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D2287L00028 (EVA-26645)

Statistical Analysis Plan for the Implementation of the US PRECISION AIRQ®, Asthma Checklist, and Educational Resources (PRECISION Program) into Clinical Practice Using Telehealth and In-Person Platforms

D2287L00028 (EVA-26645)

Draft Statistical Analysis Plan for the Implementation of the US PRECISION AIRQ®, Asthma Checklist, and Educational Resources (PRECISION Program) into Clinical Practice Using Telehealth and In-Person Platforms

AZ Study Statistician

PPD

2/25/2022
Date

Evidera Statistical Oversight

PPD

Feb 25, 2022
Date

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LIST OF IN-TEXT TABLES/FIGURES

LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

Abbreviation/Term	Definition
ACE	Asthma Clinical Experience Questionnaire
CCI	[redacted]
AIRQ™	Asthma Impairment and Risk Questionnaire
CRF	Case report form
ED	Emergency department
FQHC	Federally qualified health care
HCP	Health care provider
OCS	Oral corticosteroids
CCI	[redacted]
PDF	Portable document format
pMDI	Pressurized Metered-Dose Inhaler
SCS	Systemic corticosteroid
SD	Standard deviation
US	United States

AMENDMENT HISTORY

Date	Brief description of change
27 Sep 23	A SAP addendum was added to the document (displayed in Appendix B)

1. OBJECTIVES

1.1 Primary Objectives

The goal of this project is to assess the process (ease of use and challenges to health care professionals [HCP] and patients) and potential benefits (ability to capture and take action to remediate previously unrecognized morbidity) of implementing the Asthma Impairment and Risk Questionnaire (AIRQ®), Asthma Checklist, and educational resources (PRECISION program) into clinical practice during telehealth and in-person visits.

This study is descriptive and there will be no formal hypothesis testing for the primary objective.

1.2 Secondary Objective

The secondary objectives of this study are:

1. To assess clinic visit experiences of patients with asthma and when the AIRQ®, Asthma Checklist, and educational resources (PRECISION program) are utilized as part of a telehealth or in-person visit with their HCP
2. To explore change in AIRQ® scores from the initial visit to follow-up visit(s) (when available)

1.3 Exploratory Objectives

Exploratory objectives include the following:

Additional exploratory analyses may occur to address additional clinically or psychometrically relevant questions of this sample.

2. STUDY DESIGN AND SAMPLE SIZE

This community program intervention study will examine the process of integrating the AIRQ®, Asthma Checklist, and educational resources (PRECISION program) into clinical practice using in-person or telehealth visits. Providers' use of patients' responses to the AIRQ®, Asthma Checklist, and educational resources to guide treatment and asthma work-up and management will be examined. All participants will be enrolled in the study by February 2022. Study duration for each site will be 12 months, including a nine month study implementation phase (starting when the last patient is enrolled at the site) and an additional three months of follow-up to assess the sustainability of using the PRECISION program in clinical practice (sustainability stage). The nine-month implementation stage will allow for potential follow-up visits for each enrolled patient. The three-month sustainability stage will allow for sites to continue to implement the PRECISION program in their clinical practice and for sites to describe any continued benefits of using the PRECISION program at their site.

Approximately 15 to 20 clinical sites will be recruited to participate in this study, categorized into the following practice clusters: (1) primary care site (e.g., private practice, FQHC; 2) specialty care site (pulmonary, asthma/immunology); and (3) novel sites (e.g., pharmacy, nurse practitioners, nurse educators, prescribers and non-prescribers, telehealth component of Allergy and Asthma Network).. Sites will be able to conduct in-person and telehealth visits for initial and follow-up visit(s).

During the clinic visit (telehealth or in-person), HCPs will assess the patients' responses to the AIRQ® questions, discuss the results with the patient, and use the Assess component of the Asthma Checklist (as appropriate per HCP judgment). Before completing the initial study visit, patients will be asked if they would be willing to complete additional questions and, for those who agree, sites will send them an electronic survey link (via YouGov) that will include the following questionnaires: the Asthma Clinic Experience (ACE) Questionnaire, CCI Sociodemographic Questionnaire. If a follow-up visit (telehealth or in-person) is conducted during the follow-up period, the clinical site will administer the AIRQ® three-month recall version (regardless of timing of follow-up visit). Sites/HCPs will complete a Clinical Case Report Form (CRF) after the initial visit and after the first follow-up visit (if conducted) for each participant. For the initial and first follow-up visit for which patients complete an AIRQ®, HCPs will be required to review the Assess component of the Asthma Checklist and provide their responses on the CRF; while sites are encouraged to use the AIRQ® for any additional follow-up visits during the study and to provide documentation of the AIRQ® scores, additional CRFs will not be completed by the HCPs.

Additionally, Evidera will host a 30-minute conference call with each clinical site for up to four timepoints (touchpoints) to discuss the implementation of PRECISION tools (i.e., frequency of visits to and the number of portable document format (PDF) file views from study website), assess whether sites are meeting their targets for using the telehealth platform, address site questions, and discuss any challenges of implementing the PRECISION program. These meetings will take place at Months 1, 2, 3 (optional), and 6 and will be used to identify any sites that may benefit from participating in a re-training session. The optional Month 3 touchpoint will be based on whether the site has any difficulties with the study.

Study Population: Clinic staff will invite patients age ≥13 years with an HCP-confirmed asthma diagnosis who present for a clinic visit (telehealth or in-person) to complete the AIRQ® and participant questionnaires. Each site will aim to recruit approximately 50 to 75 patients with a total sample size ranging from approximately 750 to 1,500 patients. The number of patients recruited from each site may be modified (i.e., able to recruit > 75 patients) to ensure that the target study sample size is obtained.

Inclusion Criteria: Patients must meet all of the following criteria to be eligible for enrollment:

1. ≥13 years of age at the time of enrollment
2. Prior diagnosis of HCP-confirmed asthma
3. Able to read, understand, and speak English or Spanish sufficiently to self-complete or be administered the AIRQ™ via telephone, desktop computer, or mobile device (e.g., smartphone, iPad)
4. Provide consent (adults/parents/guardians) and assent (age 13 to 17 years) to participate in the study

Exclusion Criteria: Patients meeting any of the following criteria will not be included in the study:

1. Current diagnosis of active chronic obstructive pulmonary disease or any lower respiratory diagnosis other than asthma
2. Has a cognitive impairment, hearing difficulty, acute psychopathology, medical condition, or insufficient knowledge of the English or Spanish language that, in the opinion of the investigator, would interfere with their ability to agree to participate and/or complete the AIRQ™ or other study questionnaires.

2.1 Sample Size Estimations

As the primary aim of this study is to assess the process and feasibility of implementing the AIRQ™, Asthma Checklist, and education resources (PRECISION program) using a telehealth or in-person platform, inferential statistics will not be conducted as part of the primary endpoint, and a formal sample size estimation is not applicable. Each site will target approximately 50 patients with asthma; however, all sites will be capped at 75 patients per site. This cap may be modified depending on individual site recruitment to ensure the targeted sample size is met. Implementing the AIRQ®, Asthma Checklist, and educational resources (PRECISION program) among approximately 50 patients per site will provide sites with enough experience to provide feedback on the outcomes, barriers, benefits, challenges, ease of implementation, and areas for improvement for future integration as a telehealth platform.

3. ANALYSIS SET

- **All enrolled patients**: All enrolled patients who have completed the initial visit with the AIRQ®
- **Web-survey analysis dataset:** All enrolled patients who complete the initial visit and the web survey
- **Primary care cluster dataset:** All enrolled patients at a primary care site who complete the initial visit and the web survey CCI [redacted].
- **Exacerbation dataset:** Includes EMR or claims data for enrolled patients who completed the initial visit and have available pre-post exacerbation data.
- **Follow-up analysis set:** All enrolled patients who completed the initial visit with the AIRQ® and have at least one follow-up visit completed in the nine-month implementation period with the follow-up AIRQ® . Patients are not required to have a follow-up visit.
- **HCP analysis set:** All health care providers trained on the study who complete the post-study survey and/or qualitative interview

4. EXPOSURE(S) AND OUTCOMES

4.1 Exposures

4.1.1 Definition of Primary Drug Exposure

Not applicable; no drug administered.

4.1.2 Definition of Comparison Drug Exposure

Not applicable; no drug administered.

4.1.3 Participant-completed Exposures

Patients will complete the following measures.

4.1.3.1 AIRQ®

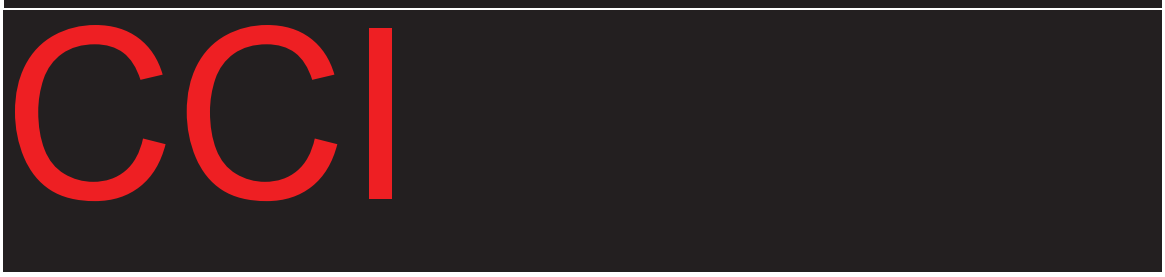
The AIRQ® includes 10 questions concerning patient medication use, asthma symptoms, medical visits, and tests. All response options are in yes/no format with a two-week recall for symptom-based impairment questions (items 1–7) and 12-month recall for exacerbation-based risk questions (items 8–10). The AIRQ® was developed iteratively, and a targeted review of research articles, current asthma guidelines and screeners, grey literature, and a secondary analysis of qualitative patient data informed the initial development of the AIRQ®. Five clinical experts, representing primary care and specialty care (including an allergist/immunologist, two pulmonologists, a nurse PhD researcher, and a family practitioner), academic and community practices, and five geographic regions of the United States (US), participated in five web-based focus groups to further develop the AIRQ®. The AIRQ® was subsequently presented at six advisory board meetings, in which more than 141 clinical experts, practitioners, asthma educators, and patient advocates reviewed and provided additional suggestions for refinement. All participants will complete the AIRQ® at their initial visit, whether in-person or via telehealth. Scoring information is located in Appendix A.

4.1.3.2 Follow-up AIRQ® (AIRQ® 3-month recall version)

A three-month recall version for the exacerbation items of the AIRQ® reduces the risk questions' (items 8–10) recall period to three rather than 12 months. Patients will complete the follow-up AIRQ® at all follow-up visits during the nine-month implementation period (if applicable).

4.1.3.3 ACE Questionnaire

The ACE Questionnaire is a self-administered electronic questionnaire that includes eight questions using a four-point Likert scale (strongly agree, agree, disagree, strongly disagree) and one open-ended question regarding additional comments about their visit or the AIRQ®. Patients who agree will be sent this questionnaire via an e-mailed survey link following their initial visit. Patients are asked to think about how completing the AIRQ® as part of their in-person or telehealth visit may have affected their experience when answering the questions.



4.1.3.6 Sociodemographic Questionnaire

Sites will collect basic participant demographic information on the Clinical CRF—age, gender, and race. Participants who agree will be asked to complete additional demographic questions. This form collects the participant's ethnicity, living situation, employment, and education, and will be used to describe the sample and assist with interpreting the results. Patients will be sent this questionnaire via an e-mailed web-link following their initial visit.

4.1.4 Clinician-completed Exposures

4.1.4.1 Clinical Case Report Form

For each participant, the clinical site will complete a Clinical CRF during the initial site telehealth or in-person visit. The Clinical CRF serves to characterize patients based on their asthma history, current medications, time since most recent spirometry, the HCP's rating of the patient's asthma severity and control, 12-month history of chart-reported exacerbations (when available), Assess component of the Asthma Checklist, and a treatment plan based on AIRQ® score at the initial visit (step-up/step down/no change).

4.1.4.2 Follow-up Clinical Case Report Form

A Follow-up Clinical CRF will be completed for patients with a follow-up visit (telehealth; in-person) during the follow-up period, which will document the HCP's rating of the patient's asthma severity and control, chart-reported exacerbations (when available), Assess component of the Asthma Checklist, and a treatment plan based on follow-up AIRQ® score at follow-up visit (e.g., step-up/step down/no change, referral). If sites submit more than one Follow-up Clinical CRF for a patient, the CRF from the first follow-up visit will be included in the primary analyses; additional follow-up AIRQ® assessments will be used to evaluate frequency of use. Novel sites where patients are participating in several asthma coaching sessions will be instructed to complete the Follow-up Clinical CRF for the patient's final session.

4.1.5 Clinical Site Touchpoint Questions

Evidera will conduct 30-minute conference calls with each clinical site for up to four timepoints (touchpoints) to discuss the use of PRECISION tools, address site questions, and discuss a set of discussion questions that focus on the facilitators and barriers/challenges of implementing the PRECISION program (educational resources). The same touchpoint implementation questions will be asked to all clinical staff participating in each scheduled meeting: Months 1, 2, 3 (optional), and 6.

4.1.6 Post-study Survey

All HCPs who participated in at least 10 telehealth or in-person visits will be invited to complete the Post-study Survey (paper form). The purpose of this survey is to obtain feedback on the implementation of the AIRQ® within each site's clinical practice (telehealth platform and in-person visit).

4.1.7 Semi-structured Interview Guide

A semi-structured interview guide will be used by the interviewer to obtain information from the principal investigator and key clinical site staff, including one non-prescriber where available, to gain a deeper understanding of the feasibility of implementing the AIRQ® via telehealth and in-person, as well as sustainability of using the PRECISION program in their clinical practice. Up to three interviews will be conducted per site. The semi-structured interview guide will include an introduction and specific questions/probes designed to facilitate discussion and optimize consistency across interviews. The interview guide will elicit from site personnel the process for implementing the AIRQ®, and recommendations for improving processes related to telehealth and in-person implementation. Also, any specific initiatives that were integrated into various practices will be discussed. Additional unscripted probes may also be used to gain further information or clarification.

4.2 Outcomes

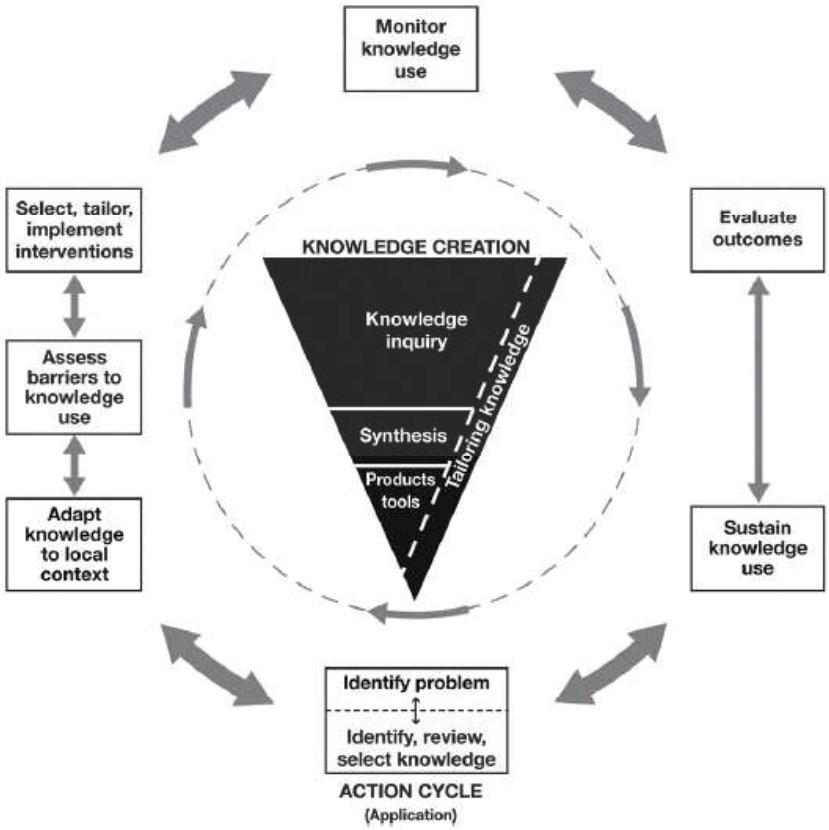
4.2.1 Primary Outcome

To address the primary objective of assessing the process and potential benefits when integrating the AIRQ® PRECISION program on a telehealth or in-person platform, the following outcomes will be assessed:

- **Post-study Telehealth Survey**: Descriptive statistics (n, frequency, mean, and standard deviation [SD]) will be used to summarize the results from the Post-study Survey.
- **Qualitative Interviews:** Results from the qualitative interviews will be summarized in a tabular format, with key recommendations, advantages, and disadvantages grouped. Specifically, barriers, benefits, challenges, ease of implementation, and areas for improvement will be summarized. Also, the summary will capture if the PRECISION program has been utilized in clinical practice post-implementation, or what would need to be done to support the continued use of the PRECISION program in their clinical practice.
- **Implementation Touchpoint Discussion with Sites:** Key findings from the implementation questions discussed during the clinical site touchpoint meetings (including barriers and subsequent ways in which these barriers were addressed) will be summarized.

Qualitative findings from the interviews and implementation touchpoints will be interpreted in the context of the Knowledge-to-Action Framework (Graham et al. 2006; Singh et al. 2020), which describes a process to translate new knowledge into sustainable evidence-based interventions that can be applied in clinical practice (In-text Figure 1). In this context, the findings will be used in the action cycle to identify challenges, barriers, and benefits to implementing the AIRQ® and PRECISION tools into clinical practice. The knowledge will be evaluated in local contexts (e.g., practice clusters) and will be monitored throughout the implementation and sustainability period.

In-text Figure 1. Knowledge-to-Action Framework



4.2.2 Secondary Outcome(s)

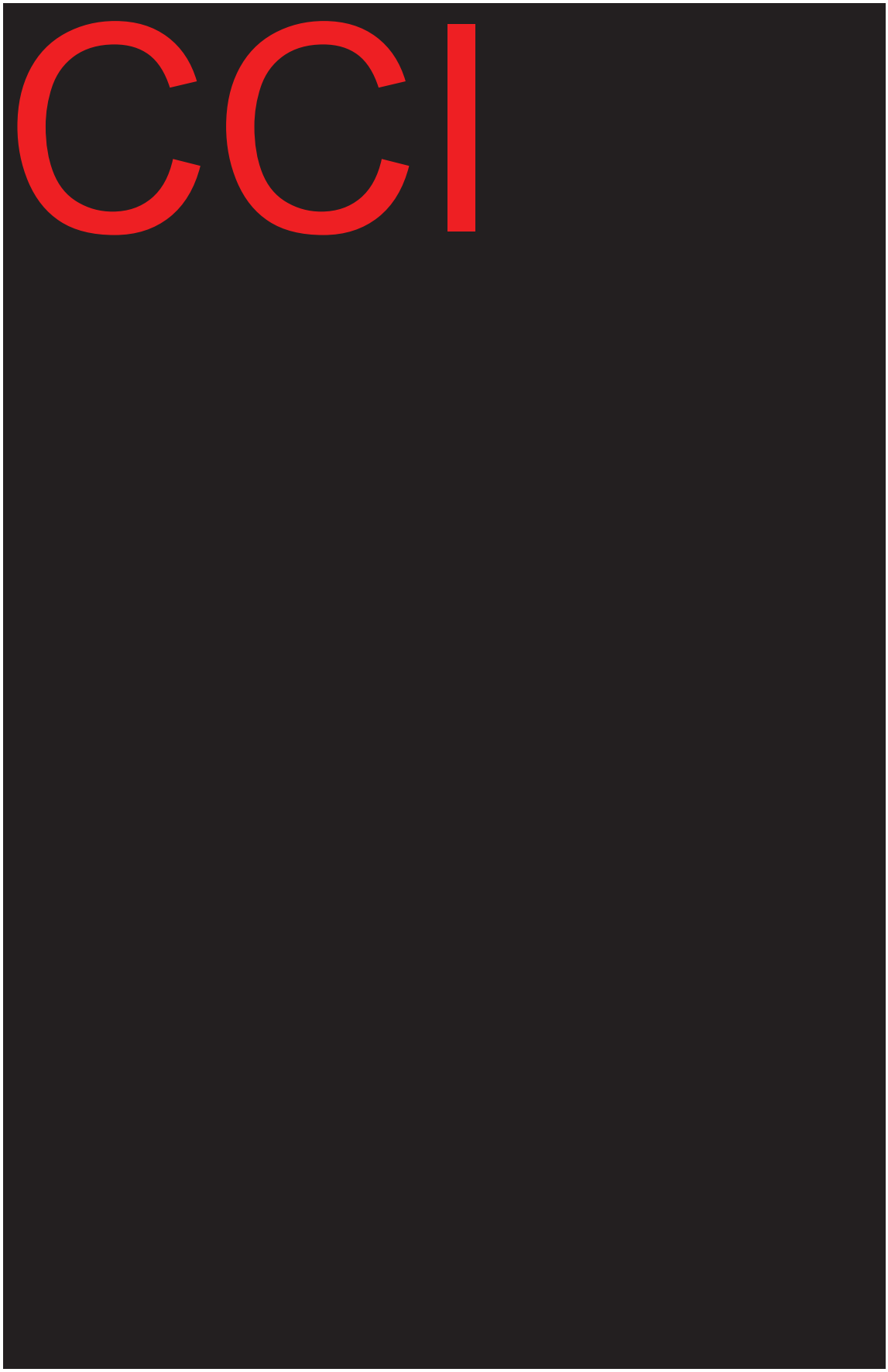
1. To address the secondary objective of assessing patient telehealth or in-person visit satisfaction when the AIRQ® is initiated as part of a telehealth or in-person visit with their HCP, the following outcomes will be assessed:
    - ACE Questionnaire Responses: Descriptive statistics (n, frequency, mean, and SD) will be used to summarize by item for all items. In addition,

2. To explore change in AIRQ® scores from initial visit to follow-up visits:
    - AIRQ® (initial study visit)
    - Follow-up AIRQ® (follow-up visits)

Results will be presented by practice cluster and platform used (e.g. telehealth vs in-person).

4.2.3 Exploratory Outcome(s)

CCI [redacted]



4.3 Other Variables and Covariates

The sample will be characterized by practice cluster: (1) primary care sites (e.g., private practice, FQHC); (2) specialty care sites (pulmonary, asthma/immunology); and (3) novel sites (e.g., pharmacy, nurse practitioners, nurse educators, prescribers and non-prescribers, telehealth component of Allergy and Asthma Network.

5. ANALYSIS METHODS

5.1 Statistical Methods – General Aspects

An overall data disposition figure (Figure 1) will be generated on all enrolled patients to describe total enrolled/consented, total sample included/excluded from analyses, and finally key data (AIRQ®) availability status. In the data disposition figure, the total sample who had a follow-up visit will be reported by practice cluster. A patient disposition table will also be developed to descriptively characterize the sample in terms of total patients enrolled, age group, and language by site and practice cluster (Table 1a to Table 1c). Descriptive statistics (n, frequency, mean, median, and SD) will be used to characterize the sample in terms of the patient-reported sociodemographic and clinical characteristics (e.g., age, sex, education, etc.) (Table 2a and Table 2b, respectively), overall and by practice cluster. Descriptive statistics (n, frequency, mean, median, and SD) will be used to characterize the sample overall and by cluster type in terms of clinician-reported patient characteristics, clinical characteristics, and visit information (Tables 3a to 3f).

Descriptive statistics (n, mean [SD], median, range) will also be used to present the results (overall and by practice cluster) for the AIRQ® total and control level scores (Table 4a). AIRQ® scores will also be summarized by visit platform (telehealth vs. in-person), exacerbation history, education level, language (sample size permitting), age, sex and NAEPP step level (Table 4b to 4h). Descriptive statistics (n, mean, SD, median range) will be presented for CCI [redacted] Descriptive statistics (n, mean [SD], median, range) will be presented for CCI [redacted]. Descriptive statistics (n, %) will be presented for the ACE Questionnaire (item scores) by practice cluster, visit platform, AIRQ® control score, exacerbation history, education level, language, age, sex, and NEPP step level (Table 7 series). Item responses and scores on the patient-reported outcome measures (AIRQ®, CCI [redacted] and ACE) will be compared across groups (practice cluster, visit platform, exacerbation history, education level, language, age, sex and NAEPP step level). For continuous variables, ANOVA will be used to compare mean scores across groups; pairwise comparisons between means will be performed using Scheffe's test adjusting for multiple comparisons for more than two groups. For categorical data, chi-square analyses will be used to compare frequencies by groups. No adjustments will be made for multiple groups.

For the follow-up analysis dataset, a patient disposition table will be developed to descriptively characterize the follow-up analysis set in terms of age group, language, race, and education by practice cluster (Table 8a). The mean time to first follow-up visit will be described (n, %) in Table 8b. For the primary care and specialty clusters, the first follow-up clinical CRF will be completed at the patient's first follow-up visit. For the novel cluster sites where patients are receiving multiple asthma coaching sessions, the follow-up clinical CRF will be completed at their final coaching session.

Descriptive statistics (n, %) will be used to describe patients with a follow-up visit by AIRQ® control level at initial visit (Tables 8c). Descriptive statistics (n, %) will also be used to describe patients with a follow-up visit by exacerbation history, education level, language, age, sex, and NAEPP step level at the initial visit (Tables 8d to 8i). Descriptive statistics (n, %) will be used to describe patients with a follow-up visit by HCP actions at the initial visit overall and by practice cluster (Table 8j to 8m).

Clinical characteristics and visit information from the first follow-up visit will be presented using descriptive statistics (n, mean [SD], median, range) (Tables 9a to 9e). Descriptive statistics (n, mean [SD], median, range) will also be used to present the results (overall and by practice cluster) for the first follow-up AIRQ® scores and control levels (Table 10a). AIRQ® scores from the first follow-up

visit will also be summarized by visit platform (telehealth vs. in-person), exacerbation history, education level, language, age, sex and NAEPP step level (Table 10b to 10h). In Table 10i, descriptive statistics (mean, SD, median, range) will be used to detail the average number of AIRQs® completed by patients overall and in each practice cluster. In Table 10j, AIRQ® scores from the patient's final follow-up (if more than 1 follow-up AIRQ) will be summarized.

5.1.1 Primary Objective: Assess the Process and Potential Benefits of Implementing the AIRQ™, Asthma Checklist, and Educational Resources (PRECISION Program) into Clinical Practice

This analysis will be conducted on the HCP analysis set of clinicians who completed the post-study survey. Descriptive statistics (n, %) will be used to summarize the proportion of responses for each of the categorical items on the post-study survey (e.g., How would you rate the overall ease of implementing the AIRQ™ into your clinical practice using the telehealth platform?). Descriptive statistics (mean [SD], median, range) will be used to summarize the number of patients treated using the PRECISION program (Table 11). Results will be presented overall and by practice cluster.

Qualitative analyses will be conducted to evaluate the frequency of descriptive free-text responses to open-ended questions on the post study survey (e.g., What features of the PRECISION program do you think could be improved?) (Table 12 series), from the qualitative interviews with key site staff and clinicians (Table 13 series), and from the implementation touchpoint calls with key site staff and clinicians (Table 14 series).

5.1.2 Secondary Objective(s): 1) To Assess Patient Visit Satisfaction When the AIRQ™ Is Initiated as Part of a Telehealth or In-Person visit with Their HCP; 2) To explore change in AIRQ® scores from the initial visit to follow-up visit(s)

To assess patient satisfaction with AIRQ®, descriptive statistics (n, %) will be used to summarize patient responses to the ACE Questionnaire overall and by practice cluster (Table 7a). Scores will also be summarized by visit platform (in-person vs. telehealth), AIRQ® control level, education level, age, exacerbation history, and patient language (Table 7 series).

AIRQ® score and control level at the initial visit and Follow-up AIRQ® score and control level at follow-up visit(s) will be explored overall and by practice cluster, and presented using descriptive statistics (n, frequency, mean, SD) (Table 4a,Table 10a and Table 10j). The change in AIRQ® between initial visit and first follow-up visit will be evaluated using paired t-tests for the overall sample, and by practice cluster (Table 15). If the sample size allows, change in AIRQ® score will also be evaluated based on elapsed time from initial visit to follow-up by groups (e.g., 0–3 months; 4–6 months; 7–9 months). In Table 16, shift analyses will be conducted to evaluate change in AIRQ® control score between the initial and first follow-up visit. The frequency of patients improving, maintaining or worsening in AIRQ® control level from initial to first follow-up visit will be described in Table 17. Similarly, shift analyses for AIRQ® control score between the initial and final follow-up visit will be presented in Table 18, and the frequency of patients improving, maintaining or worsening in AIRQ® control level from initial to final follow-up visit will be described in Table 19. If the sample size for additional AIRQ® completions after the first follow-up allows, an additional exploratory analysis will be to explore the trajectory of change in AIRQ® score in relation to visit number and other clinical variables.

5.1.3 Exploratory Objective(s): CCI

6. BIAS

6.1 Methods to Minimize Bias

Given that completing the ACE Questionnaire is optional, the potential for response bias (e.g., patients who like the telehealth platform may be more inclined to complete the survey) may be introduced into this study. This will be noted when interpreting the results. Additionally, patients who have a follow-up assessment may be more severe than those who do not; thus, change scores may not be representative of the entire sample, which will also be noted when interpreting results.

6.2 Adjustment for Multiple Comparisons

Not applicable.

7. INTERIM ANALYSES

Not applicable.

8. REFERENCES

Graham ID, Logan J, Harrison MB, Straus SE, Tetroe J, Caswell W, Robinson N. Lost in knowledge translation: time for a map? J *Contin Educ Health Prof*. 2006;26(1):13–24.

CCI [redacted]

CCI [redacted]

CCI [redacted]

Singh S, Surani S, McGuinness S, Eudicone J, Gilbert I, Subramanian S. Current practice patterns, challenges, and educational needs of asthma care providers in the United States. *J Asthma*. 2020 May 19:1-10.

Appendix A. Scoring Information

AIRQ®

The AIRQ® includes 10 questions with Yes/No responses. A total AIRQ® score is generated by summing the number of "Yes" responses. The scores for the AIRQ® range from 0–10. Patients with scores of 0 or 1 are considered "well-controlled," patients with scores of 2–4 are considered "not well-controlled," and patients with scores of 5–10 are considered "very poorly controlled."

ACE

There are eight questions on the ACE with Likert scale responses (Strongly Agree, Agree, Disagree, Strongly Disagree), and one open-ended question. There is no total score for the ACE. Scores for each individual item will be described by frequency.

NAEPP Step Coding

<table>
<tr><th>Code</th><th colspan="2">Maintenance Therapy</th><th>Rescue therapy</th></tr>
<tr><td>Step 1</td><td colspan="2">No daily medication checked</td><td>SABA alone with no maintenance therapy[a]</td></tr>
<tr><td rowspan="4">Step 2</td><td colspan="2">Low-dose ICS</td><td rowspan="3">SABA with maintenance therapy[b]</td></tr>
<tr><td colspan="2">Theophylline Preparations</td></tr>
<tr><td colspan="2">Leukotriene modifier</td></tr>
<tr><td colspan="2">No daily medication checked</td><td>ICS+ SABA as rescue therapy alone

Fixed dose combination fast-acting LABA/ICS alone as recue</td></tr>
<tr><td rowspan="5">Step 3</td><td colspan="2">Medium/High-dose ICS</td><td rowspan="13">For Steps 3 through 6, step assignment is based on maintenance therapy only.</td></tr>
<tr><td colspan="2">Low-dose ICS + LAMA</td></tr>
<tr><td colspan="2">Low-dose ICS+ leukotriene modifier</td></tr>
<tr><td colspan="2">Low-dose ICS + theophylline preparation</td></tr>
<tr><td colspan="2">Low dose ICS + LABA</td></tr>
<tr><td rowspan="4">Step 4</td><td colspan="2">Medium-dose ICS/LABA</td></tr>
<tr><td colspan="2">Medium dose ICS + LAMA</td></tr>
<tr><td colspan="2">Medium/high dose ICS + theophylline</td></tr>
<tr><td colspan="2">Medium/high dose ICS + leukotriene modifier</td></tr>
<tr><td rowspan="2">Step 5</td><td colspan="2">High-dose ICS/LABA + LAMA</td></tr>
<tr><td colspan="2">High-dose ICS/LABA</td></tr>
<tr><td>Step 6[c]</td><td>Any maintenance therapy AND</td><td>Chronic oral systemic corticosteroids

OR

Biologic</td></tr>
</table>

[a] Possible alternative: “SABA as rescue therapy via nebulizer without other rescue or maintenance therapies” or “Primatene Mist as rescue and no maintenance therapy”

[b] Possible Alternative: “SABA as rescue therapy via nebulizer with other rescue maintenance therapies” or “Primatene Mist as rescue with maintenance therapy(s)”

Appendix B. Revisions to Select Analyses Initially Detailed in this SAP

Due to the nature of the data collected or to enhance clarity of presentation or interpretation of findings, some revisions were made to select analyses initially specified in the SAP. These revisions are detailed below:

- Novel site results were displayed in separate tables (N table series)
- All analyses by language were not conducted since the AIRQ was only administered in English language.
- There was no data on PRECISION education resource views/downloads for the specialty care cluster so tables 22c and 23c could not be run
- Some analyses could not be conducted due to the small sample size, e.g., for Tables 23e-23j, Tables 29b1-b3, Tables 29e-t, Table 30a, Table N4d, Tables N6b-N6i, Tables N7b-N7i, Table N8e, N10d, N22f, N23e, N29e-N29t or due to lack of data (i.e., no telehealth visits[redacted] or medical record history data available for the novel site so Table N3c, N4b, N4c, N5, N8d, N9b, N10b, N10c, N22e, N23e could not be presented).
- There was only one follow-up visit per patient so some analyses could not be presented (Table 24 and Table N24 series) or were modified (Table 25)
- Some tables duplicated content from other tables and are not presented (content for the Table 26, 27, N26 and N27 series can be found in the Table 20, 21, N20 and N21 series)
- Inferential statistical tests (e.g., ANOVA, chi-square test) were run to determine if differences between the practice clusters were statistically significant for Table 3e and Tables 8 series, Tables 10 series, Table 20 series
- A Bowker's test was used instead of a Cochran's Q test to evaluate if there were within-patient changes in OCS use (Table 31b) as the Cochran's Q test was not suitable 9 (only provides a method for testing three or more binary matched pairs).

SIGNATURES

ASTRAZENECA SIGNATURES

D2287L00028 PRECISION Study 4 – Implementation

Statistical Analysis Plan for the Implementation of the US PRECISION AIRQ®, Asthma Checklist, and Educational Resources (PRECISION Program) into Clinical Practice Using Telehealth and In-Person Platforms: Addendum

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This statistical analysis plan addendum has been subjected to an internal AstraZeneca review.

I agree to the terms of this statistical analysis plan.

AstraZeneca Study Statistician

Evidera Statistical Oversight

DocuSign

Certificate Of Completion

Envelope Id: 062AA0E6AD534AABBDE7BD14E9A628B5
Status: Completed
Subject: Complete with DocuSign: EVA-26645 Implementation Study SAP_v1.1_Addendum.docx
Source Envelope:
Document Pages: 24
Signatures: 2
Certificate Pages: 2
Initials: 0
AutoNav: Enabled
EnvelopeId Stamping: Enabled
Time Zone: (UTC) Monrovia, Reykjavik

PPD

Record Tracking

PPD

PPD

Location: DocuSign

Signer Events	Signature	Timestamp
PPD	PPD	PPD

Electronic Record and Signature Disclosure:
Not Offered via DocuSign

PPD

PPD

PPD

Electronic Record and Signature Disclosure:
Not Offered via DocuSign

In Person Signer Events	Signature	Timestamp
Editor Delivery Events	**Status**	**Timestamp**
Agent Delivery Events	**Status**	**Timestamp**
Intermediary Delivery Events	**Status**	**Timestamp**
Certified Delivery Events	**Status**	**Timestamp**
Carbon Copy Events	**Status**	**Timestamp**
Witness Events	**Signature**	**Timestamp**
Notary Events	**Signature**	**Timestamp**

Envelope Summary Events	Status	Timestamps
Envelope Sent	Hashed/Encrypted	19-Oct-2023 | 18:16
Envelope Updated	Security Checked	19-Oct-2023 | 20:09
Envelope Updated	Security Checked	19-Oct-2023 | 20:09

Envelope Summary Events	Status	Timestamps
Certified Delivered	Security Checked	19-Oct-2023 | 20:27
Signing Complete	Security Checked	19-Oct-2023 | 20:27
Completed	Security Checked	19-Oct-2023 | 20:27

Payment Events	Status	Timestamps