is obtained by a maximum expiration followed by a maximum inspiration. The patient performs a forced breathing maneuver.
Depending on the results of the oscillometry or spirometry testing, reversibility testing can also be conducted using the ALDS device. When the ALDS suggest execution of a reversibility test, this is performed according to the ERS guideline with use of 400 μg Salbutamol as the bronchodilator.[13]
The ALDS is registered as a medical device (class IIa) and manufactured in Germany and released for the European Common Market (CE).
An extended version of the ALDS is expected to be released in the spring of 2025. This version will include the possibility to measure FeNO as well.

The ALDS provides a physiological interpretation of all the tests performed using the ALDS. This interpretation is based on the quality of the tests and the results. This algorithm follows the literature and is part of the medical device regulation package.

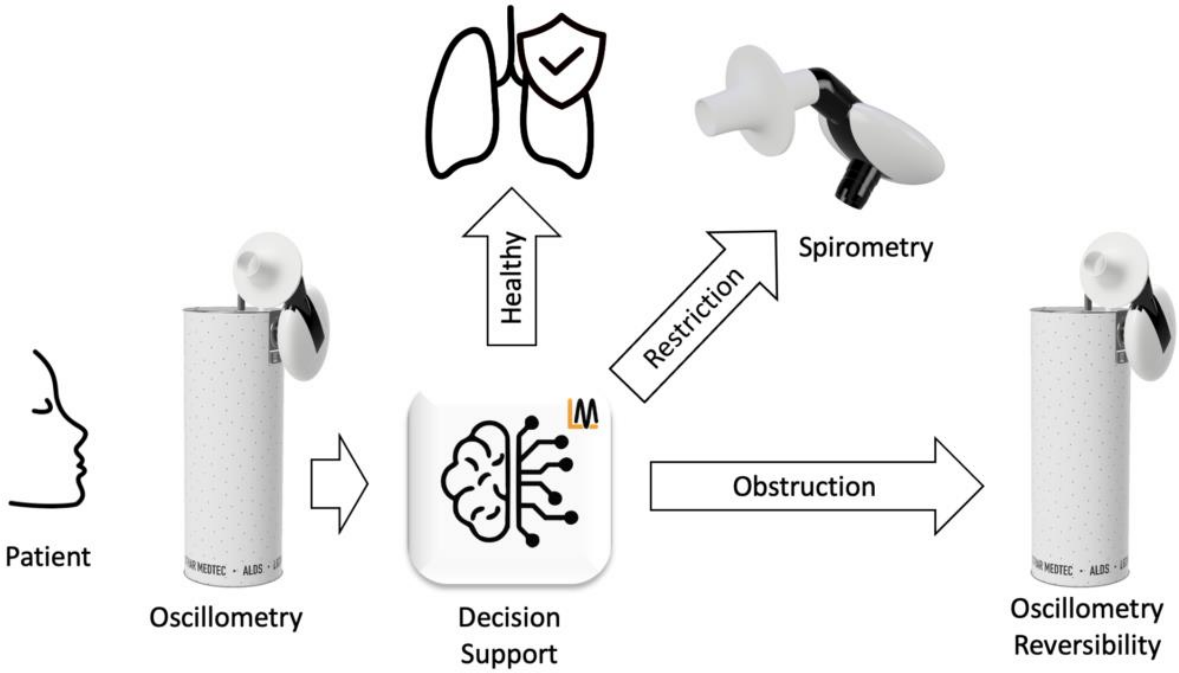

Figure 2. Oscillometry and spirometry performed with the ALDS system including decision support by the ALDS

5.3 FeNO

The FeNO test or exhaled nitric oxide test is a non-invasive way to estimate epithelial damage and airway inflammation. Nitric oxide is a gas which is produced by cells which are involved in inflammation associated with eosinophilic or allergic asthma[14]. It is suggested that FeNO is a marker for ICS responsiveness, however, further research is needed to support this suggestion [15,16].
The FeNO test is preformed using the Fenom PRO device or equivalent. The device is a point-of-care breath analyser that uses electrochemical technology to measure the fraction of FeNO using the ATS/ERS guidelines for measurement of NO. To perform the test the Healthcare professional and the participant follow the instruction on the screen of the Fenom PRO device or equivalent.

Patients are asked to exhale into the device for 10 seconds. The device and associated training will be provided to by GPRI.
The lung function measurement and FeNO test together take approximately 20 minutes. The FeNO test will be performed before the spirometry or oscillometry.
FeNO is also currently being included in a new version of the ALDS device (ALDS pro). If available at the moment of study visits, the ALDS pro device can be used to perform the FeNO test instead of the Fenom PRO device or equivalent.

5.4 Blood Eosinophil counts (bEOS counts)

Patients' blood Eos counts are measured by a Point-of-Care (POC) (finger prick) test using the HemoCue® WBC DIFF System. The HemoCue® WBC DIFF device is a validated device to assess Eos counts in airways diseases.[17] A traditional laboratory test is not needed. It takes about 5 minutes to perform this POC test and an additional 5 minutes for the device to analyse the results.

5.5 Chronic Airways Assessment Test

The Chronic Airways Assessment Test (CAAT) is an 8-item PRO developed to measure health status in asthma and COPD (appendix 4).[18] The instrument uses semantic differential 6-point response scales which are defined by contrasting adjectives to capture the impact of asthma and COPD. Content includes items related to cough, phlegm, chest tightness, breathlessness going up hills/stairs, activity limitation at home, confidence leaving home, sleep and energy. A CAAT total score is the sum of item responses. Scores range from 0-40 with higher scores indicative of greater impact on health status.

5.6 Oxford Asthma Attack Risk Scale

The Oxford Asthma Attack Risk Scale (ORACLE) score is a prototype risk stratification assessment based on five variables which include biomarkers (FeNO and bEOS), current asthma treatment intensity, and other clinical risk factors. The score describes the predicted number of severe asthma attacks to occur in the following year if treatment is not changed and proposed personalised anti-inflammatory and non-inflammatory treatment strategies based on a patient's inflammatory phenotype.[3]

5.7 eCRF

Results of the AsthmaOptimiser, ALDS and other tests will be stored in an electronic case report form (eCRF) following country specific regulations.

5.8 Patient report

After the full visit consultation, the patient will receive a personalised report including high level results of the AsthmaOptimiser and other performed tests. Where ethics committees allow, in addition to the results, the patient will also receive a list of studies being conducted in their region which the patient might be eligible for based on their results. This list will also include a link to an information movie produced by GPRI to inform the patient about the potential added value of participating in a clinical trials in general, including the potential advantage for the

individual patient as well as for the whole patient population. Patients can contact one of the trial sites participating in the trial in the patients surrounding themselves by using the easy application options for each specific study. In addition, patients will receive a phone call by the local study team a few days after the OptimAIR study visit to give them an opportunity to ask questions about participation and to ask if they are interested in referral to one of the trials. In addition, patients are asked for permission to share their contact details with the nearby trial study teams.

5.9 Healthcare provider report

After the patient's short or full visit consultation, the healthcare professional will receive a report including the results of the visit. When the patient completed the full visit, the report will include a list of treatment and management advice following the GINA guideline. The healthcare provider will also receive a list of clinical trials in the surrounding area that their patient might be eligible for. The list will include a link to more information for the healthcare professional regarding the specific trials.

5.10 GPRI Respiratory Registry

For patients attending the full visit, follow-up will be conducted after 3, and 6 months using the Respiratory Registry. Every 3 months patients will receive an online invitation to fill in a digital questionnaire including questions regarding their exacerbations during the past 3 months, potential changes in medication use and the CAAT, ACQ-6, and tai-10 questionnaires. If patients are not able to fill in the questionnaire digitally, they can request a paper version of the questionnaire. In case patients do not respond to the invitation after 3 months they will get a phone call of the local study team.
Patients only participating in the short visit will be given the option to also enter the Respiratory Registry and will receive the same questionnaire.

6. METHODS

6.1 Study parameters/endpoints

6.1.1 Main study endpoint

The primary endpoint is the number and distribution of identified opportunities to optimize treatment and management based on GINA guidance.

The endpoint will be assessed in all patients in which the OptimAIR consultation has been performed.

6.1.2 Secondary study endpoints

The following secondary endpoints will be assessed:

- Number and type of changes made to inhaled medication
- Number of changes of inhaler device made based upon technique optimisation
- Number and type of recommendations made to lifestyle changes (eg smoking cessation)
- Change from baseline in CAAT score after 12 weeks
- Change from baseline in ACQ-6 score after 12 weeks

These endpoints will be assessed in all patients in which the consultation using the AsthmaOptimiser has been performed and who completed the questionnaire after 12 weeks via the GPRI Respiratory Registry.

6.1.3 Exploratory study endpoints

The following exploratory endpoints will be assessed:

- Distribution of ORACLE risk score

This endpoint will be assessed in all patients in which the consultation using the AsthmaOptimiser has been performed and the ORACLE score has been calculated.

- Number of patients identified based on ICS use, lung function and biomarkers that would be eligible for non-ICS treatment in clinical trials

This endpoint will be assessed in all patients in which the consultation using the AsthmaOptimiser has been performed.

- Willingness to participate in interventional clinical trials when approached through OptimAIR visit

This endpoint will be assessed in all patients in which the consultation using the AsthmaOptimiser has been performed and who completed the questionnaire after 12 weeks via the GPRI Respiratory Registry.

- Change in CAAT score in patients eligible and participating in clinical trials versus patients eligible but not participating in clinical trials after 6 months

This endpoint will be assessed in all patients in which the consultation using the AsthmaOptimiser has been performed and who completed the questionnaire after 6 months via the GPRI Respiratory Registry.

6.2 Study procedures

Patient eligibility for the OptimAIR study will be assessed during pre-screening call by phone or during a pre-screening visit at the own healthcare professional or by a local study team. Patient eligibility check can also be performed based on information available in the Electronical Medical System of a healthcare professional, in this case the patient will be contacted and informed about the study.

A visit for the OptimAIR study will be conducted by the patient's own healthcare professional or by a local study team. The visit starts with explaining the purpose of the study and signing informed consent.

The study visit consist of two parts, of which the second (full visit) is dependent of the results during the first part (short visit):

Short visit:
During the short visit, patient's demographic characteristics and exacerbation history over the past 12 months are collected and current asthma control will be assessed using the ACQ-6 and CAAT (appendix 3 and 4), and oscillometry will be performed. Based on the outcome of the short visit there are two options:

1. Well controlled asthma, defined as ACQ-6 score ≤ 0.75 and normal oscillometry (ALDS result "normal lung function"). The visit for the patient is finished. The patient will be followed via the Respiratory registry after 3 and 6 months.
2. Uncontrolled asthma, defined as ACQ-6 score > 0.75 OR no normal lungfunction based on the ALDS report. The patient will continue to the full visit.

Full visit:
During the full visit the AsthmaOptimiser will be used and all procedures described in chapter 5 will be conducted (see also Schedule of assessments, Table 1). The order of assessments within the AsthmaOptimiser will be advised as follows:

- FeNO
- Spirometry (pre)
- bEOS counts
- ACQ-6
- Oscillometry (post)
- Spirometry (post)
- CAAT
- ORACLE score

Three and six months after the OptimAIR visit the patient will receive an invitation to fill in a digital questionnaire including questions regarding their exacerbations during the past 3 months, potential changes in medication use and the CAAT questionnaire.

Table 1. Schedule of Assessments OptimAIR study

Schedule of assessments					
Visit	Visit 0*	Visit 1* short^	Visit 1* full^	Follow up 1	Follow up 2
Time (months)	0	0	0	3	6
Invitation + Informed consent					
Invitation and informed consent provided	X				
Informed consent procedure		X			
OptimAIR study visit					
Demographics		X			
ACQ-6		X		X	X
CAAT		X		X	X
Oscillometry (pre)		X			
FeNO			X		
Spirometry (pre)			X		
blood EOS counts			X		
Exacerbation history			X	X	X
Type, adherence and attitudes inhalation medication			X	X	X
Inhaler technique			X		
Risk factor assessment			X		
Oscillometry (post)			X		
Spirometry (post)			X		
ORACLE score			X		
Lifestyle recommendations			X	X	X

* V0 and V1 can be at the same moment if regulations allow
^ All patients will start with the short visit, full visit will be dependent on results of short visit

6.3 Withdrawal of individual patients

Patients can leave the study at any time for any reason if they wish to do so without any consequences.

6.4 Replacement of individual patients after withdrawal

Patients that left the study, e.g. during the study visit or non-responsive during the follow-up period, will not be replaced.

7. SAFETY REPORTING

7.1 Temporary halt for reasons of subject safety

In accordance with section 10, subsection 4, of the WMO, the sponsor will suspend the study if there is sufficient ground that continuation of the study will jeopardise subject health or safety. The investigator will take care that all subjects are kept informed.

7.2 AEs and SAEs

7.2.1 Adverse events (AEs)

Adverse events are defined as any undesirable experience occurring to a subject during the study, whether or not considered related to the study procedures. All adverse events reported spontaneously by the patient or observed by the healthcare provider or study team will be recorded.

Only AEs that occur during the consultation/study visit will be required to be reported.

7.2.2 Serious adverse events (SAEs)

A serious adverse event is any untoward medical occurrence or effect that

- results in death;
- is life threatening (at the time of the event);
- requires hospitalisation or prolongation of existing inpatients' hospitalisation;
- results in persistent or significant disability or incapacity;
- is a congenital anomaly or birth defect; or
- any other important medical event that did not result in any of the outcomes listed above due to medical or surgical intervention but could have been based upon appropriate judgement by the investigator.

An elective hospital admission will not be considered as a serious adverse event.

The healthcare provider performing the study visit will report all SAEs to the sponsor without undue delay after obtaining knowledge of the events. Only SAEs that occur during the consultation/study visit will be required to be reported.
The sponsor will report the SAEs to the accredited METC that approved the protocol, within 7 days of first knowledge for SAEs that result in death or are life threatening followed by a period of maximum of 8 days to complete the initial preliminary report. If applicable, all other SAEs will be reported in line listings after study closure.

8. STATISTICAL ANALYSIS

8.1 Primary study parameter

The primary endpoint is the number and distribution of identified opportunities to optimize treatment based on the GINA guidelines. These opportunities are provided by the AsthmaOptimiser results after the patient's consultation. Multiple management suggestions can be given by the AsthmaOptimiser (e.g. address adherence & address inhalation technique). We will report all combinations that are given within the study population. The combination of guideline-based treatment opportunities variable is nominal, and we will report frequency and percentage of the combinations of identified opportunities.

8.2 Secondary study parameters

The secondary endpoints are:

- Number and type of changes made to inhaled medication
- Number of changes of inhaler device made based upon technique optimisation
- Number and type of recommendations made to lifestyle changes (eg smoking cessation)

We will report frequencies and percentages of the number and eventually type of changes and recommendations. Numbers will be presented per country.

- Change from baseline in CAAT score after 12 weeks
- Change from baseline in ACQ-6 score after 12 weeks

The change in CAAT and ACQ-6 score will be assessed using linear mixed-effects models. Analysis will be done with and without adjustment for potential confounders, such as age, sex, country and asthma severity. Analysis will additionally be stratified based on country.

8.3 Exploratory study parameters

The exploratory endpoints are:

- Distribution of ORACLE risk score

This will be presented descriptively using mean ORACLE risk scores. Numbers will be presented per country.

- Number of patients identified based on ICS use, lung function and biomarkers that would be eligible for non-ICS treatment in clinical trials
- Willingness to participate in interventional clinical trials when approached through OptimAIR visit

The number of patients identified to be eligible for and willingness to participate in clinical trials will be presented descriptively using frequencies and percentages. Numbers will be presented per country and clinical trial.

- Change in CAAT score in patients eligible and participating in clinical trials versus patients eligible but not participating in clinical trials in the registry after 6 months

The change in CAAT score will be assessed using linear mixed-effects models. Analysis will be done with and without adjustment for potential confounders, such as age, sex, country and asthma severity. Analysis will additionally be stratified based on country and clinical trial.

9. ETHICAL CONSIDERATIONS

9.1 Regulation statement

This study will be conducted in accordance with the principles of the declaration of Helsinki (version October 2013).

9.2 Informed consent

9.2.1 Informed consent procedure

The healthcare professional (HCP) or member of the local study team will explain the nature of the study to the patient after he or she has expressed interest in participating. Patients or their legally authorized representative will receive either a digital or hard copy of the Patient Information Sheet and Informed Consent Form (ICF). Patients must be informed that their participation is voluntary, and they are free to refuse to participate and may withdraw their consent at any time and for any reason during the study without any consequences. Depending on the specific regulations in patient's country, the informed consent procedure may either be directly initiated or after the minimum consideration period. If applicable, before signing, the HCP will explain the study again. Patients can ask any questions they may have. Upon satisfactory clarification of all questions, patients will be given the option to sign the ICF. Signatures can be provided either on paper or digitally.

9.2.2 Paper-based consent

The patient and HCP will sign the ICF on paper at the site. Following the signing process, one ICF will be retained at the site in accordance with Good Clinical Practice (GCP) standards, while the other will be provided to the patient.

9.2.3 Electronic Consent

Signing the ICF electronically will be facilitated through the eConsent module of the designated Electronic Data Capture (EDC) system. The patient and HCP will sign the ICF using the study tablet. The eConsent module will comply with 21 CFR Part 11 regulations for electronic signatures and will incorporate encryption measures. HCP's will undergo two-factor authentication prior to signing the ICF. Upon completion of the signing process, the patient will receive a digital copy of the signed ICF.

9.2.4 Electronic Data Capture System

Regardless of whether the ICF signature is electronic or paper-based, visits data will be collected in an EDC system.

The medical record must include a statement that informed consent was obtained for the OptimAIR study and the date it was obtained.
The ICF will contain a separate section detailing the storage and utilization of data gathering during the study, aimed at selecting and potentially inviting patients to participate in other research studies. Patients will be informed of their freedom to decline participation in this additional use of their data in the future and retain the right to withdraw consent at any time and for any reason without any consequences.

9.3 Benefits and risks assessment, group relatedness

The AsthmaOptimiser e-health tool provides the healthcare professionals with personalized, guideline-based management suggestions to optimize the asthma treatment, but patients will always receive medical treatment as determined by their physician. The AsthmaOptimiser may help to structurally implement evidence-based guidelines and to tailor care to the individual patients which may benefit their health.
If based on results of the OptimAIR study patient might be eligible for one of the clinical trials, referral to and application for those trials will be voluntary and completely based on the patient's own discission.
The risk of participating in the OptimAIR study is negligible because most study procedures can be classified as usual care. All participants will use their own medication and will not be randomly allocated to an experimental intervention. The blood eosinophil count requires a point-of-care test (finger prick) which could be considered a minor inconvenience to the patient.

9.4 Potential biases and limitations

The current protocol includes patients with uncontrolled moderate to severe asthma, based on medication and previous exacerbations. This excludes patients with mild asthma. Therefore the results and management advices of the AsthmaOptimiser are only applicable for the first patient group and can not automatically be translated to the second population.
The current study will be performed in at least three countries with different health care systems. This could affect the treatment preferences of a patients healthcare professional and the willingness to follow the advices given by the AsthmaOptimiser. Also the patient preferences might be different between the countries due to cultural differences. This can be taken into account in the analisis of the study results.

10. ADMINISTRATIVE ASPECTS, MONITORING AND PUBLICATION

10.1 Handling and storage of data

Data from the AsthmaOptimiser will be stored according to the medical information regulation by Lothar Medtech which complies with class IIa for continuous operation according to Annex IX of the Directive, also complies with the essential requirements according to EN ISO 13485:2016. medical devices - quality management systems - requirements for regulatory purposes. Certification authority: TUEV SUED (CE0123) Certificate numbers: G10 102194 0002 Rev. 1
The data collected in the AsthmaOptimiser will be transferred securely to the Electronic Data Capture system.
Research data for the current study will be collected during the study visit using the AsthmaOptimiser and the other procedures and during follow-up for the GPRI Respiratory register, as specified in table 1. All research data will be directly entered into an Electronic Data Capture system (EDC). The data collection software Castor or a comparable vendor will be used to ensure the adequate entry, management, and storage of the collected data. The selected EDC system will have an audit trail that enables the tracking of changes. Furthermore, the system enables the application of validation rules (e.g. halts when a value is incorrectly filled out e.g. an age value that is smaller than 18 or when a data field is accidently skipped). This will minimize errors and missing values on questionnaires. The selected EDC system should comply with all applicable laws and regulations, including ICH E6 Good Clinical Practice (GCP), 21 CFR Part 11, EU Annex 11, General Data Protection Regulation (GDPR), HIPAA (US), ISO 9001 and ISO 27001. Data handling and storage will comply with the General Data Protection Regulation (GDRP). The investigator will ensure protection of patient's personal data in compliance with the Personal Data Protection Act and that all reports, publications, patient samples and any other study disclosures do not reveal the identity of the patient, except where required by laws. Patients are identified only by a patient identification number or site identification number to maintain patient confidentiality. All patient study records will be kept safely in an access- controlled area. Identification code lists linking patient names to patient identification numbers should preferably be stored separate from patient records. In case of data transfer, the sponsor or its representative will maintain high standards of confidentiality and protection of patient personal data. Clinical information will not be released without the written permission of the patient, except for monitoring by clinical quality assurance auditors or other authorized personnel appointed by the sponsor, by appropriate IRB members, and by inspectors from regulatory authorities.

10.2 Public disclosure and publication policy

The study will be registered with the Heads of Medicine Agencies – European Medicine Agency (HMA-EMA) catalogue of Real World Data (RWD) studies, which focuses on observational research (https://catalogues.ema.europa.eu/catalogue-rwd-studies). We aim to disseminate the results of this study through conference abstracts in line with the CCMO statement on publication policy.

11. REFERENCES

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12. Appendices

12.1 Appendix 1. IPCRG conference Dublin 2021. Results CAPTURE study[19]

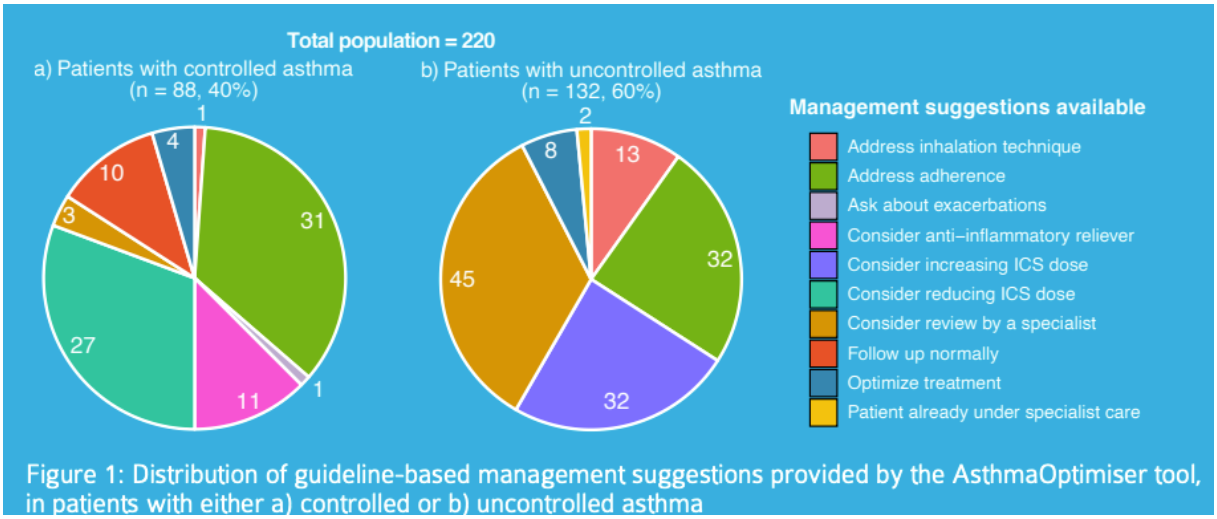
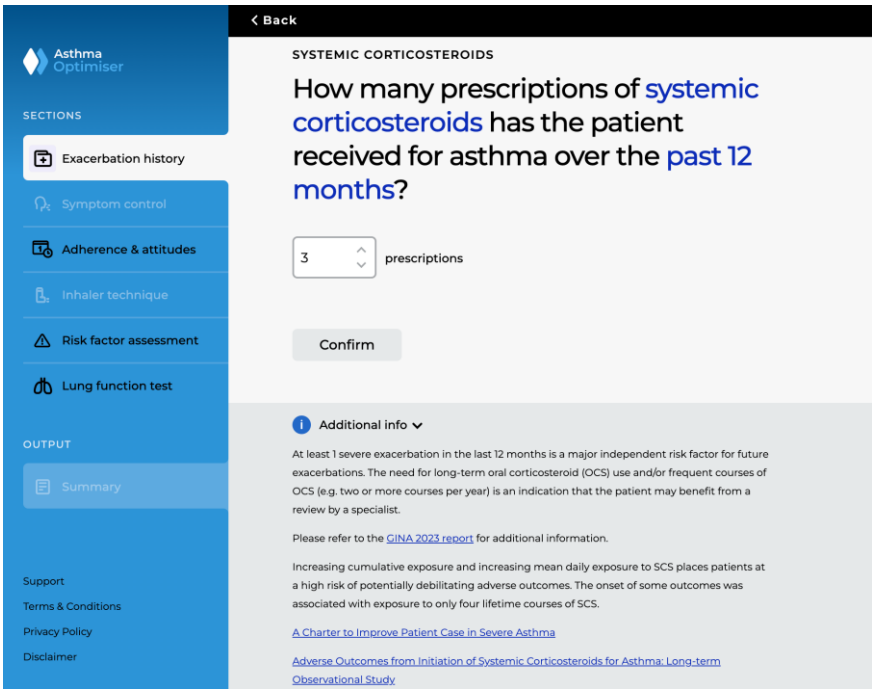
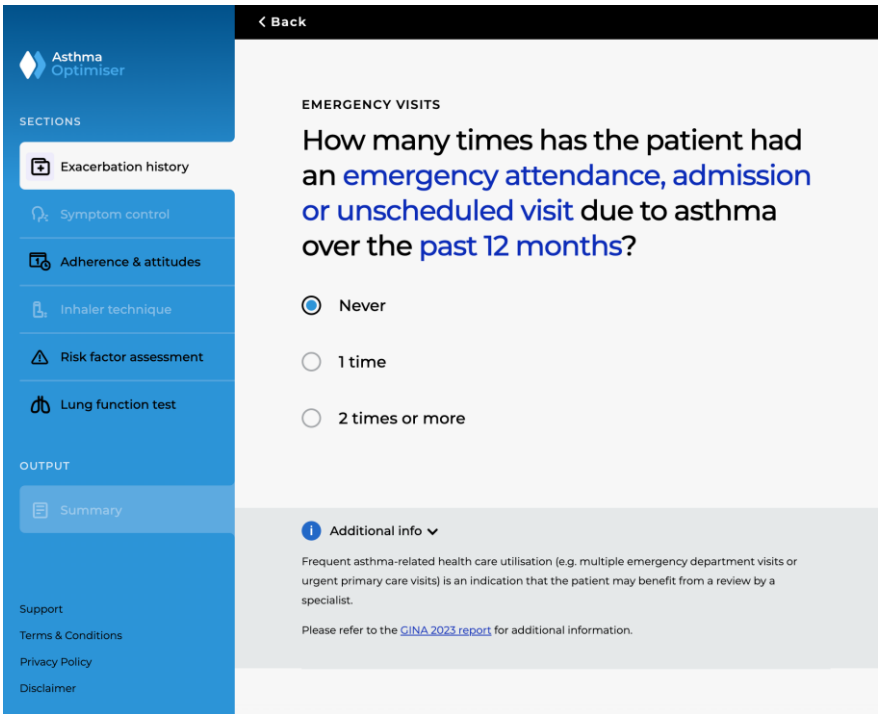
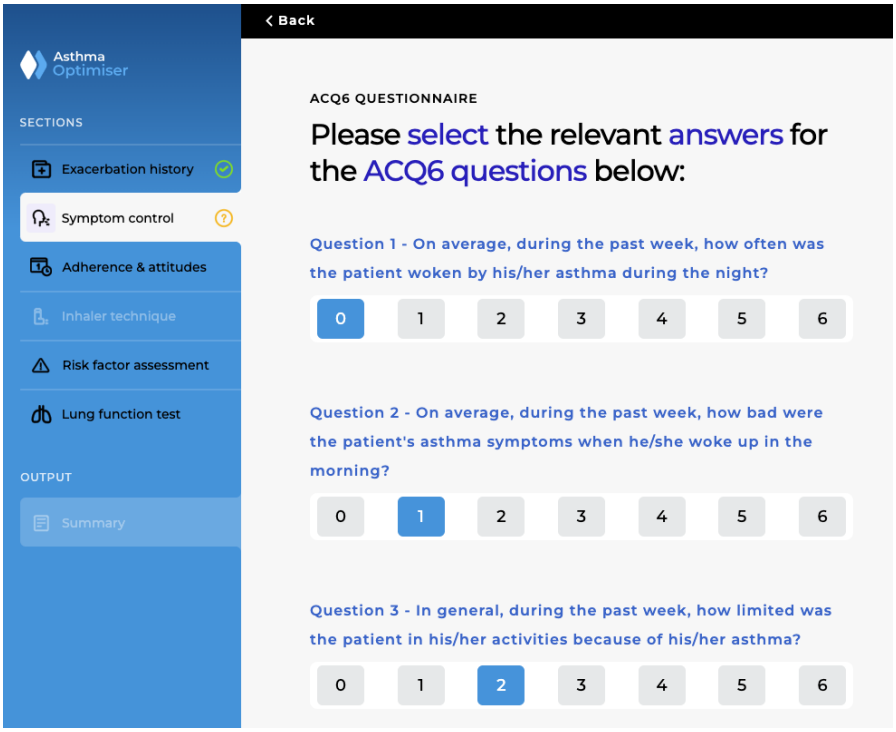


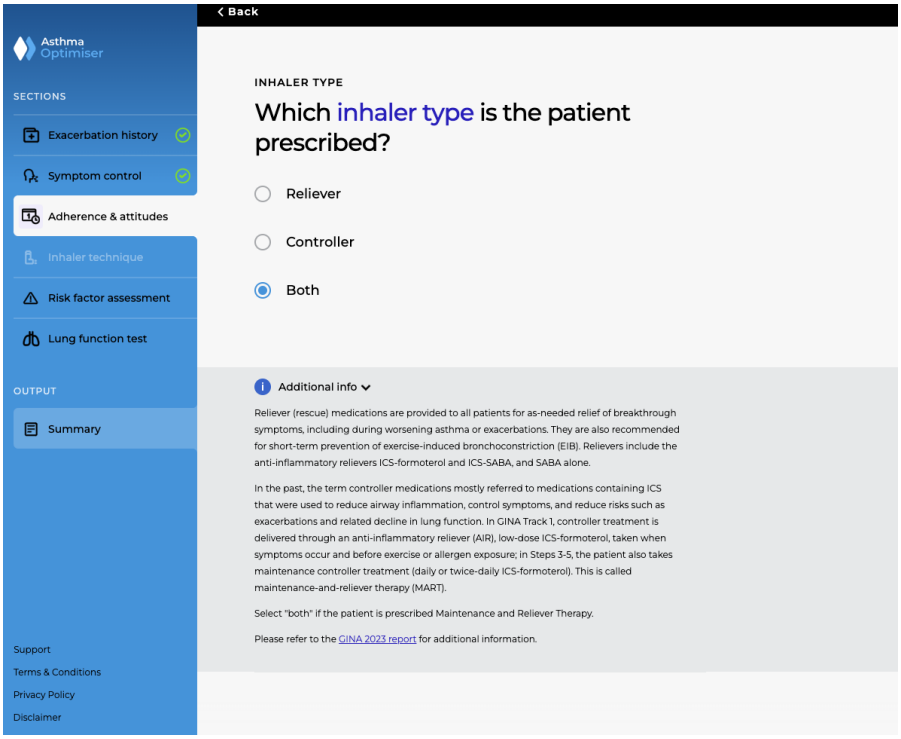
Figure 1: Distribution of guideline-based management suggestions provided by the AsthmaOptimiser tool, in patients with either a) controlled or b) uncontrolled asthma

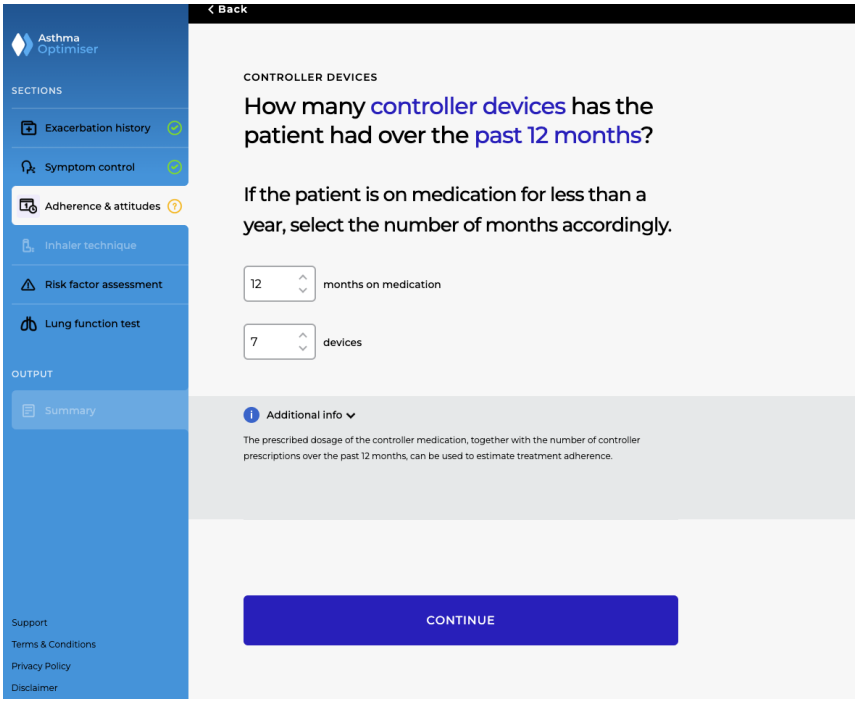
12.2 Appendix 2. Screenshot AsthmaOptimiser

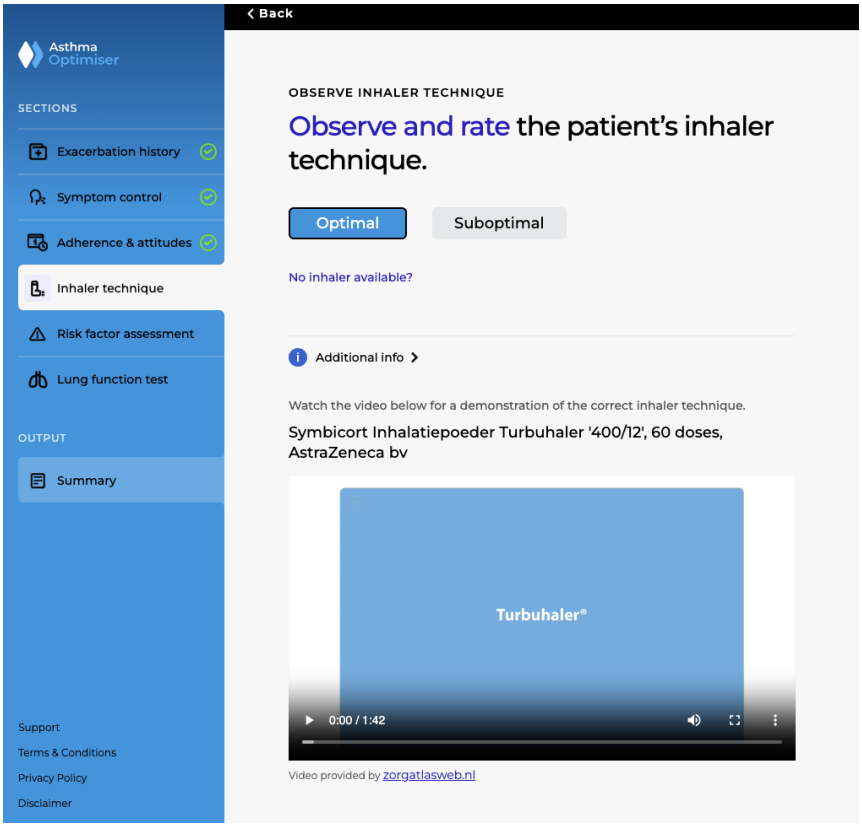


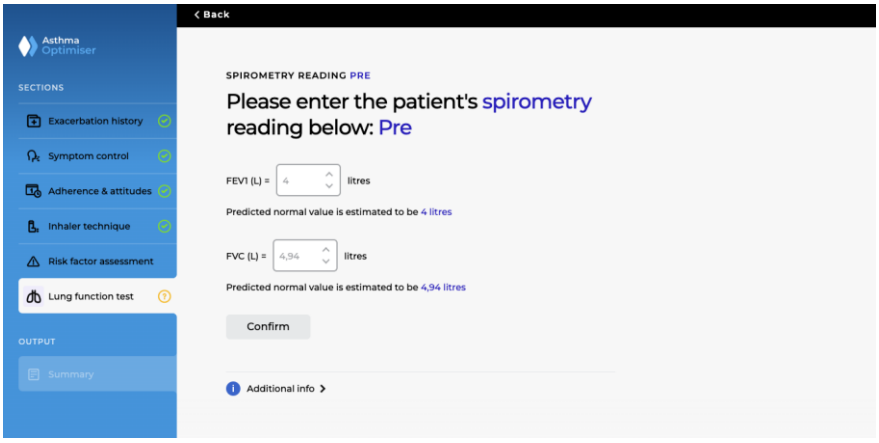


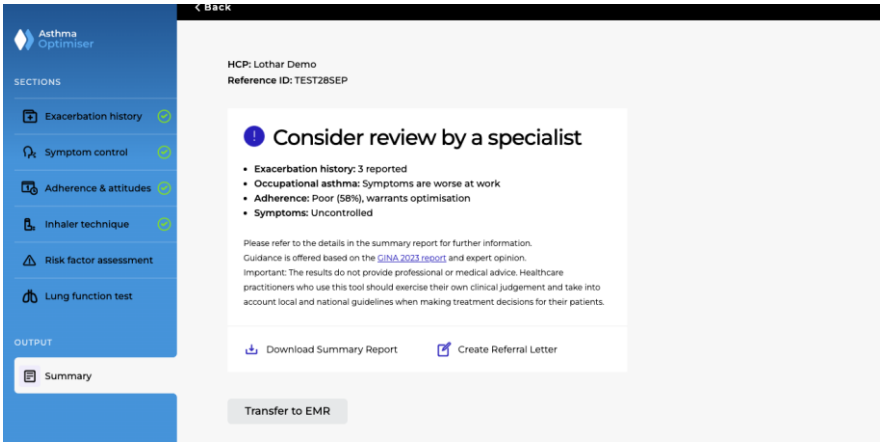

Back
Asthma Optimiser
SECTIONS
Exacerbation history
Symptom control
Adherence & attitudes
Inhaler technique
Risk factor assessment
Lung function test
OUTPUT
Summary
ACQ6 QUESTIONNAIRE
Please select the relevant answers for the ACQ6 questions below:
Question 1 - On average, during the past week, how often was the patient woken by his/her asthma during the night?
0 1 2 3 4 5 6
Question 2 - On average, during the past week, how bad were the patient's asthma symptoms when he/she woke up in the morning?
0 1 2 3 4 5 6
Question 3 - In general, during the past week, how limited was the patient in his/her activities because of his/her asthma?
0 1 2 3 4 5 6

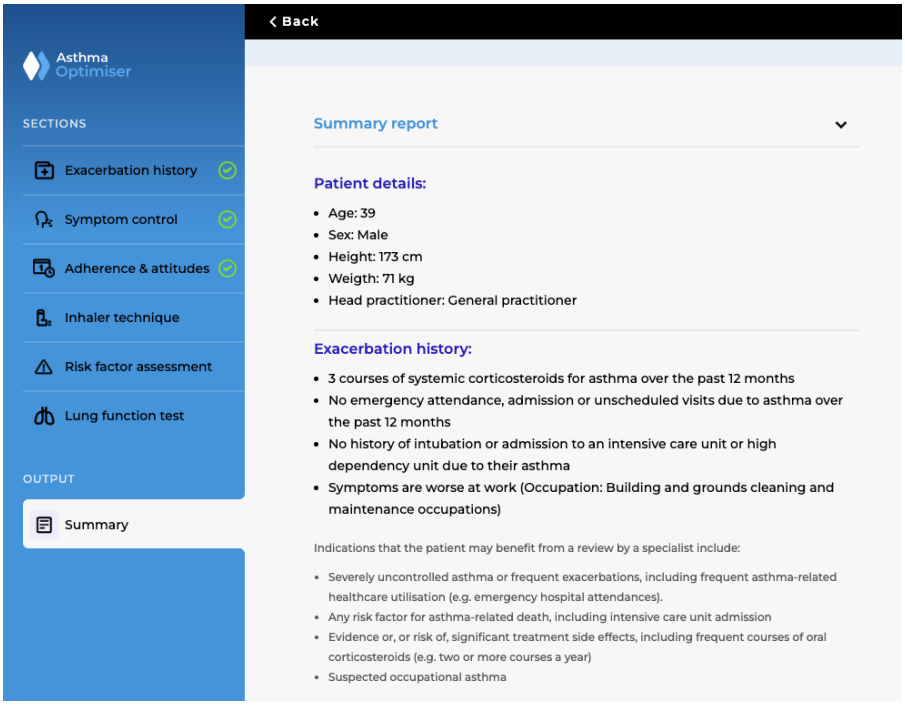

Back
Asthma Optimiser
SECTIONS
Exacerbation history
Symptom control
Adherence & attitudes
Inhaler technique
Risk factor assessment
Lung function test
OUTPUT
Summary
Support
Terms & Conditions
Privacy Policy
Disclaimer
INHALER TYPE
Which inhaler type is the patient prescribed?
Reliever
Controller
Both
Additional info
Reliever (rescue) medications are provided to all patients for as-needed relief of breakthrough symptoms, including during worsening asthma or exacerbations. They are also recommended for short-term prevention of exercise-induced bronchoconstriction (EIB). Relievers include the anti-inflammatory relievers ICS-formoterol and ICS-SABA, and SABA alone.
In the past, the term controller medications mostly referred to medications containing ICS that were used to reduce airway inflammation, control symptoms, and reduce risks such as exacerbations and related decline in lung function. In GINA Track 1, controller treatment is delivered through an anti-inflammatory reliever (AIR), low-dose ICS-formoterol, taken when symptoms occur and before exercise or allergen exposure; in Steps 3-5, the patient also takes maintenance controller treatment (daily or twice-daily ICS-formoterol). This is called maintenance-and-reliever therapy (MART).
Select "both" if the patient is prescribed Maintenance and Reliever Therapy.
Please refer to the GINA 2023 report for additional information.

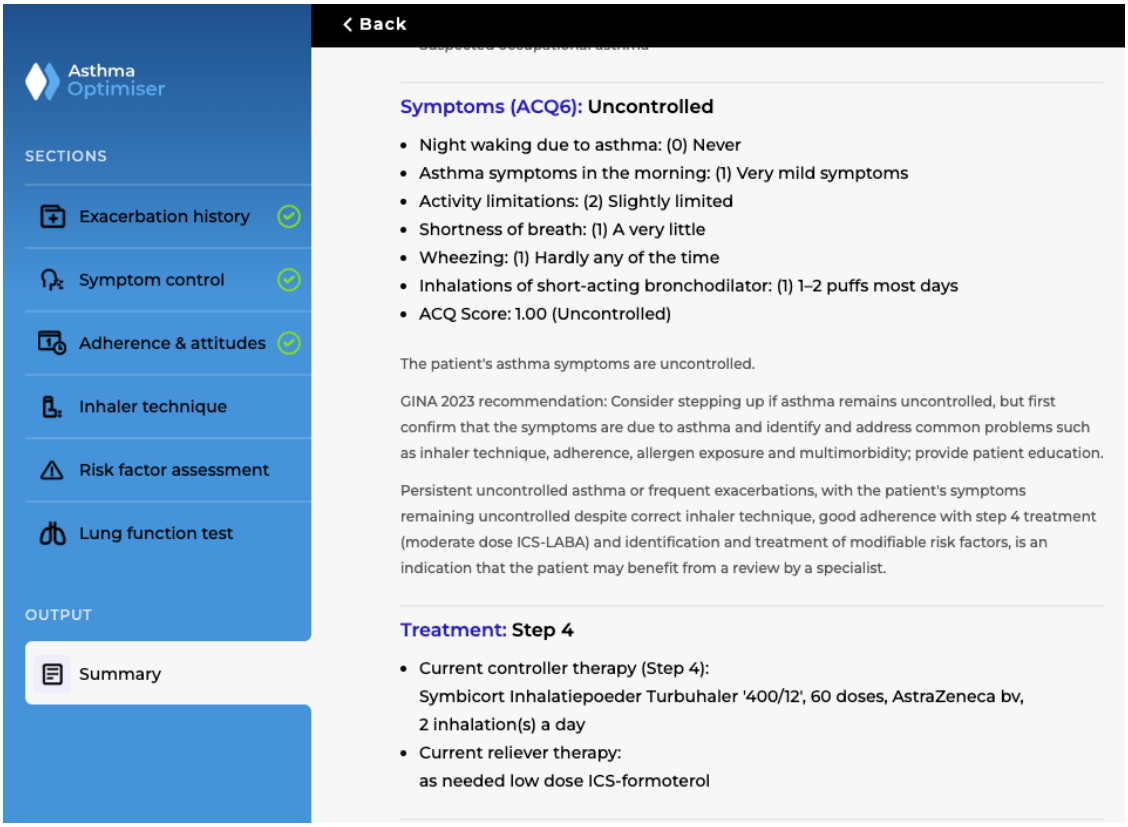

Back
Asthma Optimiser
SECTIONS
Exacerbation history
Symptom control
Adherence & attitudes
Inhaler technique
Risk factor assessment
Lung function test
OUTPUT
Summary
Support
Terms & Conditions
Privacy Policy
Disclaimer
CONTROLLER DEVICES
How many controller devices has the patient had over the past 12 months?
If the patient is on medication for less than a year, select the number of months accordingly.
12
months on medication
7
devices
Additional info
The prescribed dosage of the controller medication, together with the number of controller prescriptions over the past 12 months, can be used to estimate treatment adherence.
CONTINUE

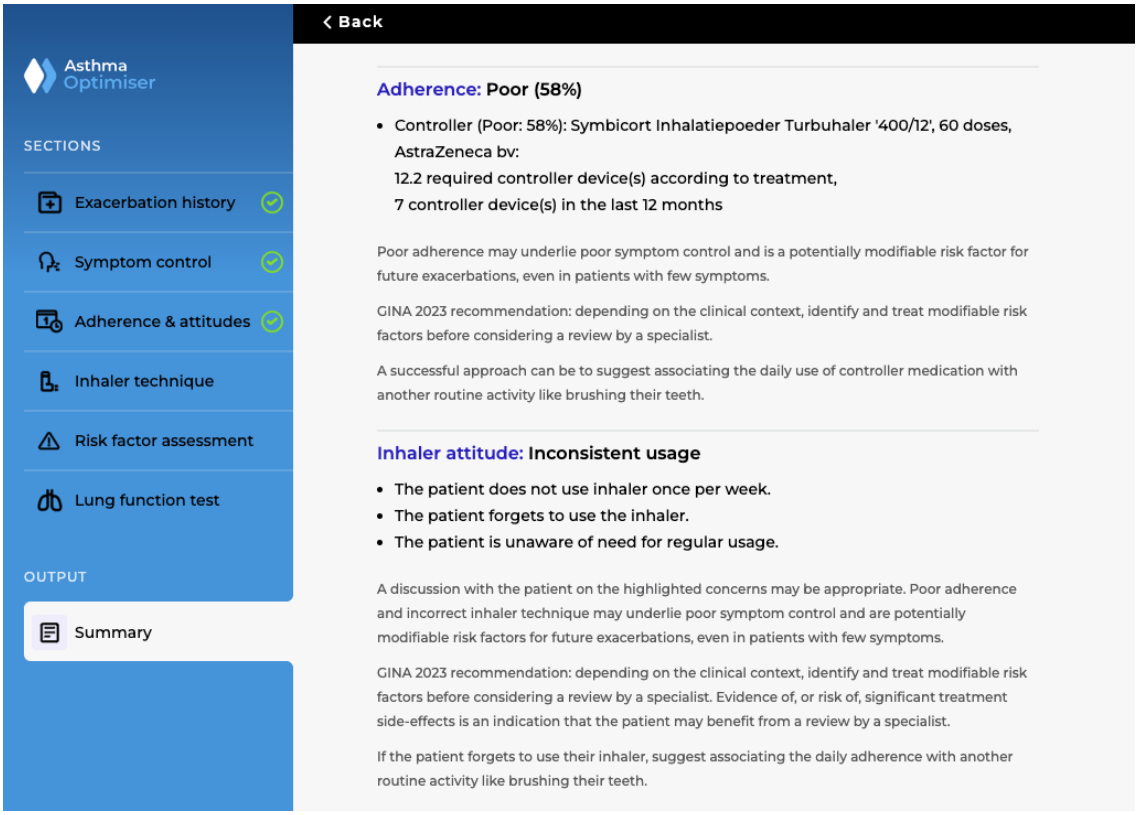

Back
Asthma Optimiser
SECTIONS
Exacerbation history
Symptom control
Adherence & attitudes
Inhaler technique
Risk factor assessment
Lung function test
OUTPUT
Summary
Support
Terms & Conditions
Privacy Policy
Disclaimer
OBSERVE INHALER TECHNIQUE
Observe and rate the patient's inhaler technique.
Optimal
Suboptimal
No inhaler available?
Additional info
Watch the video below for a demonstration of the correct inhaler technique.
Symbicort Inhalatiepoeder Turbuhaler '400/12', 60 doses, AstraZeneca bv
Turbuhaler®
0:00 / 1:42
Video provided by zorgatlasweb.nl

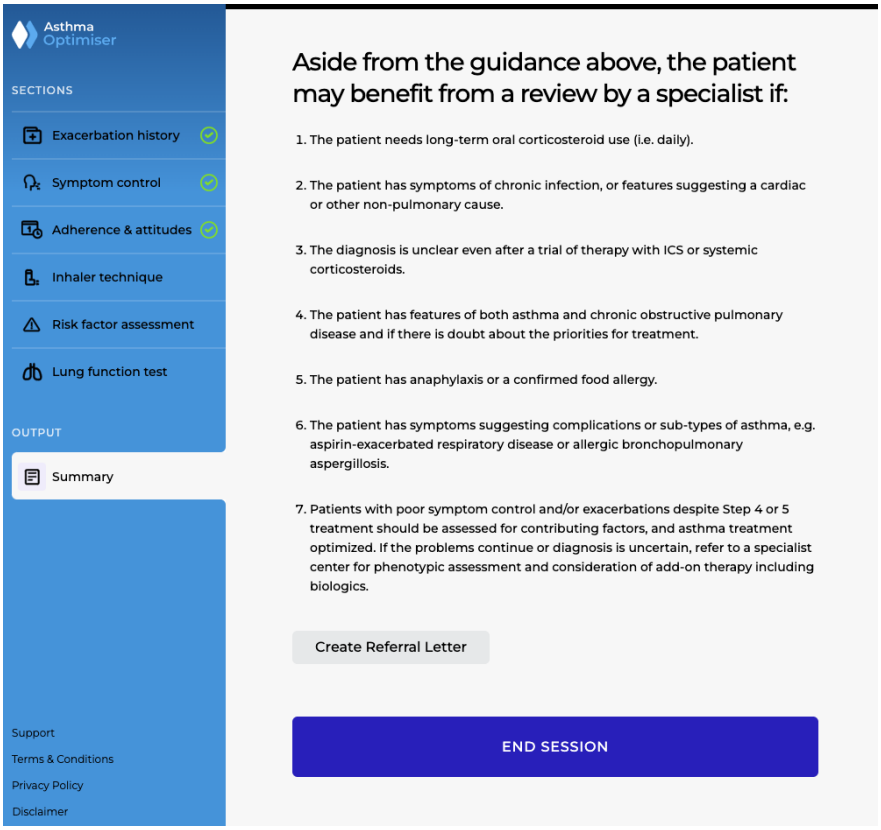

Back
Asthma Optimiser
SECTIONS
Exacerbation history
Symptom control
Adherence & attitudes
Inhaler technique
Risk factor assessment
Lung function test
OUTPUT
Summary
SPIROMETRY READING PRE
Please enter the patient's spirometry reading below: Pre
FEV1 (L) = 4 litres
Predicted normal value is estimated to be 4 litres
FVC (L) = 4,94 litres
Predicted normal value is estimated to be 4,94 litres
Confirm
Additional info


Back
Asthma Optimiser
SECTIONS
Exacerbation history
Symptom control
Adherence & attitudes
Inhaler technique
Risk factor assessment
Lung function test
OUTPUT
Summary
HCP: Lothar Demo
Reference ID: TEST28SEP
Consider review by a specialist
Exacerbation history: 3 reported
Occupational asthma: Symptoms are worse at work
Adherence: Poor (58%), warrants optimisation
Symptoms: Uncontrolled
Please refer to the details in the summary report for further information.
Guidance is offered based on the GINA 2023 report and expert opinion.
Important: The results do not provide professional or medical advice. Healthcare practitioners who use this tool should exercise their own clinical judgement and take into account local and national guidelines when making treatment decisions for their patients.
Download Summary Report
Create Referral Letter
Transfer to EMR


Back
Asthma Optimiser
SECTIONS
Exacerbation history
Symptom control
Adherence & attitudes
Inhaler technique
Risk factor assessment
Lung function test
OUTPUT
Summary
Summary report
Patient details:
Age: 39
Sex: Male
Height: 173 cm
Weigth: 71 kg
Head practitioner: General practitioner
Exacerbation history:
3 courses of systemic corticosteroids for asthma over the past 12 months
No emergency attendance, admission or unscheduled visits due to asthma over the past 12 months
No history of intubation or admission to an intensive care unit or high dependency unit due to their asthma
Symptoms are worse at work (Occupation: Building and grounds cleaning and maintenance occupations)
Indications that the patient may benefit from a review by a specialist include:
Severely uncontrolled asthma or frequent exacerbations, including frequent asthma-related healthcare utilisation (e.g. emergency hospital attendances).
Any risk factor for asthma-related death, including intensive care unit admission
Evidence or, or risk of, significant treatment side effects, including frequent courses of oral corticosteroids (e.g. two or more courses a year)
Suspected occupational asthma


Back
Asthma Optimiser
SECTIONS
Exacerbation history
Symptom control
Adherence & attitudes
Inhaler technique
Risk factor assessment
Lung function test
OUTPUT
Summary
Symptoms (ACQ6): Uncontrolled
Night waking due to asthma: (0) Never
Asthma symptoms in the morning: (1) Very mild symptoms
Activity limitations: (2) Slightly limited
Shortness of breath: (1) A very little
Wheezing: (1) Hardly any of the time
Inhalations of short-acting bronchodilator: (1) 1–2 puffs most days
ACQ Score: 1.00 (Uncontrolled)
The patient's asthma symptoms are uncontrolled.
GINA 2023 recommendation: Consider stepping up if asthma remains uncontrolled, but first confirm that the symptoms are due to asthma and identify and address common problems such as inhaler technique, adherence, allergen exposure and multimorbidity; provide patient education.
Persistent uncontrolled asthma or frequent exacerbations, with the patient's symptoms remaining uncontrolled despite correct inhaler technique, good adherence with step 4 treatment (moderate dose ICS-LABA) and identification and treatment of modifiable risk factors, is an indication that the patient may benefit from a review by a specialist.
Treatment: Step 4
Current controller therapy (Step 4):
Symbicort Inhalatiepoeder Turbuhaler '400/12', 60 doses, AstraZeneca bv,
2 inhalation(s) a day
Current reliever therapy:
as needed low dose ICS-formoterol


Back
Asthma Optimiser
SECTIONS
Exacerbation history
Symptom control
Adherence & attitudes
Inhaler technique
Risk factor assessment
Lung function test
OUTPUT
Summary
Adherence: Poor (58%)
Controller (Poor: 58%): Symbicort Inhalatiepoeder Turbuhaler '400/12', 60 doses, AstraZeneca bv:
12.2 required controller device(s) according to treatment,
7 controller device(s) in the last 12 months
Poor adherence may underlie poor symptom control and is a potentially modifiable risk factor for future exacerbations, even in patients with few symptoms.
GINA 2023 recommendation: depending on the clinical context, identify and treat modifiable risk factors before considering a review by a specialist.
A successful approach can be to suggest associating the daily use of controller medication with another routine activity like brushing their teeth.
Inhaler attitude: Inconsistent usage
The patient does not use inhaler once per week.
The patient forgets to use the inhaler.
The patient is unaware of need for regular usage.
A discussion with the patient on the highlighted concerns may be appropriate. Poor adherence and incorrect inhaler technique may underlie poor symptom control and are potentially modifiable risk factors for future exacerbations, even in patients with few symptoms.
GINA 2023 recommendation: depending on the clinical context, identify and treat modifiable risk factors before considering a review by a specialist. Evidence of, or risk of, significant treatment side-effects is an indication that the patient may benefit from a review by a specialist.
If the patient forgets to use their inhaler, suggest associating the daily adherence with another routine activity like brushing their teeth.


Asthma
Optimiser
SECTIONS
Exacerbation history
Symptom control
Adherence & attitudes
Inhaler technique
Risk factor assessment
Lung function test
OUTPUT
Summary
Support
Terms & Conditions
Privacy Policy
Disclaimer
Aside from the guidance above, the patient may benefit from a review by a specialist if:
1. The patient needs long-term oral corticosteroid use (i.e. daily).
2. The patient has symptoms of chronic infection, or features suggesting a cardiac or other non-pulmonary cause.
3. The diagnosis is unclear even after a trial of therapy with ICS or systemic corticosteroids.
4. The patient has features of both asthma and chronic obstructive pulmonary disease and if there is doubt about the priorities for treatment.
5. The patient has anaphylaxis or a confirmed food allergy.
6. The patient has symptoms suggesting complications or sub-types of asthma, e.g. aspirin-exacerbated respiratory disease or allergic bronchopulmonary aspergillosis.
7. Patients with poor symptom control and/or exacerbations despite Step 4 or 5 treatment should be assessed for contributing factors, and asthma treatment optimized. If the problems continue or diagnosis is uncertain, refer to a specialist center for phenotypic assessment and consideration of add-on therapy including biologics.
Create Referral Letter
END SESSION

12.3 Appendix 3 – ACQ-6 questionnaire

The ACQ-6 will be provided in the patients local language.

ASTHMA CONTROL QUESTIONNAIRE© Page 1 of 2

Please answer questions 1 - 6.

Circle the number of the response that best describes how you have been during the past week.

1.	On average, during the past week, how often were you **woken by your asthma** during the night?	0 Never 1 Hardly ever 2 A few times 3 Several times 4 Many times 5 A great many times 6 Unable to sleep because of asthma
2.	On average, during the past week, how **bad were your asthma symptoms when you woke up** in the morning?	0 No symptoms 1 Very mild symptoms 2 Mild symptoms 3 Moderate symptoms 4 Quite severe symptoms 5 Severe symptoms 6 Very severe symptoms
3.	In general, during the past week, how **limited were you in your activities** because of your asthma?	0 Not limited at all 1 Very slightly limited 2 Slightly limited 3 Moderately limited 4 Very limited 5 Extremely limited 6 Totally limited
4.	In general, during the past week, how much **shortness of breath** did you experience because of your asthma?	0 None 1 A very little 2 A little 3 A moderate amount 4 Quite a lot 5 A great deal 6 A very great deal

QUESTIONS 1 – 6 ONLY : MODIFIED SEPTEMBER 2010 ENGLISH FOR UK

ASTHMA CONTROL QUESTIONNAIRE© Page 2 of 2

5.	In general, during the past week, how much of the time did you **wheeze?**	0 Never 1 Hardly any of the time 2 A little of the time 3 A moderate amount of the time 4 A lot of the time 5 Most of the time 6 All the time
6.	On average, during the past week, how many **puffs/inhalations of short-acting bronchodilator** (eg. Ventolin/Bricanyl) have you used each day? *(If you are not sure how to answer this question, please ask for help)*	0 None 1 1 - 2 puffs/inhalations most days 2 3 - 4 puffs/inhalations most days 3 5 - 8 puffs/inhalations most days 4 9 - 12 puffs/inhalations most days 5 13 - 16 puffs/inhalations most days 6 More than 16 puffs/inhalations most days

QUESTIONS 1 – 6 ONLY : MODIFIED SEPTEMBER 2010 ENGLISH FOR UK

12.4 Appendix 4 – CAAT questionnaire

The CAAT will be provided in the patients local language.

How is your Pulmonary Disease? Take the Chronic Airways Assessment Test (CAAT)

This questionnaire will help you and your healthcare professional measure the impact of your Pulmonary Disease is having on your wellbeing and daily life. Your answers and test score, can be used by you and your healthcare professional to help improve the management of your Pulmonary Disease and get the greatest benefit from treatment.

Example:

I am very happy	0 **X** 2 3 4 5	I am sad

			SCORE
I never cough	0 1 2 3 4 5	**I cough all the time**	
I have no phlegm (mucus) in my chest at all	0 1 2 3 4 5	**My chest is full of phlegm (mucus)**	
My chest does not feel tight at all	0 1 2 3 4 5	**My chest feels very tight**	
When I walk up a hill or one flight of stairs I am not breathless	0 1 2 3 4 5	**When I walk up a hill or one flight of stairs I am very breathless**	
I am not limited doing any activities at home	0 1 2 3 4 5	**I am very limited doing activities at home**	
I am confident leaving my home despite my lung condition	0 1 2 3 4 5	**I am not at all confident leaving my home because of my lung condition**	
I sleep soundly	0 1 2 3 4 5	**I don't sleep soundly because of my lung condition**	
I have lots of energy	0 1 2 3 4 5	**I have no energy at all**	
			TOTAL SCORE

CAAT – Universal/English
CAAT_AU1.0_eng-ori.docx

OptimAIR_master_protocol_v4_15Feb2025

Final Audit Report 2025-02-17

Created:	2025-02-17
By:	Iris van Geer (iris.van.geer@gpri.nl)
Status:	Signed
Transaction ID:	CBJCHBCAABAAzGgYprJgdbYKRkHggD0E7zDVRT1Fdxs5

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