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Responsive Asthma Care for Teens (ReACT): Development protocol for an adaptive mobile health intervention for adolescents with asthma

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Abstract

Introduction: Asthma is a leading cause of youth morbidity in the United States, affecting > 8% of youth. Adherence to inhaled corticosteroids (ICS) can prevent asthma-related morbidity; however, the typical adolescent with asthma takes fewer than 50% of their prescribed doses. Adolescents are uniquely vulnerable to suboptimal asthma self-management due to still-developing executive functioning capabilities that may impede consistent self-regulation and weaken attempts to use problem solving to overcome barriers to ICS adherence.

Methods and analysis: The aims of this project are to improve adherence to ICS as an important step toward better self-management among adolescents ages 13-17 diagnosed with asthma by merging the efficacious behavior change strategies found in behavioral health interventions with scalable, adaptive mHealth technologies to create the Responsive Asthma Care for Teens program (ReACT). ReACT intervention content will be developed through an iterative user-centered design process that includes conducting 1) one-on-one interviews with 20 teens with asthma; 2) crowdsourced feedback from a nationally representative panel of 100 adolescents with asthma; and 3) an advisory board of youth with asthma, a pediatric pulmonologist, and a behavioral health expert. In tandem, we will work with an existing technology vendor to program ReACT algorithms to allow for tailored intervention delivery. We will conduct usability testing of an alpha version of ReACT with a sample of 20 target users to assess acceptability and usability of our mHealth intervention.

Ethics and dissemination: Institutional Review Board approval was obtained at the University of Kansas and the University of Florida. We will submit study findings for presentation at national research conferences that are well attended by a mix of psychologists, allied health professionals, and physicians. We will publish study findings in peer-reviewed journals read by members of the psychology, nursing, and pulmonary communities.

Strengths and limitations of this study

- Intervention content will be developed first with theory and evidence-based decision-making and refined via an iterative, user-centered approach with target users and key stakeholders.
- Adaptive algorithms will be programmed into an existing, patient-facing asthma management platform.
- Intervention usability and acceptability will be stringently assessed prior to efficacy testing to allow for modifications and improvements.
- Although we will have data on patient preferences, usability, and acceptability, the current protocol is not designed to evaluate the efficacy of the ReACT program; this limitation will be addressed in a future randomized controlled trial.

Introduction

Asthma affects over 8% of youth and is a leading cause of morbidity.[1,2] Some asthma symptoms and health care utilization could be prevented via consistent engagement in disease self-management behaviors (e.g., symptom recognition and monitoring, appropriate administration of medications).[2,3] Adherence to daily controller medications, such as inhaled corticosteroids, is central to control asthma and reduce morbidity for youth with persistent asthma.[2] ICS adherence rates with adolescents are often < 50%,[4,5] placing them at significant risk for reduced lung function, increased morbidity, and poor quality of life.[4,6]

Effective disease management in asthma involves avoiding triggers that cause symptoms, monitoring symptoms when they occur, and, for those with persistent symptoms, taking controller medications to address inflammation and reduce symptom frequency.[2] The complexity of the asthma treatment regimen coupled with still-developing executive functioning and problem solving abilities makes adolescents vulnerable to suboptimal asthma self-management through self-regulation defecits.[7–11] Self-regulation theory as applied in this context posits that intrapersonal and external factors influence the degree to which an adolescent will engage in disease management strategies to achieve a desired end point or goal (**Figure 1)**. One of the major challenges for adolescents from a self-regulation theory perspective is that sustained self-management requires an ongoing and effortful process of observing, judging, and reacting to three distinct but reciprocally related processes. Regarding adherence to ICS, observing refers to the self-monitoring of one's medication adherence (e.g., '*I took my controller medication 5 of the 14 times I was supposed to last week*'), judging refers to internal appraisals of the person's behavior set against a goal (e.g., '*That is bad! I took less than half of my prescribed doses last* *week.'*), and reactions refer to the response to observations and reactions (e.g., *'I am going to ask my mom to help me remember my medication every morning and after dinner.'*).

The utility and application of self-regulation theory is well-supported in asthma.[12–16] Clark and colleagues demonstrated in a large cohort of families of children with asthma (*n* = 637) that self-observations, self-judgments, and self-reactions were interrelated across time and predictive of disease management strategies, healthcare utilization, and quality of life in a 5-year prospective study.[17] Intrapersonal factors, including asthma knowledge, attitudes (e.g., motivation), and feelings (e.g., mood, stress), and external factors such as the social and family environment, have consistently been associated with asthma management behaviors and disease outcomes.[13,18–23] The effortful processes of observation and judgement are both linked to disease management strategies and more frequent engagement in self-monitoring (i.e., self-observation), goal setting, and higher self-efficacy for asthma management which are themselves related to positive asthma outcomes. Therefore, the requisite strategies for adhering to ICS typically require sustained cognitive effort and are less likely to be possessed by adoescents who are required to use their evolving cognitive resources for other developmentally normative tasks (e.g., navigating social situations, schoolwork). In practice, efficacious interventions cultivate self-regulatory skills by providing scaffolded support in self-monitoring medication use, setting adherence goals, and delivering regular feedback on progress. Often parents are engaged in the initialinitial learning and later practice and maintenance as they are a major part of the system that supports the adolescent from day-to-day.

Similar to the problem of underdeveloped self-regulatory skill, it is common for adolescents with persistent asthma to be met with barriers to ICS adherence that they may not have the experience or cognitive development to effectively problem-solve.[24,25] For instance, even developmentally normative tasks such as having several tests in one week may be novel enough to overwhelm an adolescent's developing problem-solving ability. Efficacious behavioral interventions often attempt to actively reframe ICS adherence as central to an adolescent's self-concept (e.g., better lung function will allow you to pursue your interests). Once adolescents see adherence as helping them reach their own personal goals rather than as a chore, they are sufficiently motivated to learn skills that can help ensure adherence to ICS. To this end, adolescents are taught to identify intrapersonal and external barriers to adherence and problem solve around those barriers. Beyond simply teaching a formula for problem-solving, many effective adherence promotion programs tailor intervention content to personally salient barriers and help the adolescent identify and implement strategies specifically designed to increase the chances of regimen success. [26,27,28]

A persistent problem in this approach is the difficulty of relying on infrequent face-to-face visits (e.g., for clinical care) to implement interventions. Smartphones are habitually carried by >70% of adolescents[29]; as such, mobile technology provides a readily available medium to approximate the features of efficacious behavioral health interventions[30,31] by leveraging passive monitoring, data listening, preprogrammed algorithms, and content libraries focused on improving self-regulation and problem solving skills.[32,33] Despite their potential, existing mobile health (mHealth) interventions have been largely developed without the benefit of behavioral theory, use reminder-based approaches to behavior change, and lack the kinds of tailored problem-solving training that characterizes efficacious in-person interventions.[34,35] We believe that this, at least in part, helps explain why existing mHealth interventions for asthma medication adherence have yet to demonstrate their efficacy beyond active controls.[36,37]

There is a clear need for a mHealth intervention that merges digital delivery modalities with the theory-based behavioral framework, full-featured tailoring, and adaptive dosing found in efficacious in-person treatments. Recent technological advances have catalyzed the development of mobile-based intervention platforms that deliver tailored support to individuals in a timely fashion.[38,39] We propose to extend this work to pediatric asthma by developing ReACT, an innovative adaptive mHealth intervention that provides scaffolded self-regulation and problem solving training when adolescents' adherence data indicate they need additional support the most. We will outline how ReACT content will be developed, refined, and tested through an iterative user-centered design process guided by theory and prior evidence.

Methods and Analysis

Objectives

The aims of the study are: 1) conduct a hybrid user-centered and evidence-based design process to develop ReACT content and features and use information from the design process to create libraries of intervention content; 2) test the acceptability and usability of ReACT in a sample of 20 adolescents with persistent asthma. We hypothesize that ReACT will be an acceptable and usable mHealth adherence promotion intervention as determined by high satisfaction ratings and themes from think aloud testing and qualitative one-on-one interviews with target users.

Project Overview

This multi-site study will take place at two universities and their affiliated clinics. Features and intervention content of ReACT will be developed concurrently. We will work with a technology vendor to add functionality for ReACT to an existing mHealth adherence monitoring platform. We will use a strong theoretical framework and prior evidence combined with a series of user-centered design phases to determine what intervention content should populate the ReACT system (Design Phase 1). Study team members and an advisory board will then refine intervention content and complete preliminary usability testing of ReACT (Design Phase 2). Finally, we will conduct acceptability and usability testing using an alpha version of ReACT. See **Figure 2** for the study timeline.

Core ReACT Functionality

We will create ReACT by expanding the capabilities of an existing Android and iOS compatible mobile phone app that uses an integrated mobile sensor designed to fit onto an asthma metered dose inhaler (MDI) or diskus. The sensor works passively to sense when ICS or short-acting beta-agonist (SABA) medications are dispensed. Bluetooth is used to pass the information to the app, which has a set of optional features (e.g., provide feedback about adherence) that can be turned on as intervention parameters dictate. **Figure 3** outlines an adolescent's intervention experience through ReACT. Building from theory and prior evidence, core ReACT components in sequence are: 1) core education on asthma management and skills training content on goal setting and problem solving, 2) conditional activation of ReACT features when an adolescent is <80% adherent to their ICS, 3) an evidence-based goal-setting algorithm that shapes adherence to dosing recommendations over time, 4) timely assessment of an adolescent's barriers to adherence, and 5) delivery of tailored problem solving training based on recent and salient barriers.

ReACT will begin with an orientation module within the app that guides the users through the platform, core educational and skills training modules, and passive monitoring of medications. Adolescents will complete an asthma education module based on NHLBI guidelines[40] to ensure that they have an understanding of the importance of medication adherence as a means to avoid asthma-related impairments. Adolescents will receive skills training on empirically-supported techniques consistent with our guiding self-regulation theory. Goal setting content will use a SMART (Specific, Measurable, Attainable, Relevant, Time-Bound) goal framework. Problem-solving skills training will focus on orienting to the problem, defining and formulating the problem, generating alternative solutions, deciding on a course of action, and implementation of a solution.[41,42] We will use engaging videos created by the team to deliver content. Participants will complete the orientation modules with study staff to encourage engagement and provide assistance if necessary.

ReACT will use passive sensing to objectively monitor rates of adolescent ICS adherence throughout the intervention period. Active intervention elements in ReACT will activate only when an adolescent falls below a clinically derived 80% adherence threshold[43] based on a 7-day rolling average, thus reducing intervention fatigue.[39] If an adolescent has < 80% adherence to ICS based on the 7-day rolling average, they will be prompted to view graphical feedback about their patterns of ICS adherence and SABA use. ReACT will then prompt the adolescent to set a goal for adherence in the next 7-day period, a strategy with demonstrated efficacy in previous asthma adherence interventions.[44] The algorithm will only allow goals that are reasonable given performance over the past week to avoid overly ambitious and unattainable goals. Each evening, the adolescent will receive a feedback message about how much their adherence that day moved them toward their goal.

ReACT will identify contextual barriers to ICS adherence by also initiating an assessment as soon as the 7-day rolling average indicates that adherence is < 80%. Adolescents will be given a brief electronic momentary assessment (EMA) survey of barriers identified from our pilot data and Design Phase 1 to identify what barrier the problem-solving content should be tailored to address. Participants will answer brief questions regarding barriers that got in the way of taking their ICS followed by a rank order item denoting which one to make the focus of their problem-solving efforts. Once a barrier is identified, ReACT will deliver problem-solving content tailored to that specific barrier. For instance, if an adolescent has identified and chooses to work on stress as their top barrier to ICS adherence, the tailored problem solving will deliver structured problem-solving training using a flexible system of branching that is tailored to stress specifically. To execute this feature, ReACT will have several content banks that use the same structure. To illustrate the user experience, a possible problem-solving intervention could include: 1) defining the problem: participants will be presented with a standard message reflecting the problem they identified in the EMA survey 2) setting a realistic, achievable goal: several goals will be presented and the participant will choose one and receive feedback on their choice; 3) generating multiple solutions: the participant will be asked to choose from a list of possible solutions for the goal that they selected in step #2; 4) evaluating pros and cons: participants will evaluate the pros and cons of multiple solutions listed in step #3; 5) selecting a solution: participants will choose the solution that may work the best; 6) making an action plan: participants will select from a list of action plans that correspond to the solution they have selected; 7) evaluating the outcome: after a week participants will be asked whether they implemented the solution selected in #6.

Once an adolescent receives intervention content, ReACT will deliver a survey two days later to assess content use. If the participant responds that they used the intervention strategy, ReACT will assess for the participant's confidence in their ability to repeat the plan in the future. If the participant has not used the strategy, they will receive a supportive prompt with options to review the content they saw last time, see the same content in a different media format, review a different set of content on the same topic, or set a goal to use the strategies by a specific time in the next two days. The Tailored Problem-Solving Process (**Figure 3**) will only run once in a given 7-day window to avoid overwhelming participants with content and ensure that participants can only be presented two content modules in a given 7-day period. Another program safeguard to reduce overwhelming participants with content is a restriction in the number of content modules in a given 7-day period (≤2). This mirrors normative approaches for in-person interventions during which only one or two new concepts would be introduced each week.

Participants and Recruitment

Participants. Participants will include four separate samples of 13-17-year-old adolescents with asthma and their caregivers. Twenty adolescent-caregiver dyads will complete individual interviews, 100 adolescents will provide crowdsourced feedback via a national online panel, four adolescent-caregiver dyads will participate in advisory board meetings, and 20 adolescent-caregiver dyads will complete user testing of ReACT. We intend that at least half of adolescent participants in the interviews and advisory boards will be from racial and ethnic minority groups.

Inclusion and Exclusion Criteria. For interviews, advisory boards, and user testing, adolescents must have a physician-verified diagnosis of current asthma with persistent symptoms requiring regular ICS use for ≥ 6 months. They must have a daily ICS or ICS/LABA prescription, and they and their caregivers must speak and read English. Asthma status and prescription information will be verified via the electronic medical record. Families will be excluded from the study if the adolescent is currently involved in an asthma management intervention, has a comorbid chronic health condition that may impact lung function, or has a significant cognitive impairment or developmental delay that interferes with study completion. For crowdsourced feedback, inclusion will be determined at the level of a national online panel, which will screen participants for persistent asthma.

Recruitment. Participants will be recruited through university-affiliated clinics and via flyers. IRB approved flyers will be posted or made available in clinics, community organizations, schools, physician offices, and common areas. Flyers will encourage families and nurses to call our research office to learn about the project, determine initial eligibility, and if eligible, schedule an in-person screening visit where informed consent will be collected prior to study enrollment. Research staff will be available to meet with participants during a scheduled clinic visit to provide a study overview, complete in-person screening for eligibility, and invite participation. In the event that a family is unable to complete screening during a clinic visit, research staff will request permission for a member of the study team to contact patients for screening using an IRB-approved "consent-to-contact" form. A member of the study staff will then call interested participants to provide a study overview and invite participation.

ReACT Development

Patient and Public Involvement. Adolescents diagnosed with asthma, their caregivers, and pediatric asthma providers are involved in all stages of ReACT development please see below subsections for descriptions of involvement.

Design Phase 1: Content Development. We have developed a list of common barriers to ICS adherence from our own pilot data and the extant pediatric asthma literature. Our goal for Design Phase 1 is to use individual interviews with adolescents diagnosed with asthma to translate these barriers into terms easily understood by adolescents, develop a final list of barriers to adherence, and subsequently develop a library of intervention content to overcome adherence barriers that is informed by self-regulation theory. Individual interview participants and their caregivers will also complete asthma-related measures to for sample description purposes and to obtain preliminary data on constructs of interest to the project (see **Table 1**).

The study team will create an individual interview guide that will be used to identify what barriers to adherence are most salient to adolescents with asthma, and to solicit their opinion about the types of intervention content that they would prefer to receive when experiencing these barriers. Prior to the start of individual interviews, pediatric asthma providers (e.g., pulmonologists, nurses) will provide feedback on the interview guide. All interviews will be audio recorded and conducted with self-regulation theory in mind. If a component of self-regulation theory is not discussed, we will probe for content in the omitted domain to facilitate development of intervention content. Interviews will be transcribed and evaluated by the study team (see Data Analysis section).

Research staff with experience developing digital intervention content will leverage information gathered during Design Phase 1 to develop a library of intervention content for each barrier identified in the interviews and quantitative analysis of our pilot data. We anticipate that intervention content will include a combination of skills training videos, brief text content, educational videos, and images. Delivery modality (SMS, app, etc.) will be discussed with the advisory board.

Design Phase 2: Refinement of Content and Preliminary Usability Testing. In Design Phase 2 we will refine intervention content generated in Design Phase 1 through 1) nationally crowdsourced feedback from adolescents with asthma and 2) advisory board meetings. Preliminary usability testing and iterative refinement will be conducted with our advisory board meetings (described below).

Nationally crowdsourced feedback will be solicited via an online panel and survey-technology provider. Participants will review intervention content and rate its appropriateness using a dichotomous "Yes" (I like the message as it is) or "No" (change it to make it better) response choice. Content receiving ≥ 60% "No" votes will be discarded, and those with ≤ 39% "No" votes will be accepted as final intervention content. Content with 40-59% "No" votes will be revised or clarified while retaining any theoretically or empirically derived concepts.[45 45] We will design surveys to take no more than 30 minutes each. If necessary, we will split the content into two surveys to keep the administration time < 30 minutes. Although adolescent stakeholders will be involved in developing ReACT intervention content rated during crowdsourcing, we acknowledge that there is a possibility that a higher than expected amount of content will be viewed unfavorably during this phase. We will review crowdsourcing feedback data from an initial wave of 20 participants. In the event that > 60% of content is viewed unfavorably, we will pause crowdsourcing to develop new intervention content.

An advisory board comprised of adolescent-caregiver dyads and study staff members will convene three times. The first meeting will focus on reviewing summative data and themes that emerged from crowdsourcing phase. The second advisory board meeting will involve discussion about methods to further refine intervention content that received 40-59% "No" votes during crowdsourcing. We will incorporate modified content that reaches group consensus into applicable ReACT intervention content libraries. Preliminary usability testing will take place during the final advisory board meeting. Members will conduct hands-on testing of ReACT alongside study staff. We will use a "think aloud" approach with members as they explore components of the ReACT interface (e.g., layout, visual feedback), answer EMA questions, and view intervention content.[46] This process more closely approximates actual use, and will enable us to receive feedback in real-time. The study team will transcribe participant commentary during testing for review. Advisory board participants and their caregivers will also complete asthma-related measures to pilot data collection procedures and provide baseline descriptive statistics (see **Table 1**).

Acceptability and Usability Testing of ReACT

In the final phase, adolescents will conduct user testing with the alpha version of ReACT. The overarching goal is to gather acceptability and usability data from the perspectives of target users of ReACT. Adolescents will be oriented to ReACT by study staff and then complete a "think aloud" approach with as they interact with ReACT.[46] Study staff will ensure that participants interact with all relevant ReACT components including asthma education and skills training videos, EMA questions, and intervention content delivered in a variety of formats. Again, participant comments and suggestions during testing will be transcribed for review, and participants and their caregivers will complete asthma-related measures (see **Table 1**).

Data Analysis Plan

Individual Interviews. Study staff will transcribe individual interviews for interpretation and enter transcribed files and expanded field notes into NVivo. We will code and aggregate interviews using a theoretical thematic analysis approach to developing themes.[47–49] Our theoretical thematic analysis approach will use an a priori theoretical framework guided by self-regulation theory, informed by advisory board meetings. The investigators will mark comments identified to represent discrete thoughts or themes using a semantic analysis, and they will use an essential realist approach to arrive at themes.[47] These patterns or themes will comprise the initial set of categories. Research staff will then re-code the data using these categories and organize major themes into summary tables to inform the aims of the second advisory board meeting where we will develop an initial content library. Interviews will continue until no new themes emerge in the data coding process (i.e., saturation).[50] After the coding process is complete data will be described descriptively.

ReACT Acceptability. Acceptability of ReACT will be determined in two ways during the usability testing phase. First, the ReACT Satisfaction Questionnaire[51] will assess overall satisfaction, perceptions regarding how helpful ReACT could be in managing asthma, and whether adolescents would recommend ReACT to friends with asthma. An average rating of 3 (mostly satisfied) will be considered a successful outcome. Second, the semi-structured interviews will solicit adolescent feedback about ReACT. Our comprehensive interview guide will cover a range of topics, including: 1) perceived usefulness of ReACT; 2) how effective ReACT might be in changing asthma self-management behaviors; and 3) suggestions on further refining ReACT (e.g., incorporating other individuals). Qualitative data analysis will help determine overall project success. The process for identifying themes will be similar to the process from the earlier interview phase, but in this case we will use an entirely de novo process of identifying themes.[47] We will mark comments identified to represent discrete thoughts or themes using a semantic analysis, and we will use an essential realist approach to arrive at themes.[47] In particular, we will be attentive to themes that relate to the acceptability, usefulness, and user experience of ReACT. Themes that indicate that ReACT was perceived to be effective, appropriately tailored, and acceptable burden will be the criterion for success.

ReACT Usability. Usability will be determined in three ways. First, an average rating of 3 (agree) on the Health Information Technology Usability Evaluation Scale[52] will be a criterion for success. Second, themes from think aloud testing that suggest adolescents can navigate the ReACT interface intuitively and with minimal difficulty will be markers of success. Finally, our semi-structured interview will ask for feedback regarding: 1) the layout of the ReACT interface; 2) the navigation experience; 3) clarity of the wording; 4) clarity of the video content; and 5) ways to improve the usability and content of ReACT. Qualitative analysis that reveals themes of easy navigation and clear understanding of the goals and functionality of ReACT is the criterion for success.

Ethics and Dissemination

All aspects of the study protocol will be approved by local institutional review boards. In addition, all research team members will complete certification in topics related to the responsible conduct of research. To minimize risk from research participation, potential subjects will be fully informed regarding the purpose, process and amount of time required for participation. It is possible that research staff will identify an adolescent whose asthma appears undertreated. Research staff will review all cases with local medical personnel and facilitate a referral for evaluation and appropriate medication if indicated.

We plan to disseminate findings from the current project to multiple audiences including the local medical community and the broader scientific community via local and national presentations at relevant conferences and meetings. Beyond pediatric asthma, we also envision that the ReACT infrastructure and design process can be used to develop and test behavior change interventions in other disease populations. If successful, this would be a significant step toward the 2016 NIH-Wide Strategic Plain goal of using mHealth to "enhance health promotion and disease prevention."[53]

Author's Contributions

DAF and CCC conceived the study. DAF, CCC, SRP, ELM, and JS developed the protocol. DAF, CCC, NK, AO, CF, and AMN were involved in drafting of the article. All authors completed a critical revision of the article and approved the final text.

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Table 1

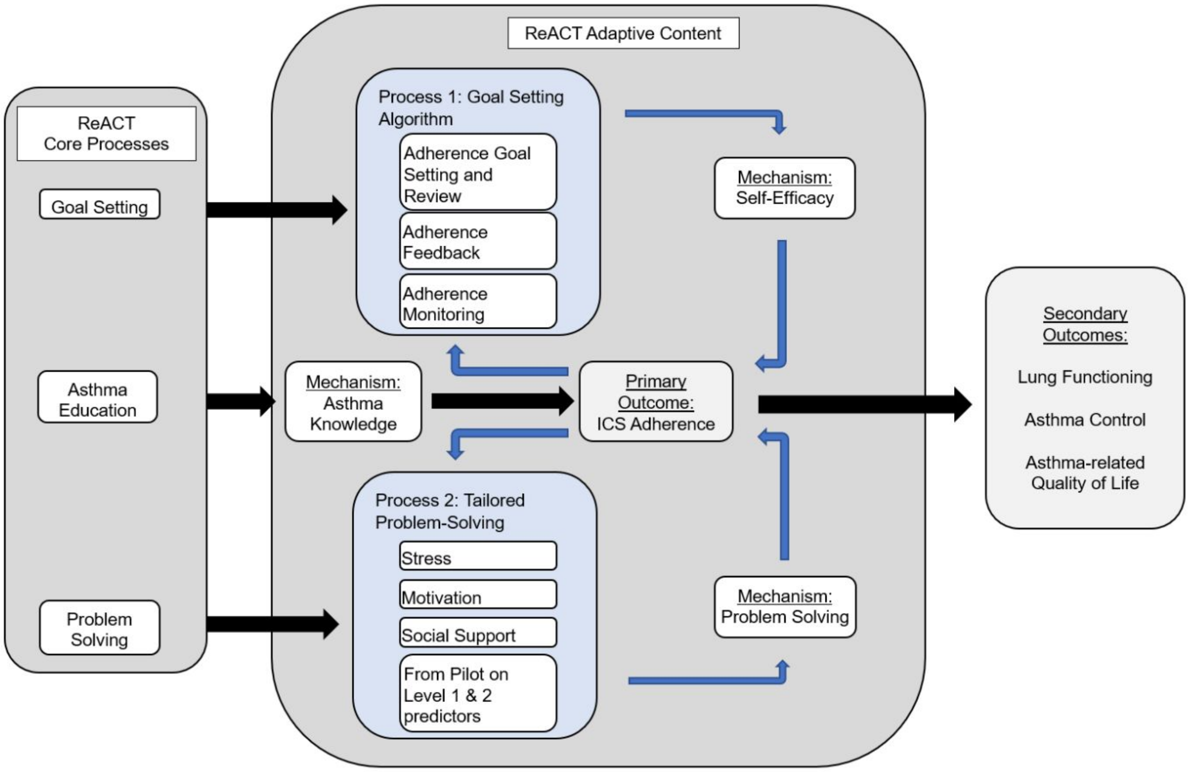
ReACT Outcome Measures

Outcome	Measure	Assessment Schedule*
Demographics	A caregiver-report questionnaire assesses adolescent and family demographic characteristics.	II, AB, UT
Asthma Morbidity	A caregiver-report questionnaire assesses frequency of asthma symptoms, exacerbations, activity limitations, missed school days due to asthma, ED visits, and hospitalizations.	II, AB, UT
Medical Information	Medical chart review assesses prescribed ICS regimen and dosage.	II, AB, UT
Asthma Knowledge & Skills	The Asthma Child Knowledge and Skills Questionnaire,[12] a modified version of the Children's Asthma Knowledge Questionnaire,[54] is a 30-item adolescent-report measure that assesses both asthma knowledge and self-assessment of skills required for taking medication.	II, AB, UT
Asthma Control	The Asthma Control Test (ACT)[55] is a 5-item, validated, adolescent-report questionnaire that assesses asthma control in past 4 weeks.	II, AB, UT
Asthma Management	The Asthma Management Efficacy Questionnaire (AME)[56] is a 14 item, validated, adolescent-report questionnaire that assesses asthma self-management behaviors.	II, AB, UT
Asthma Adherence	The Medication Adherence Report Scale for Asthma (MARS-A)[57] is a 10-item, validated, adolescent-report measure of ICS adherence.	II, AB, UT
Self-Regulation	The Treatment Self-Regulation Questionnaire (TRSQ) - Asthma[58] is a 15-item, adoelscent-report measure that assesses motivation for using controller medication.	II, AB, UT
Stress	The Adolescent Stress Questionnaire (ASQ)[59] Revised is a 58-item, validated, adolescent-report questionnaire that assesses stressors in adolescence.	II, AB, UT
Social Support	The Social Support Questionnaire (SSQ)[60] is a 27-item, validated, adolescent-report measure of social support.	II, AB, UT
Problem Solving	The Social Problem Solving Inventory-Revised: Short Form (SPSI-R:S)[61] is a 25-item, validated, adolescent-report measure that assesses problem solving orientation and skills in everyday life.	II, AB, UT
Asthma-Related Quality of Life	The Pediatric Asthma Quality of Life Questionnaire (PAQLQ)[62] is a 23-item, validated, adolescent-report questionnaire that measures extent of asthma impairment in quality of life.	II, AB, UT
Acceptability	The ReAct Satisfaction Questionnaire is an 8-item modification of the Client Satisfaction Questionnaire[51] that assesses overall participant satisfaction with the ReACT intervention. Semi-structured interviews assess what	UT

	adolescents like and do not like about ReACT, its relevance, and its perceived helpfulness with medication adherence.	
Usability	The Health Information Technology Usability Evaluation Scale[52] is a 20-item, validated questionnaire that assesses perceived usefulness, impact on disease, perceived ease of use, and user control. Think aloud testing gathers stream of consciousness data regarding thoughts and feelings of users as they complete specified tasks. Semi-structured interviews assess the the look and feel of ReACT, ease of navigation, and experience accessing intervention content.	UT

*II = Design Phase I Individual Interviews, AB = Advisory Boards, UT = User Testing

Figure 1. ReACT Conceptual Model



Note: Black arrows represent mechanistic processes occurring during the ReACT intervention period. Blue arrows indicate recursive processes happening repeatedly during the intervention period. ICS Adherence = Adherence to inhaled to corticosteroids.

Figure 2. Study Timeline

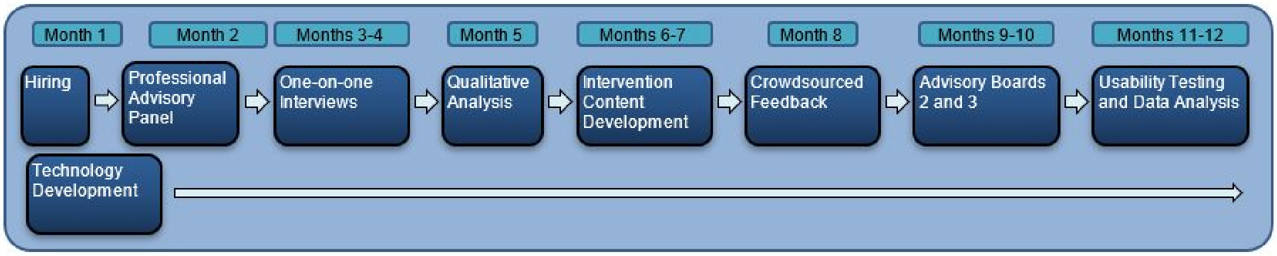
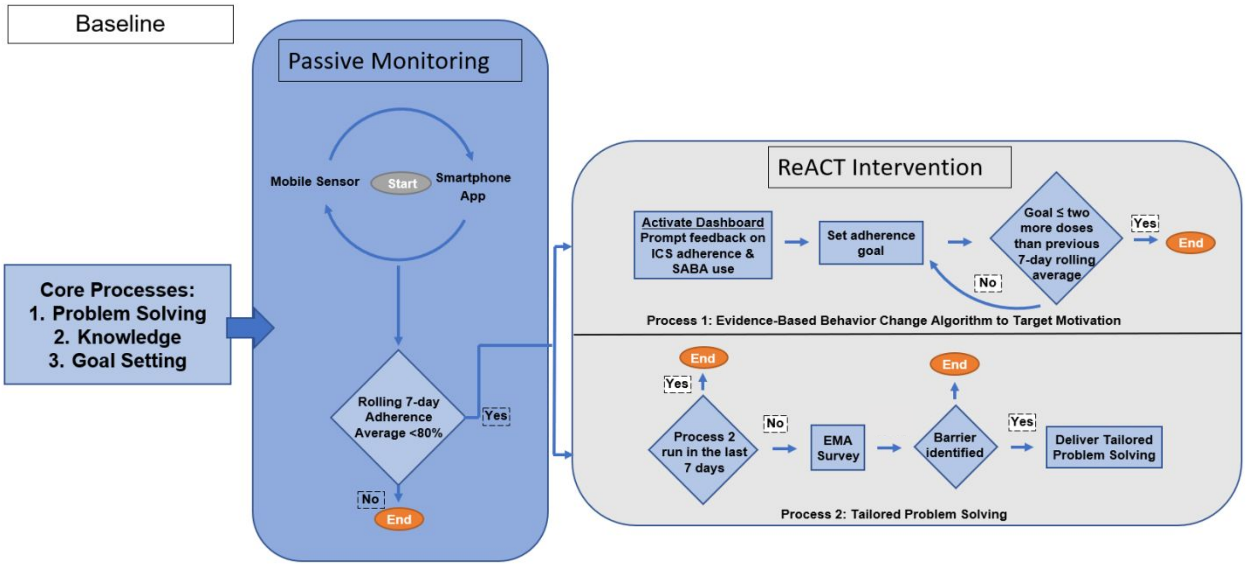


Figure 3. ReACT Participant Flow



Note: Diamonds indicate intervention decision rules. ICS = inhaled corticosteroids, SABA = short-acting beta-agonist.

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Responsive Asthma Care for Teens (ReACT): Development protocol for an adaptive mobile health intervention for adolescents with asthma

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Responsive Asthma Care for Teens (ReACT): Development protocol for an adaptive mobile health intervention for adolescents with asthma

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Abstract

Introduction: Asthma is a leading cause of youth morbidity in the United States, affecting > 8% of youth. Adherence to inhaled corticosteroids (ICS) can prevent asthma-related morbidity; however, the typical adolescent with asthma takes fewer than 50% of their prescribed doses. Adolescents are uniquely vulnerable to suboptimal asthma self-management due to still-developing executive functioning capabilities that may impede consistent self-regulation and weaken attempts to use problem solving to overcome barriers to ICS adherence.

Methods and analysis: The aims of this project are to improve adherence to ICS as an important step toward better self-management among adolescents ages 13-17 diagnosed with asthma by merging the efficacious behavior change strategies found in behavioral health interventions with scalable, adaptive mHealth technologies to create the Responsive Asthma Care for Teens program (ReACT). ReACT intervention content will be developed through an iterative user-centered design process that includes conducting 1) one-on-one interviews with 20 teens with asthma; 2) crowdsourced feedback from a nationally representative panel of 100 adolescents with asthma; and 3) an advisory board of youth with asthma, a pediatric pulmonologist, and a behavioral health expert. In tandem, we will work with an existing technology vendor to program ReACT algorithms to allow for tailored intervention delivery. We will conduct usability testing of an alpha version of ReACT with a sample of 20 target users to assess acceptability and usability of our mHealth intervention. Participants will complete a 4-week run-in period to monitor their adherence with all ReACT features turned off. Subsequently, participants will complete a 4-week intervention period with all ReACT features activated. The study started in October of 2018 and is scheduled to conclude in late 2019.

Ethics and dissemination: Institutional Review Board approval was obtained at the University of Kansas and the University of Florida. We will submit study findings for presentation at national research conferences that are well attended by a mix of psychologists, allied health professionals, and physicians. We will publish study findings in peer-reviewed journals read by members of the psychology, nursing, and pulmonary communities.

Strengths and limitations of this study

- Intervention content will be developed first with theory and evidence-based decision-making and refined via an iterative, user-centered approach with target users and key stakeholders.
- Adaptive algorithms will be programmed into an existing, patient-facing asthma management platform.
- Intervention usability and acceptability will be stringently assessed prior to efficacy testing to allow for modifications and improvements.
- Although we will have data on patient preferences, usability, and acceptability, the current protocol is not designed to evaluate the efficacy of the ReACT program; this limitation will be addressed in a future randomized controlled trial.
- While medical providers were involved in the development of interviews, content, and interpretation of results, the current protocol will not incorporate shared decision-making between patients and providers in the intervention given the focus of ReACT.

Introduction

Asthma affects over 8% of youth and is a leading cause of morbidity.[1,2] Some asthma symptoms and health care utilization could be prevented via consistent engagement in disease self-management behaviors (e.g., symptom recognition and monitoring, appropriate administration of medications).[2,3] Adherence to daily controller medications, such as inhaled corticosteroids (ICS), is central to control asthma and reduce morbidity for youth with persistent asthma.[2] ICS adherence rates with adolescents are often < 50%,[4,5] placing them at significant risk for reduced lung function, increased morbidity, and poor quality of life.[4,6] We posit that the complexity of the asthma treatment regimen coupled with still-developing executive functioning and problem solving abilities makes adolescents uniquely vulnerable to suboptimal asthma self-management through self-regulation defecits.[7–11]

The importance of self-regulation in asthma self-management is well-supported.[12–17] Because the self-regulation abilities that are needed to successfully manage one's own asthma are linked to brain regions that are still developing in adolescents (i.e., frontal lobes responsible for top-down control),external supports in the form of parents or technology may be required to ensure that dosing occurs as prescribed. Simply put, to develop self-regulation, adolescents with chronic and persistent asthma need to spend time thinking about their asthma, medication, and actively planning how to incorporate adherence into their lives. Developmentally, adolescents' executive functioning skills may not be ideally suited for this task as evidenced by data indicating that adolescents take their medication as prescribed on some occasions, and nearly every adolescent misses some doses on some occasions.[18,19]

Similar to the problem of underdeveloped self-regulatory skill, it is common for adolescents with persistent asthma to be met with barriers to ICS adherence that they may not have the experience or cognitive development to effectively problem-solve.[20,21] Indeed, intrapersonal factors such as attitudes (e.g., motivation), feelings (e.g., mood, stress), and external factors such as the social and family environment, have consistently been associated with asthma management behaviors and disease outcomes.[13,22–27] Efficacious behavioral interventions often attempt to actively reframe ICS adherence as central to an adolescent's self-concept (e.g., better lung function will allow you to pursue your interests). Once adolescents see adherence as helping them reach their own personal goals rather than as a chore, they are sufficiently motivated to learn skills that can help ensure adherence to ICS. To this end, adolescents are taught to identify intrapersonal and external barriers to adherence and problem solve around those barriers. Beyond simply teaching a formula for problem-solving, many effective adherence promotion programs tailor intervention content to personally salient barriers and help the adolescent identify and implement strategies specifically designed to increase the chances of regimen success.[28–30]

A persistent problem in this approach is the difficulty of relying on infrequent face-to-face visits (e.g., for clinical care) to implement interventions. Smartphones are habitually carried by >70% of adolescents[31]; as such, mobile technology provides a readily available medium to approximate the features of efficacious behavioral health interventions[32,33] by leveraging passive monitoring, data listening, preprogrammed algorithms, and content libraries focused on improving self-regulation and problem solving skills.[34,35] Despite their potential, existing mobile health (mHealth) interventions have been largely developed without the benefit of behavioral theory, use reminder-based approaches to behavior change, and lack the kinds of tailored problem-solving training that characterizes efficacious in-person interventions[36–38] (for a systematic evaluation of behavior change techniques in current asthma self-management applications, see [38]). We believe that this, at least in part, helps explain why very few existing mHealth interventions for asthma medication adherence have yet to demonstrate their efficacy beyond active controls.[39–41]

There is a clear need for a mHealth intervention that merges digital delivery modalities with the theory-based behavioral framework and tailoring found in efficacious in-person treatments. Recent technological advances have catalyzed the development of mobile-based intervention platforms that deliver tailored support to individuals in a timely fashion.[42,43] We propose to extend this work to pediatric asthma by developing ReACT, an innovative adaptive mHealth intervention that facilitates self-regulation by aiding adolescents in self-monitoring, goal setting, and problem solving when adolescents' adherence data indicate they need additional support the most (**Figure 1**). We will outline how ReACT content will be developed, refined, and tested through an iterative user-centered design process guided by theory and prior evidence.

Methods and Analysis

Objectives

The aims of the study are: 1) conduct a hybrid user-centered and evidence-based design process comprised of individual interviews, crowdsourcing, and advisory boards to develop ReACT content and features; 2) test the acceptability and usability of ReACT in a sample of 20 adolescents with persistent asthma. We hypothesize that ReACT will be an acceptable and usable mHealth adherence promotion intervention as determined by high acceptability and usability ratings and themes from think aloud testing and qualitative one-on-one interviews with target users.

Project Overview

This multi-site study will take place at the University of Florida, University of Kansas, and their affiliated clinics. The study commenced in October 2018 and is anticipated to be completed in late 2019. Features and intervention content of ReACT will be developed concurrently. We will work with a technology vendor to add functionality for ReACT to an existing mHealth adherence monitoring platform. We will use a strong theoretical framework and prior evidence combined with a series of user-centered design phases to determine what intervention content should populate the ReACT system (Design Phase 1). Study team members and an advisory board will then refine intervention content and complete preliminary usability testing of ReACT (Design Phase 2). Finally, we will conduct acceptability and usability testing using an alpha version of ReACT. See **Figure 2** for the study timeline.

Core ReACT Functionality

We will create ReACT by expanding the capabilities of an existing Android and iOS compatible mobile phone app that uses an integrated mobile sensor designed to fit onto an asthma metered dose inhaler (MDI) or diskus. The sensor works passively to sense when ICS or short-acting beta-agonist (SABA) medications are dispensed. Bluetooth is used to pass the information to the app, which has a set of optional features (e.g., provide feedback about adherence) that can be turned on as intervention parameters dictate. **Figure 3** outlines an adolescent's intervention experience through ReACT. Building from theory and prior evidence, core ReACT components in sequence are: 1) core education on asthma management and skills training content on goal setting and problem solving[4,44], 2) conditional activation of ReACT features when an adolescent is <80% adherent to their ICS, 3) an evidence-based goal-setting algorithm that shapes adherence to dosing recommendations over time, 4) timely assessment of an adolescent's barriers to adherence, and 5) delivery of tailored problem solving training based on recent and salient barriers. Determinants of self-regulation will be integrated into the core ReACT functionality to best scaffold support for adolescents, as outlined below.

ReACT will begin with an orientation module within the app that guides the users through the platform, core educational and skills training modules, and passive monitoring of medications. Adolescents will complete an asthma education module based on NHLBI guidelines[45] to ensure that they have an understanding of the importance of medication adherence as a means to avoid asthma-related impairments. Adolescents will receive skills training on empirically-supported techniques consistent with our guiding self-regulation theory. Goal setting content will use a SMART (Specific, Measurable, Attainable, Relevant, Time-Bound) goal framework. Problem-solving skills training will focus on orienting to the problem, defining and formulating the problem, generating alternative solutions, deciding on a course of action, and implementing a solution.[46,47] We will use engaging videos created by the team to deliver content. Participants will complete the orientation modules with study staff to encourage engagement and provide assistance if necessary.

ReACT will use passive sensing to objectively monitor rates of adolescent ICS adherence throughout the intervention period. The use of the ICS adherence sensor offloads the burden of self-monitoring such that adolescents do not have to remember or calculate their adherence. Active intervention elements in ReACT will activate only when an adolescent falls below a clinically derived 80% adherence threshold[48] based on a 7-day rolling average, thus reducing intervention fatigue.[43] If an adolescent has $< 80\%$ adherence to ICS based on the 7-day rolling average, ReACT will prompt the adolescent to set a goal for adherence in the next 7-day period, a strategy with demonstrated efficacy in previous asthma adherence interventions.[49] The algorithm will only allow goals that are reasonable given performance over the past week to avoid overly ambitious and unattainable goals. Each evening, the adolescent will receive a feedback message about how much their adherence that day moved them toward their goal, additionally facilitating the self-regulatory process of observation. Furthermore, the conditional activation of the ReACT features should support self-regulatory skills, specifically judgement, by notifying the adolescent when his or her adherence declines.

ReACT will identify contextual barriers to ICS adherence by also initiating an assessment as soon as the 7-day rolling average indicates that adherence is < 80%. Specifically, adolescents will be prompted via a push notification to complete a brief electronic momentary assessment (EMA) survey of barriers identified from our pilot data and Design Phase 1 to identify what barrier the problem-solving content should be tailored to address. Participants will answer brief questions in the app regarding barriers that got in the way of taking their ICS followed by a rank order item denoting which one to make the focus of their problem-solving efforts. Once a barrier is identified, ReACT will deliver problem-solving content in the app that is tailored to that specific barrier. For instance, if an adolescent has identified and chooses to work on stress as their top barrier to ICS adherence, the tailored problem solving will deliver structured problem-solving training using a flexible system of branching that is tailored to stress specifically. To execute this feature, ReACT will have several content banks that use the same structure. To illustrate the user experience, a possible problem-solving intervention could include: 1) defining the problem: participants will be presented with a standard message reflecting the problem they identified in the EMA survey; 2) setting a realistic, achievable goal: several goals will be presented and the participant will choose one and receive feedback on their choice; 3) generating multiple solutions: the participant will be asked to choose from a list of possible solutions for the goal that they selected in step #2; 4) evaluating pros and cons: participants will evaluate the pros and cons of multiple solutions listed in step #3; 5) selecting a solution: participants will choose the solution that may work the best; 6) making an action plan: participants will select from a list of action plans that correspond to the solution they have selected; 7) evaluating the outcome: after a week participants will be asked whether they implemented the solution selected in #6. The goal-setting and tailored problem-solving process should enhance one's reaction to suboptimal adherence by improving self-efficacy and facilitating skills to overcome their personalized adherence barriers.

Once an adolescent receives intervention content, ReACT will prompt adolescents to complete a survey in the app two days later to assess content use. If the participant responds that they used the intervention strategy, ReACT will assess the participant's confidence in their ability to repeat the plan in the future. If the participant has not used the strategy, they will receive a supportive prompt with options to review the content they saw last time, see the same content in a different media format, review a different set of content on the same topic, or set a goal to use the strategies by a specific time in the next two days. Another program safeguard is to reduce overwhelming participants with content; therefore the Tailored Problem-Solving Process (**Figure 3**) will only run once in a given 7-day window. This mirrors normative approaches for in-person interventions during which only one or two new concepts would be introduced each week.

Participants and Recruitment

Participants. Participants will include four separate samples of 13-17-year-old adolescents with asthma and their caregivers (see **Figure 4**). Twenty adolescent-caregiver dyads will complete individual interviews, 100 adolescents will provide crowdsourced feedback via a national online panel, four adolescent-caregiver dyads will participate in advisory board meetings, and 20 adolescent-caregiver dyads will complete user testing of ReACT. We intend that at least half of adolescent participants in the interviews and advisory boards will be from racial and ethnic minority groups.

Inclusion and Exclusion Criteria. For interviews, advisory boards, and user testing, adolescents must have a physician-verified diagnosis of current asthma with persistent symptoms requiring regular ICS use for ≥ 6 months. They must have a daily ICS or ICS/LABA prescription that is sensor-compatible, and they and their caregivers must speak and read English. Asthma status and prescription information will be verified via the electronic medical record. Families will be excluded from the study if the adolescent is currently involved in an asthma management intervention, has a comorbid chronic health condition that may impact lung function, or has a significant cognitive impairment or developmental delay that interferes with study completion. For crowdsourced feedback, inclusion will be determined at the level of a national online panel, which will screen participants for persistent asthma.

Recruitment. Participants will be recruited 1) through university-affiliated clinics and 2) via flyers. Research and clinic staff members with access to the Electronic Medical Record will identify eligible patients with upcoming medical appointments. During these appointments, providers with clinical relationships with the eligible participants will first approach the patients to determine their interest in hearing more about the study. Then, in coordination with the clinic staff, research staff will meet with interested patients to provide a study overview, complete in-person screening for eligibility, and invite participation. In the event that a family is unable to complete screening during a clinic visit, research staff will request permission for a member of the study team to contact patients for screening using an IRB-approved "consent-to-contact" form. A member of the study staff will then call interested participants to provide a study overview and invite participation. In addition, IRB approved flyers will be posted or made available in clinics, community organizations, schools, physician offices, and common areas. Flyers will encourage families and nurses to call our research office to learn about the project, determine initial eligibility, and if eligible, schedule an in-person screening visit where informed consent will be collected prior to study enrollment. Throughout all phases of the project, participants will be incentivized and compensated for their participation.

ReACT Development

Patient and Public Involvement. Adolescents diagnosed with asthma, their caregivers, and pediatric asthma providers are involved in all stages of ReACT development, as described below.

Design Phase 1: Content Development. We have developed a list of common barriers to ICS adherence from our own pilot data and the extant pediatric asthma literature. Our goal for Design Phase 1 is to use individual interviews with adolescents diagnosed with asthma to translate these barriers into terms easily understood by adolescents, develop a final list of barriers to adherence, and subsequently develop a library of intervention content to overcome adherence barriers that is informed by self-regulation theory. Individual interview participants and their caregivers will also complete asthma-related measures for sample description purposes and to obtain preliminary data on constructs of interest to the project (see **Table 1**). Adolescent-caregiver dyads will receive $60 for their participation.

The study team will create an individual interview guide that will be used to identify what barriers to adherence are most salient to adolescents with asthma, and to solicit their opinion about the types of intervention content that they would prefer to receive when experiencing these barriers. Prior to the start of individual interviews, at least three pediatric asthma providers (e.g., pulmonologists, nurses) will provide feedback on the interview guide. All interviews will be audio recorded and conducted with self-regulation theory in mind. If a component of self-regulation theory is not discussed, we will probe for content in the omitted domain to facilitate development of intervention content. Interviews will be transcribed and evaluated by the study team to inform digital intervention content development (see Data Analysis section).

Research staff with experience developing digital intervention content will leverage information gathered during Design Phase 1 to develop a library of intervention content for each barrier identified in the interviews and quantitative analysis of our pilot data. We anticipate that intervention content will include a combination of skills training videos, brief text content, educational videos, and images. Delivery modality (SMS, app, etc.) will be discussed with the advisory board.

Design Phase 2: Refinement of Content and Preliminary Usability Testing. In Design Phase 2 we will refine intervention content generated in Design Phase 1 through 1) nationally crowdsourced feedback from adolescents with asthma and 2) advisory board meetings. Preliminary usability testing and iterative refinement will be conducted with our advisory board meetings (described below).

Nationally crowdsourced feedback will be solicited via an online panel and survey-technology provider. Participants will be identified from panels of adolescents who have agreed to participate in research. These panels are accessed by our survey vendor through their business-to-business partnerships. Participants will be screened for persistent asthma using the following standard set of questions commonly used in epidemiological trials (e.g., National Health

Interview Survey: 1) Have you ever been told by a doctor, nurse, or other health professional that you have asthma? 2) Do you still have asthma? Affirmative answers to both questions will qualify an adolescent for participating.[50] Participants will review intervention content and rate its appropriateness using a dichotomous "Yes" (I like the message as it is) or "No" (change it to make it better) response choice. They will receive $15 for their participation. Content receiving ≥ 60% "No" votes will be discarded, and those with ≤ 39% "No" votes will be accepted as final intervention content. Content with 40-59% "No" votes will be revised or clarified while retaining any theoretically or empirically derived concepts.[51] We will design surveys to take no more than 30 minutes each. If necessary, we will split the content into two surveys to keep the administration time < 30 minutes. Although adolescent stakeholders will be involved in developing ReACT intervention content rated during crowdsourcing, we acknowledge that there is a possibility that a higher than expected amount of content will be viewed unfavorably during this phase. We will review crowdsourcing feedback data from an initial wave of 20 participants. In the event that > 60% of content is viewed unfavorably, we will pause crowdsourcing to develop new intervention content.

An advisory board comprised of adolescent-caregiver dyads and study staff members will convene three times. The first meeting will focus on reviewing summative data and themes that emerged from crowdsourcing phase. The second advisory board meeting will involve discussion about methods to further refine intervention content that received 40-59% "No" votes during crowdsourcing. We will incorporate modified content that reaches group consensus into applicable ReACT intervention content libraries. Preliminary usability testing will take place during the final advisory board meeting. Members will conduct hands-on testing of ReACT alongside study staff. We will use a "think aloud" approach with members as they explore components of the ReACT interface (e.g., layout, visual feedback), answer EMA questions, and view intervention content.[52] This process more closely approximates actual use and will enable us to receive feedback in real-time. The study team will transcribe participant commentary during testing for review. Results of the "think aloud" testing will help to inform final design decisions in ReACT.[52] For instance, whether content is delivered using SMS, in-app, push notification, or some other medium will be informed by user preferences. Advisory board participants and their caregivers will also complete asthma-related measures to pilot data collection procedures and provide baseline descriptive statistics (see **Table 1**). Adolescent-caregiver dyads will receive $50 for each advisory board meeting they attend.

Acceptability and Usability Testing of ReACT

In the final phase, adolescents will conduct user testing with the alpha version of ReACT. The overarching goal is to gather acceptability and usability data from the perspectives of target users of ReACT. A sample of 20 participants will complete a 4-week run-in period to monitor their adherence with all ReACT features turned off. Subsequently, study staff will meet with participants to complete ReACT orientation. This visit will ensure that participants are able to download and use ReACT, and that relevant ReACT components (e.g., asthma education and skills training videos) are accessed before beginning. Participants will complete asthma-related study questionnaires (see **Table** 1) and then begin a 4-week intervention period with all ReACT features activated. Notably, acceptability and usability measures will be administered at a final study visit at the conclusion of the 4-week intervention period Again, participant comments and suggestions during the final study visit will be transcribed for review.

Data Analysis Plan

Individual Interviews. Study staff will enter transcribed files and expanded notes into NVivo into NVivo. We will code and aggregate interviews using a theoretical thematic analysis approach to developing themes.[53–55] Our theoretical thematic analysis approach will use an *a priori* theoretical framework guided by self-regulation theory, informed by advisory board meetings. The investigators will mark comments identified to represent discrete thoughts or themes using a semantic analysis, and they will use an essential realist approach to arrive at themes.[53] These patterns or themes will comprise the initial set of categories. Research staff will then re-code the data using these categories and organize major themes into summary tables to inform initial development of a digital content library. Interviews will continue until no new themes emerge in the data coding process (i.e., saturation).[56] After the coding process is complete, data will be described descriptively.

ReACT Acceptability. Acceptability of ReACT will be determined in two ways during the usability testing phase. First, the ReACT Satisfaction Questionnaire[57] will assess overall satisfaction, perceptions regarding how helpful ReACT could be in managing asthma, and whether adolescents would recommend ReACT to friends with asthma on a 4-point Likert scale. An average rating of 3 (mostly satisfied) will be considered a successful outcome. Second, the semi-structured interviews will solicit adolescent feedback about ReACT. Our comprehensive interview guide will cover a range of topics, including: 1) perceived usefulness of ReACT; 2) how effective ReACT might be in changing asthma self-management behaviors; and 3) suggestions on further refining ReACT (e.g., incorporating other individuals). Qualitative data analysis will help determine overall project success. The process for identifying themes will be similar to the process from the earlier interview phase, but in this case we will use an entirely de novo process of identifying themes.[53] We will mark comments identified to represent discrete thoughts or themes using a semantic analysis, and we will use an essential realist approach to arrive at themes.[53] In particular, we will be attentive to themes that relate to the acceptability, usefulness, and user experience of ReACT. Themes that indicate that ReACT was perceived to be effective, appropriately tailored, and acceptable burden will be the criterion for success.

ReACT Usability. Usability will be determined in three ways. First, an average rating of 3 (agree) on the Health Information Technology Usability Evaluation Scale[58] will be a criterion for success. Second, themes from think aloud testing that suggest adolescents can navigate the ReACT interface intuitively and with minimal difficulty will be markers of success. Finally, our semi-structured interview will ask for feedback regarding: 1) the layout of the ReACT interface; 2) the navigation experience; 3) clarity of the wording; 4) clarity of the video content; and 5) ways to improve the usability and content of ReACT. These data will be used to inform future refinements of ReACT in advance of a subsequent trial.

Ethics and Dissemination

All aspects of the study protocol will be approved by local institutional review boards. In addition, all research team members will complete certification in topics related to the responsible conduct of research. To minimize risk from research participation, potential subjects will be fully informed regarding the purpose, process and amount of time required for participation. It is possible that research staff will identify an adolescent whose asthma appears undertreated. Research staff will review all cases with local medical personnel and facilitate a referral for evaluation and appropriate medication if indicated.

We plan to disseminate findings from the current project to multiple audiences including the local medical community and the broader scientific community via local and national presentations at relevant conferences and meetings. Beyond pediatric asthma, we also envision that the ReACT infrastructure and design process can be used to develop and test behavior change interventions in other disease populations. If successful, this would be a significant step toward the 2016 NIH-Wide Strategic Plain goal of using mHealth to "enhance health promotion and disease prevention."[59]

Limitations

The current project is a pilot feasibility, acceptability, and usability study in a targeted sample (i.e., adolescents with chronic and persistent asthma) who also have a high need for this type of intervention. As such, we will not be able to contribute knowledge about the feasibility of ReACT in all of the populations it might benefit (e.g., adults with chronic obstructive pulmonary disease). Moreover, the current project is not powered to understand heterogeneity of outcomes across sex, socioeconomic status, race, culture, and literacy levels. ReACT does not target all of the factors that might influence adherence. Specifically, structural issues such as inadequate insurance coverage will not be addressed in the current protocol. At this stage, ReACT does not involve providers at least in part because there are already other commercial systems that do a good job of achieving that function. The novelty of ReACT is to identify the developmentally appropriate individual level interventions that can increase adherence.

Author's Contributions

DAF and CCC conceived the study. DAF, CCC, SRP, SG, ELM, and JS developed the protocol. DAF, CCC, NK, AO, KF, and AMN were involved in drafting of the article. Specifically, DAF and CCC collaboratively wrote the text, NK and AO edited the text, and created figures. KF and AMN provided expertise and section edits on the statistical approach and features of problem-solving therapy. SRP, ELM, provided expertise and writing about qualitative work. JS provided expertise and writing about adaptive interventions. All authors completed a critical revision of the article and approved the final text.

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Table 1

ReACT Outcome Measures

Outcome	Measure	Assessment Schedule*
Demographics	A caregiver-report questionnaire assesses adolescent and family demographic characteristics.	II, AB, UT
Asthma Morbidity	A caregiver-report questionnaire assesses frequency of asthma symptoms, exacerbations, activity limitations, missed school days due to asthma, ED visits, and hospitalizations.	II, AB, UT
Medical Information	Medical chart review assesses prescribed ICS regimen and dosage.	II, AB, UT
Asthma Knowledge & Skills	The Asthma Child Knowledge and Skills Questionnaire,[12] a modified version of the Children's Asthma Knowledge Questionnaire,[60] is a 30-item adolescent-report measure that assesses both asthma knowledge and self-assessment of skills required for taking medication.	II, AB, UT
Asthma Control	The Asthma Control Test (ACT)[61] is a 5-item, validated, adolescent-report questionnaire that assesses asthma control in past 4 weeks.	II, AB, UT
Asthma Management	The Asthma Management Efficacy Questionnaire (AME)[62] is a 14 item, validated, adolescent-report questionnaire that assesses asthma self-management behaviors.	II, AB, UT
Asthma Adherence	The Medication Adherence Report Scale for Asthma (MARS-A)[63] is a 10-item, validated, adolescent-report measure of ICS adherence.	II, AB, UT
Self-Regulation	The Treatment Self-Regulation Questionnaire (TRSQ) - Asthma[64] is a 15-item, adolescent-report measure that assesses motivation for using controller medication.	II, AB, UT
Stress	The Adolescent Stress Questionnaire (ASQ)[65] Revised is a 58-item, validated, adolescent-report questionnaire that assesses stressors in adolescence.	II, AB, UT
Social Support	The Social Support Questionnaire (SSQ)[66] is a 27-item, validated, adolescent-report measure of social support.	II, AB, UT
Problem Solving	The Social Problem Solving Inventory-Revised: Short Form (SPSI-R:S)[67] is a 25-item, validated, adolescent-report measure that assesses problem solving orientation and skills in everyday life.	II, AB, UT
Asthma-Related Quality of Life	The Pediatric Asthma Quality of Life Questionnaire (PAQLQ)[68] is a 23-item, validated, adolescent-report questionnaire that measures extent of asthma impairment in quality of life.	II, AB, UT
Acceptability	The ReAct Satisfaction Questionnaire is an 8-item modification of the Client Satisfaction Questionnaire[57] that assesses overall participant satisfaction with the ReACT intervention. Semi-structured interviews assess what	UT

	adolescents like and do not like about ReACT, its relevance, and its perceived helpfulness with medication adherence.	
Usability	The Health Information Technology Usability Evaluation Scale[58] is a 20-item, validated questionnaire that assesses perceived usefulness, impact on disease, perceived ease of use, and user control. Think aloud testing gathers stream of consciousness data regarding thoughts and feelings of users as they complete specified tasks. Semi-structured interviews assess the the look and feel of ReACT, ease of navigation, and experience accessing intervention content.	UT

*II = Design Phase I Individual Interviews, AB = Advisory Boards, UT = User Testing

Figure Legend:

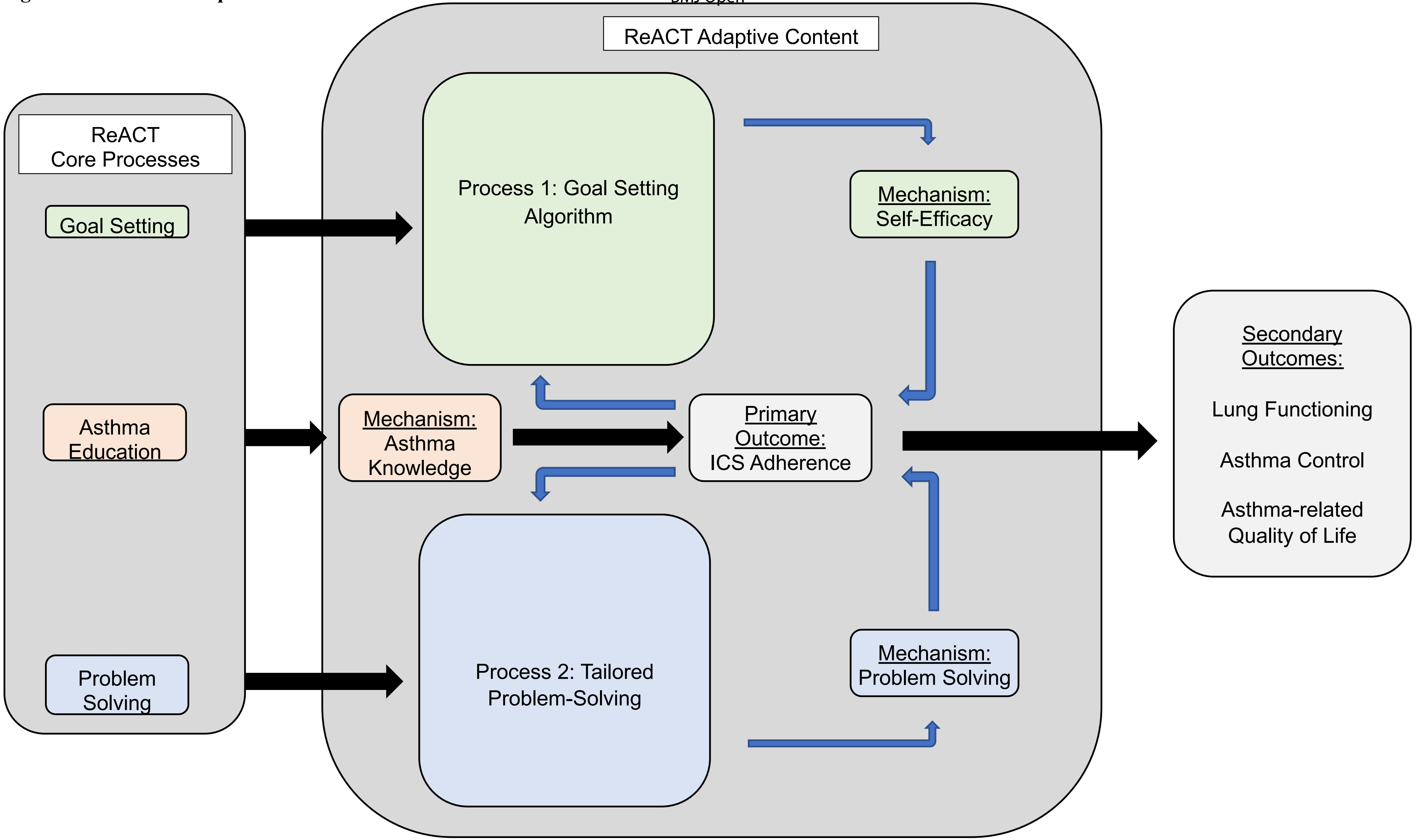
Figure 1. ReACT Conceptual Model, Note: Black arrows represent mechanistic processes occurring during the ReACT intervention period. Blue arrows indicate recursive processes happening repeatedly during the intervention period. ICS adherence = Adherence to inhaled corticosteroids.

Figure 2. Study Timeline.

Figure 3. React Participant Flow. Note: Diamonds indicate intervention decision rules. ICS = inhaled corticosteroids, SABA = short-acting beta-agonist.

Figure 4. ReACT Flow of Formative Work.

Figure 1. ReACT Conceptual Model



Note: Black arrows represent mechanistic processes occurring during the ReACT intervention period. Blue arrows indicate recursive processes happening repeatedly during the intervention period. ICS Adherence = Adherence to inhaled to corticosteroids.

Figure 2. Study Timeline

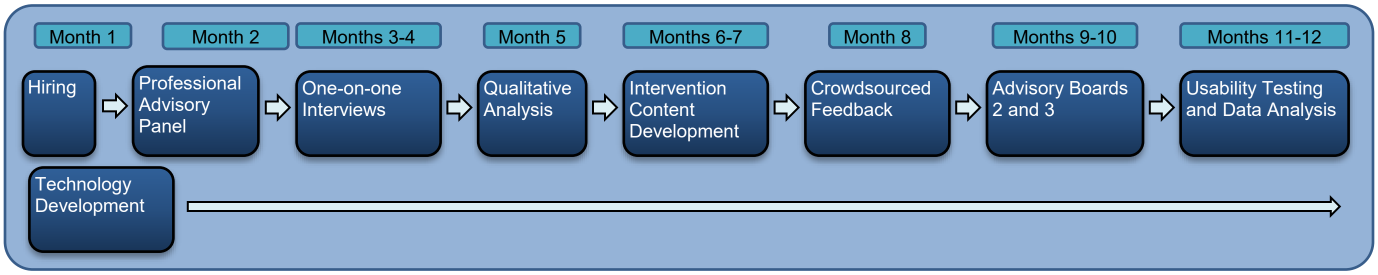
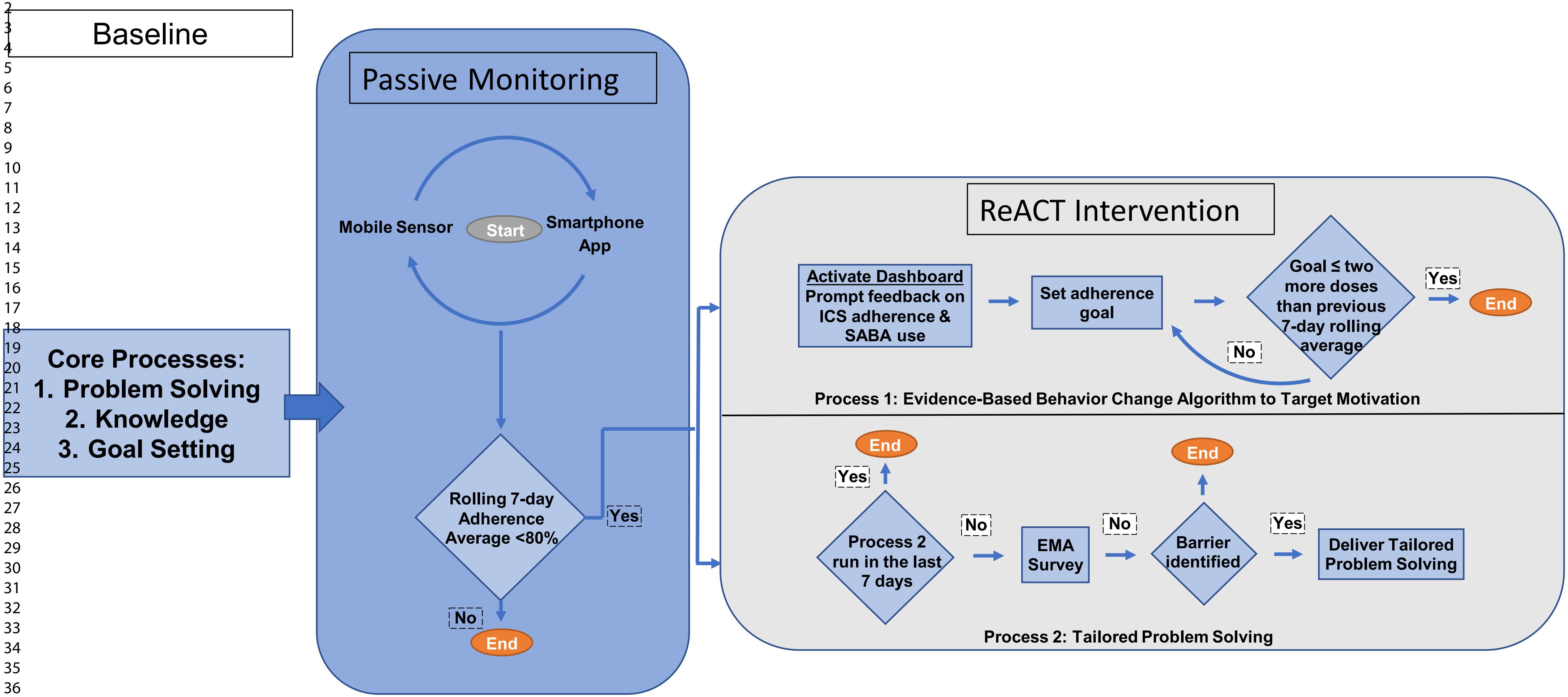
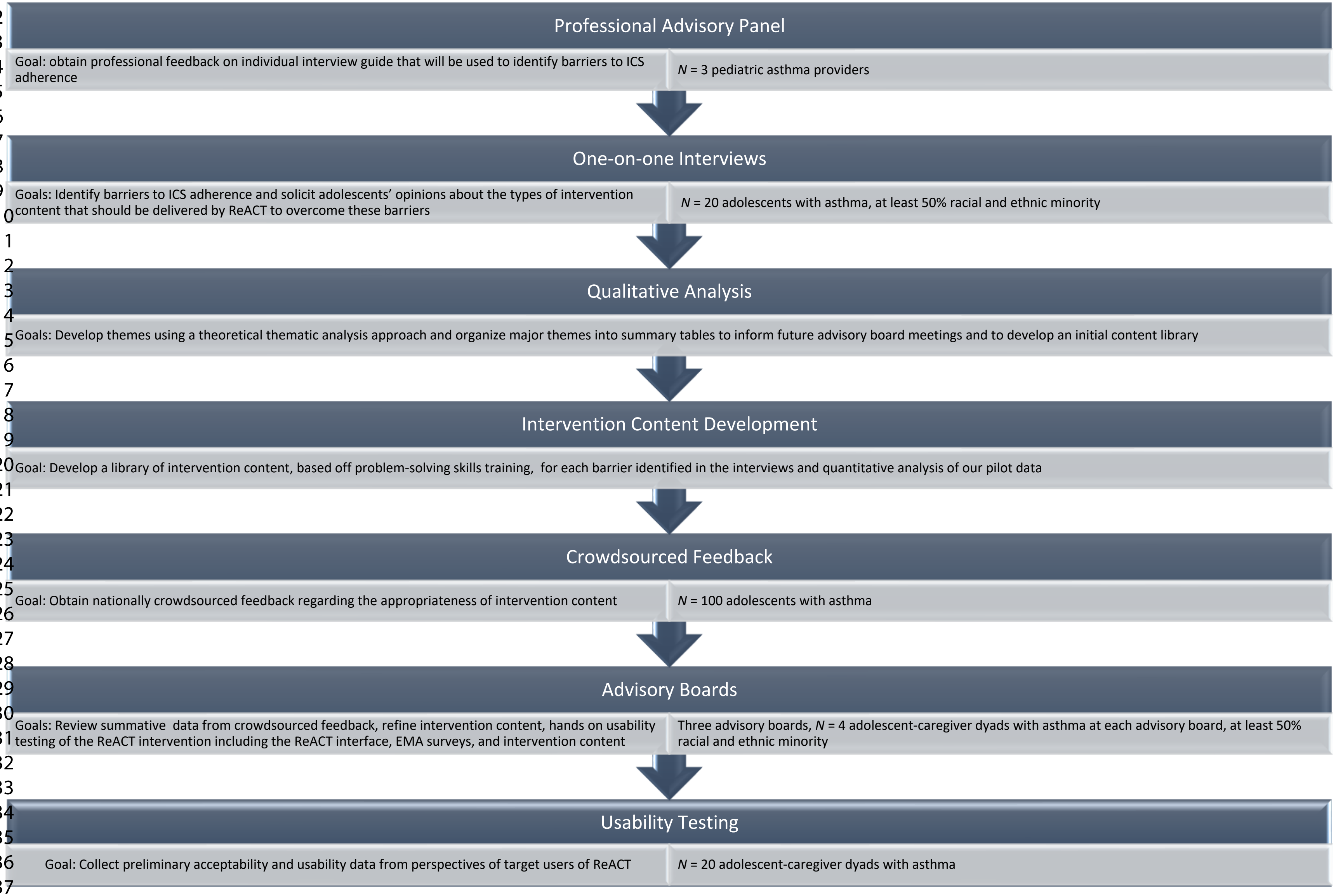


Figure 3. ReACT Participant Flow



Note: Diamonds indicate intervention decision rules. ICS = inhaled corticosteroids, SABA = short-acting beta-agonist.

Figure 4. ReACT Flow of Formative Work



Responsive Asthma Care for Teens (ReACT): Development protocol for an adaptive mobile health intervention for adolescents with asthma

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Responsive Asthma Care for Teens (ReACT): Development protocol for an adaptive mobile health intervention for adolescents with asthma

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Abstract

Introduction: Asthma is a leading cause of youth morbidity in the United States, affecting > 8% of youth. Adherence to inhaled corticosteroids (ICS) can prevent asthma-related morbidity; however, the typical adolescent with asthma takes fewer than 50% of their prescribed doses. Adolescents are uniquely vulnerable to suboptimal asthma self-management due to still-developing executive functioning capabilities that may impede consistent self-regulation and weaken attempts to use problem solving to overcome barriers to ICS adherence.

Methods and analysis: The aims of this project are to improve adherence to ICS as an important step toward better self-management among adolescents ages 13-17 diagnosed with asthma by merging the efficacious behavior change strategies found in behavioral health interventions with scalable, adaptive mHealth technologies to create the Responsive Asthma Care for Teens program (ReACT). ReACT intervention content will be developed through an iterative user-centered design process that includes conducting 1) one-on-one interviews with 20 teens with asthma; 2) crowdsourced feedback from a nationally representative panel of 100 adolescents with asthma; and 3) an advisory board of youth with asthma, a pediatric pulmonologist, and a behavioral health expert. In tandem, we will work with an existing technology vendor to program ReACT algorithms to allow for tailored intervention delivery. We will conduct usability testing of an alpha version of ReACT with a sample of 20 target users to assess acceptability and usability of our mHealth intervention. Participants will complete a 4-week run-in period to monitor their adherence with all ReACT features turned off. Subsequently, participants will complete a 4-week intervention period with all ReACT features activated. The study started in October of 2018 and is scheduled to conclude in late 2019.

Ethics and dissemination: Institutional Review Board approval was obtained at the University of Kansas and the University of Florida. We will submit study findings for presentation at national research conferences that are well attended by a mix of psychologists, allied health professionals, and physicians. We will publish study findings in peer-reviewed journals read by members of the psychology, nursing, and pulmonary communities.

Strengths and limitations of this study

- Intervention content will be developed first with theory and evidence-based decision-making and refined via an iterative, user-centered approach with target users and key stakeholders.
- Adaptive algorithms will be programmed into an existing, patient-facing asthma management platform.
- Intervention usability and acceptability will be stringently assessed prior to efficacy testing to allow for modifications and improvements.
- Although we will have data on patient preferences, usability, and acceptability, the current protocol is not designed to evaluate the efficacy of the ReACT program; this limitation will be addressed in a future randomized controlled trial.
- While medical providers were involved in the development of interviews, content, and interpretation of results, the current protocol will not incorporate shared decision-making between patients and providers in the intervention given the focus of ReACT.

Introduction

Asthma affects over 8% of youth and is a leading cause of morbidity.[1,2] Some asthma symptoms and health care utilization could be prevented via consistent engagement in disease self-management behaviors (e.g., symptom recognition and monitoring, appropriate administration of medications).[2,3] Adherence to daily controller medications, such as inhaled corticosteroids (ICS), is central to control asthma and reduce morbidity for youth with persistent asthma.[2] ICS adherence rates with adolescents are often < 50%,[4,5] placing them at significant risk for reduced lung function, increased morbidity, and poor quality of life.[4,6] We posit that the complexity of the asthma treatment regimen coupled with still-developing executive functioning and problem solving abilities makes adolescents uniquely vulnerable to suboptimal asthma self-management through self-regulation defects.[7–11]

The importance of self-regulation in asthma self-management is well-supported.[12–17] Because the self-regulation abilities that are needed to successfully manage one's own asthma are linked to brain regions that are still developing in adolescents (i.e., frontal lobes responsible for top-down control),external supports in the form of parents or technology may be required to ensure that dosing occurs as prescribed. Simply put, to develop self-regulation, adolescents with chronic and persistent asthma need to spend time thinking about their asthma, medication, and actively planning how to incorporate adherence into their lives. Developmentally, adolescents' executive functioning skills may not be ideally suited for this task as evidenced by data indicating that adolescents take their medication as prescribed on some occasions, and nearly every adolescent misses some doses on some occasions.[18,19]

Similar to the problem of underdeveloped self-regulatory skill, it is common for adolescents with persistent asthma to be met with barriers to ICS adherence that they may not have the experience or cognitive development to effectively problem-solve.[20,21] Indeed, intrapersonal factors such as attitudes (e.g., motivation), feelings (e.g., mood, stress), and external factors such as the social and family environment, have consistently been associated with asthma management behaviors and disease outcomes.[13,22–27] Efficacious behavioral interventions often attempt to actively reframe ICS adherence as central to an adolescent's self-concept (e.g., better lung function will allow you to pursue your interests). Once adolescents see adherence as helping them reach their own personal goals rather than as a chore, they are sufficiently motivated to learn skills that can help ensure adherence to ICS. To this end, adolescents are taught to identify intrapersonal and external barriers to adherence and problem solve around those barriers. Beyond simply teaching a formula for problem-solving, many effective adherence promotion programs tailor intervention content to personally salient barriers and help the adolescent identify and implement strategies specifically designed to increase the chances of regimen success.[28–30]

A persistent problem in this approach is the difficulty of relying on infrequent face-to-face visits (e.g., for clinical care) to implement interventions. Smartphones are habitually carried by >70% of adolescents[31]; as such, mobile technology provides a readily available medium to approximate the features of efficacious behavioral health interventions[32,33] by leveraging passive monitoring, data listening, preprogrammed algorithms, and content libraries focused on improving self-regulation and problem solving skills.[34,35] Despite their potential, existing mobile health (mHealth) interventions have been largely developed without the benefit of behavioral theory, use reminder-based approaches to behavior change, and lack the kinds of tailored problem-solving training that characterizes efficacious in-person interventions[36–38] (for a systematic evaluation of behavior change techniques in current asthma self-management applications, see [38]). We believe that this, at least in part, helps explain why very few existing mHealth interventions for asthma medication adherence have yet to demonstrate their efficacy beyond active controls.[39–41]

There is a clear need for a mHealth intervention that merges digital delivery modalities with the theory-based behavioral framework and tailoring found in efficacious in-person treatments. Recent technological advances have catalyzed the development of mobile-based intervention platforms that deliver tailored support to individuals in a timely fashion.[42,43] We propose to extend this work to pediatric asthma by developing ReACT, an innovative adaptive mHealth intervention that facilitates self-regulation by aiding adolescents in self-monitoring, goal setting, and problem solving when adolescents' adherence data indicate they need additional support the most (**Figure 1**). We will outline how ReACT content will be developed, refined, and tested through an iterative user-centered design process guided by theory and prior evidence.

Methods and Analysis

Objectives

The aims of the study are: 1) conduct a hybrid user-centered and evidence-based design process comprised of individual interviews, crowdsourcing, and advisory boards to develop ReACT content and features; 2) test the acceptability and usability of ReACT in a sample of 20 adolescents with persistent asthma. We hypothesize that ReACT will be an acceptable and usable mHealth adherence promotion intervention as determined by high acceptability and usability ratings and themes from think aloud testing and qualitative one-on-one interviews with target users.

Project Overview

This multi-site study will take place at the University of Florida, University of Kansas, and their affiliated clinics. The study commenced in October 2018 and is anticipated to be completed in late 2019. Features and intervention content of ReACT will be developed concurrently. We will work with a technology vendor to add functionality for ReACT to an existing mHealth adherence monitoring platform. We will use a strong theoretical framework and prior evidence combined with a series of user-centered design phases to determine what intervention content should populate the ReACT system (Design Phase 1). Study team members and an advisory board will then refine intervention content and complete preliminary usability testing of ReACT (Design Phase 2). Finally, we will conduct acceptability and usability testing using an alpha version of ReACT. See **Figure 2** for the study timeline.

Core ReACT Functionality

We will create ReACT by expanding the capabilities of an existing Android and iOS compatible mobile phone app that uses an integrated mobile sensor designed to fit onto an asthma metered dose inhaler (MDI) or diskus. The sensor works passively to sense when ICS or short-acting beta-agonist (SABA) medications are dispensed. Bluetooth is used to pass the information to the app, which has a set of optional features (e.g., provide feedback about adherence) that can be turned on as intervention parameters dictate. **Figure 3** outlines an adolescent's intervention experience through ReACT. Building from theory and prior evidence, core ReACT components in sequence are: 1) core education on asthma management and skills training content on goal setting and problem solving[4,44], 2) conditional activation of ReACT features when an adolescent is <80% adherent to their ICS, 3) an evidence-based goal-setting algorithm that shapes adherence to dosing recommendations over time, 4) timely assessment of an adolescent's barriers to adherence, and 5) delivery of tailored problem solving training based on recent and salient barriers. Determinants of self-regulation will be integrated into the core ReACT functionality to best scaffold support for adolescents, as outlined below.

ReACT will begin with an orientation module within the app that guides the users through the platform, core educational and skills training modules, and passive monitoring of medications. Adolescents will complete an asthma education module based on NHLBI guidelines[45] to ensure that they have an understanding of the importance of medication adherence as a means to avoid asthma-related impairments. Adolescents will receive skills training on empirically-supported techniques consistent with our guiding self-regulation theory. Goal setting content will use a SMART (Specific, Measurable, Attainable, Relevant, Time-Bound) goal framework. Problem-solving skills training will focus on orienting to the problem, defining and formulating the problem, generating alternative solutions, deciding on a course of action, and implementing a solution.[46,47] We will use engaging videos created by the team to deliver content. Participants will complete the orientation modules with study staff to encourage engagement and provide assistance if necessary.

ReACT will use passive sensing to objectively monitor rates of adolescent ICS adherence throughout the intervention period. The use of the ICS adherence sensor offloads the burden of self-monitoring such that adolescents do not have to remember or calculate their adherence. Active intervention elements in ReACT will activate only when an adolescent falls below a clinically derived 80% adherence threshold[48] based on a 7-day rolling average, thus reducing intervention fatigue.[43] If an adolescent has $< 80\%$ adherence to ICS based on the 7-day rolling average, ReACT will prompt the adolescent to set a goal for adherence in the next 7-day period, a strategy with demonstrated efficacy in previous asthma adherence interventions.[49] The algorithm will only allow goals that are reasonable given performance over the past week to avoid overly ambitious and unattainable goals. Each evening, the adolescent will receive a feedback message about how much their adherence that day moved them toward their goal, additionally facilitating the self-regulatory process of observation. Furthermore, the conditional activation of the ReACT features should support self-regulatory skills, specifically judgement, by notifying the adolescent when his or her adherence declines.

ReACT will identify contextual barriers to ICS adherence by also initiating an assessment as soon as the 7-day rolling average indicates that adherence is < 80%. Specifically, adolescents will be prompted via a push notification to complete a brief electronic momentary assessment (EMA) survey of barriers identified from our pilot data and Design Phase 1 to identify what barrier the problem-solving content should be tailored to address. Participants will answer brief questions in the app regarding barriers that got in the way of taking their ICS followed by a rank order item denoting which one to make the focus of their problem-solving efforts. Once a barrier is identified, ReACT will deliver problem-solving content in the app that is tailored to that specific barrier. For instance, if an adolescent has identified and chooses to work on stress as their top barrier to ICS adherence, the tailored problem solving will deliver structured problem-solving training using a flexible system of branching that is tailored to stress specifically. To execute this feature, ReACT will have several content banks that use the same structure. To illustrate the user experience, a possible problem-solving intervention could include: 1) defining the problem: participants will be presented with a standard message reflecting the problem they identified in the EMA survey; 2) setting a realistic, achievable goal: several goals will be presented and the participant will choose one and receive feedback on their choice; 3) generating multiple solutions: the participant will be asked to choose from a list of possible solutions for the goal that they selected in step #2; 4) evaluating pros and cons: participants will evaluate the pros and cons of multiple solutions listed in step #3; 5) selecting a solution: participants will choose the solution that may work the best; 6) making an action plan: participants will select from a list of action plans that correspond to the solution they have selected; 7) evaluating the outcome: after a week participants will be asked whether they implemented the solution selected in #6. The goal-setting and tailored problem-solving process should enhance one's reaction to suboptimal adherence by improving self-efficacy and facilitating skills to overcome their personalized adherence barriers.

Once an adolescent receives intervention content, ReACT will prompt adolescents to complete a survey in the app two days later to assess content use. If the participant responds that they used the intervention strategy, ReACT will assess the participant's confidence in their ability to repeat the plan in the future. If the participant has not used the strategy, they will receive a supportive prompt with options to review the content they saw last time, see the same content in a different media format, review a different set of content on the same topic, or set a goal to use the strategies by a specific time in the next two days. Another program safeguard is to reduce overwhelming participants with content; therefore the Tailored Problem-Solving Process (**Figure 3**) will only run once in a given 7-day window. This mirrors normative approaches for in-person interventions during which only one or two new concepts would be introduced each week.

Participants and Recruitment

Participants. Participants will include four separate samples of 13-17-year-old adolescents with asthma and their caregivers (see **Figure 4**). Twenty adolescent-caregiver dyads will complete individual interviews, 100 adolescents will provide crowdsourced feedback via a national online panel, four adolescent-caregiver dyads will participate in advisory board meetings, and 20 adolescent-caregiver dyads will complete user testing of ReACT. We intend that at least half of adolescent participants in the interviews and advisory boards will be from racial and ethnic minority groups.

Inclusion and Exclusion Criteria. For interviews, advisory boards, and user testing, adolescents must have a physician-verified diagnosis of current asthma with persistent symptoms requiring regular ICS use for $\geq$ 6 months. They must have a daily ICS or ICS/LABA prescription that is sensor-compatible, and they and their caregivers must speak and read English. Asthma status and prescription information will be verified via the electronic medical record. Families will be excluded from the study if the adolescent is currently involved in an asthma management intervention, has a comorbid chronic health condition that may impact lung function, or has a significant cognitive impairment or developmental delay that interferes with study completion. For crowdsourced feedback, inclusion will be determined at the level of a national online panel, which will screen participants for persistent asthma.

Recruitment. Participants will be recruited 1) through university-affiliated clinics and 2) via flyers. Research and clinic staff members with access to the Electronic Medical Record will identify eligible patients with upcoming medical appointments. During these appointments, providers with clinical relationships with the eligible participants will first approach the patients to determine their interest in hearing more about the study. Then, in coordination with the clinic staff, research staff will meet with interested patients to provide a study overview, complete in-person screening for eligibility, and invite participation. In the event that a family is unable to complete screening during a clinic visit, research staff will request permission for a member of the study team to contact patients for screening using an IRB-approved "consent-to-contact" form. A member of the study staff will then call interested participants to provide a study overview and invite participation. In addition, IRB approved flyers will be posted or made available in clinics, community organizations, schools, physician offices, and common areas. Flyers will encourage families and nurses to call our research office to learn about the project, determine initial eligibility, and if eligible, schedule an in-person screening visit where informed consent will be collected prior to study enrollment. Throughout all phases of the project, participants will be incentivized and compensated for their participation.

ReACT Development

Patient and Public Involvement. Adolescents diagnosed with asthma, their caregivers, and pediatric asthma providers are involved in all stages of ReACT development, as described below.

Design Phase 1: Content Development. We have developed a list of common barriers to ICS adherence from our own pilot data and the extant pediatric asthma literature. Our goal for Design Phase 1 is to use individual interviews with adolescents diagnosed with asthma to translate these barriers into terms easily understood by adolescents, develop a final list of barriers to adherence, and subsequently develop a library of intervention content to overcome adherence barriers that is informed by self-regulation theory. Individual interview participants and their caregivers will also complete asthma-related measures for sample description purposes and to obtain preliminary data on constructs of interest to the project (see **Table 1**). Adolescent-caregiver dyads will receive $60 for their participation.

The study team will create an individual interview guide that will be used to identify what barriers to adherence are most salient to adolescents with asthma, and to solicit their opinion about the types of intervention content that they would prefer to receive when experiencing these barriers. Prior to the start of individual interviews, at least three pediatric asthma providers (e.g., pulmonologists, nurses) will provide feedback on the interview guide. All interviews will be audio recorded and conducted with self-regulation theory in mind. If a component of self-regulation theory is not discussed, we will probe for content in the omitted domain to facilitate development of intervention content. Interviews will be transcribed and evaluated by the study team to inform digital intervention content development (see Data Analysis section).

Research staff with experience developing digital intervention content will leverage information gathered during Design Phase 1 to develop a library of intervention content for each barrier identified in the interviews and quantitative analysis of our pilot data. We anticipate that intervention content will include a combination of skills training videos, brief text content, educational videos, and images. Delivery modality (SMS, app, etc.) will be discussed with the advisory board.

Design Phase 2: Refinement of Content and Preliminary Usability Testing. In Design Phase 2 we will refine intervention content generated in Design Phase 1 through 1) nationally crowdsourced feedback from adolescents with asthma and 2) advisory board meetings. Preliminary usability testing and iterative refinement will be conducted with our advisory board meetings (described below).

Nationally crowdsourced feedback will be solicited via an online panel and survey-technology provider. Participants will be identified from panels of adolescents who have agreed to participate in research. These panels are accessed by our survey vendor through their business-to-business partnerships. Participants will be screened for persistent asthma using the following standard set of questions commonly used in epidemiological trials (e.g., National Health

Interview Survey: 1) Have you ever been told by a doctor, nurse, or other health professional that you have asthma? 2) Do you still have asthma? Affirmative answers to both questions will qualify an adolescent for participating.[50] Participants will review intervention content and rate its appropriateness using a dichotomous “Yes” (I like the message as it is) or “No” (change it to make it better) response choice. They will receive $15 for their participation. Content receiving ≥ 60% “No” votes will be discarded, and those with ≤ 39% “No” votes will be accepted as final intervention content. Content with 40-59% “No” votes will be revised or clarified while retaining any theoretically or empirically derived concepts.[51] We will design surveys to take no more than 30 minutes each. If necessary, we will split the content into two surveys to keep the administration time < 30 minutes. Although adolescent stakeholders will be involved in developing ReACT intervention content rated during crowdsourcing, we acknowledge that there is a possibility that a higher than expected amount of content will be viewed unfavorably during this phase. We will review crowdsourcing feedback data from an initial wave of 20 participants. In the event that > 60% of content is viewed unfavorably, we will pause crowdsourcing to develop new intervention content.

An advisory board comprised of adolescent-caregiver dyads and study staff members will convene three times. The first meeting will focus on reviewing summative data and themes that emerged from crowdsourcing phase. The second advisory board meeting will involve discussion about methods to further refine intervention content that received 40-59% “No” votes during crowdsourcing. We will incorporate modified content that reaches group consensus into applicable ReACT intervention content libraries. Preliminary usability testing will take place during the final advisory board meeting. Members will conduct hands-on testing of ReACT alongside study staff. We will use a “think aloud” approach with members as they explore components of the ReACT interface (e.g., layout, visual feedback), answer EMA questions, and view intervention content.[52] This process more closely approximates actual use and will enable us to receive feedback in real-time. The study team will transcribe participant commentary during testing for review. Results of the “think aloud” testing will help to inform final design decisions in ReACT.[52] For instance, whether content is delivered using SMS, in-app, push notification, or some other medium will be informed by user preferences. Advisory board participants and their caregivers will also complete asthma-related measures to pilot data collection procedures and provide baseline descriptive statistics (see **Table 1**). Adolescent-caregiver dyads will receive $50 for each advisory board meeting they attend.

Acceptability and Usability Testing of ReACT

In the final phase, adolescents will conduct user testing with the alpha version of ReACT. The overarching goal is to gather acceptability and usability data from the perspectives of target users of ReACT. A sample of 20 participants will complete a 4-week run-in period to monitor their adherence with all ReACT features turned off. Subsequently, study staff will meet with participants to complete ReACT orientation. This visit will ensure that participants are able to download and use ReACT, and that relevant ReACT components (e.g., asthma education and skills training videos) are accessed before beginning. Participants will complete asthma-related study questionnaires (see **Table** 1) and then begin a 4-week intervention period with all ReACT features activated. Notably, acceptability and usability measures will be administered at a final study visit at the conclusion of the 4-week intervention period Again, participant comments and suggestions during the final study visit will be transcribed for review.

Data Analysis Plan

Individual Interviews. Study staff will enter transcribed files and expanded notes into NVivo. We will code and aggregate interviews using a theoretical thematic analysis approach to developing themes.[53–55] Our theoretical thematic analysis approach will use an *a priori* theoretical framework guided by self-regulation theory, informed by advisory board meetings. The investigators will mark comments identified to represent discrete thoughts or themes using a semantic analysis, and they will use an essential realist approach to arrive at themes.[53] These patterns or themes will comprise the initial set of categories. Research staff will then re-code the data using these categories and organize major themes into summary tables to inform initial development of a digital content library. Interviews will continue until no new themes emerge in the data coding process (i.e., saturation).[56] After the coding process is complete, data will be described descriptively.

ReACT Acceptability. Acceptability of ReACT will be determined in two ways during the usability testing phase. First, the ReACT Satisfaction Questionnaire[57] will assess overall satisfaction, perceptions regarding how helpful ReACT could be in managing asthma, and whether adolescents would recommend ReACT to friends with asthma on a 4-point Likert scale. An average rating of 3 (mostly satisfied) will be considered a successful outcome. Second, the semi-structured interviews will solicit adolescent feedback about ReACT. Our comprehensive interview guide will cover a range of topics, including: 1) perceived usefulness of ReACT; 2) how effective ReACT might be in changing asthma self-management behaviors; and 3) suggestions on further refining ReACT (e.g., incorporating other individuals). Qualitative data analysis will help determine overall project success. The process for identifying themes will be similar to the process from the earlier interview phase, but in this case we will use an entirely de novo process of identifying themes.[53] We will mark comments identified to represent discrete thoughts or themes using a semantic analysis, and we will use an essential realist approach to arrive at themes.[53] In particular, we will be attentive to themes that relate to the acceptability, usefulness, and user experience of ReACT. Themes that indicate that ReACT was perceived to be effective, appropriately tailored, and acceptable burden will be the criterion for success.

ReACT Usability. Usability will be determined in three ways. First, an average rating of 3 (agree) on the Health Information Technology Usability Evaluation Scale[58] will be a criterion for success. Second, themes from think aloud testing that suggest adolescents can navigate the ReACT interface intuitively and with minimal difficulty will be markers of success. Finally, our semi-structured interview will ask for feedback regarding: 1) the layout of the ReACT interface; 2) the navigation experience; 3) clarity of the wording; 4) clarity of the video content; and 5) ways to improve the usability and content of ReACT. These data will be used to inform future refinements of ReACT in advance of a subsequent trial.

Ethics and Dissemination

All aspects of the study protocol will be approved by local institutional review boards. In addition, all research team members will complete certification in topics related to the responsible conduct of research. To minimize risk from research participation, potential subjects will be fully informed regarding the purpose, process and amount of time required for participation. It is possible that research staff will identify an adolescent whose asthma appears undertreated. Research staff will review all cases with local medical personnel and facilitate a referral for evaluation and appropriate medication if indicated.

We plan to disseminate findings from the current project to multiple audiences including the local medical community and the broader scientific community via local and national presentations at relevant conferences and meetings. Beyond pediatric asthma, we also envision that the ReACT infrastructure and design process can be used to develop and test behavior change interventions in other disease populations. If successful, this would be a significant step toward the 2016 NIH-Wide Strategic Plain goal of using mHealth to "enhance health promotion and disease prevention."[59]

Limitations

The current project is a pilot feasibility, acceptability, and usability study in a targeted sample (i.e., adolescents with chronic and persistent asthma) who also have a high need for this type of intervention. As such, we will not be able to contribute knowledge about the feasibility of ReACT in all of the populations it might benefit (e.g., adults with chronic obstructive pulmonary disease). Moreover, the current project is not powered to understand heterogeneity of outcomes across sex, socioeconomic status, race, culture, and literacy levels. The protocol will not incorporate shared decision-making between patients and providers in the intervention given the focus of ReACT. ReACT does not target all of the factors that might influence adherence. Specifically, structural issues such as inadequate insurance coverage will not be addressed in the current protocol. At this stage, ReACT does not involve providers at least in part because there are already other commercial systems that do a good job of achieving that function. The novelty of ReACT is to identify the developmentally appropriate individual level interventions that can increase adherence.

Author's Contributions

DAF and CCC conceived the study. DAF, CCC, SRP, SG, ELM, SP, and JS developed the protocol. DAF, CCC, NK, AO, KF, and AMN were involved in drafting of the article. Specifically, DAF and CCC collaboratively wrote the text, NK and AO edited the text, and created figures. KF and AMN provided expertise and section edits on the statistical approach and features of problem-solving therapy. SRP, ELM, provided expertise and writing about qualitative work. JS provided expertise and writing about adaptive interventions. All authors completed a critical revision of the article and approved the final text.

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Data availability statement

There are no data.

Competing interest

There are no competing interests for any author.

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Table 1

ReACT Outcome Measures

Outcome	Measure	Assessment Schedule*
Demographics	A caregiver-report questionnaire assesses adolescent and family demographic characteristics.	II, AB, UT
Asthma Morbidity	A caregiver-report questionnaire assesses frequency of asthma symptoms, exacerbations, activity limitations, missed school days due to asthma, ED visits, and hospitalizations.	II, AB, UT
Medical Information	Medical chart review assesses prescribed ICS regimen and dosage.	II, AB, UT
Asthma Knowledge & Skills	The Asthma Child Knowledge and Skills Questionnaire,[12] a modified version of the Children's Asthma Knowledge Questionnaire,[60] is a 30-item adolescent-report measure that assesses both asthma knowledge and self-assessment of skills required for taking medication.	II, AB, UT
Asthma Control	The Asthma Control Test (ACT)[61] is a 5-item, validated, adolescent-report questionnaire that assesses asthma control in past 4 weeks.	II, AB, UT
Asthma Management	The Asthma Management Efficacy Questionnaire (AME)[62] is a 14 item, validated, adolescent-report questionnaire that assesses asthma self-management behaviors.	II, AB, UT
Asthma Adherence	The Medication Adherence Report Scale for Asthma (MARS-A)[63] is a 10-item, validated, adolescent-report measure of ICS adherence.	II, AB, UT
Self-Regulation	The Treatment Self-Regulation Questionnaire (TRSQ) - Asthma[64] is a 15-item, adolescent-report measure that assesses motivation for using controller medication.	II, AB, UT
Stress	The Adolescent Stress Questionnaire (ASQ)[65] Revised is a 58-item, validated, adolescent-report questionnaire that assesses stressors in adolescence.	II, AB, UT
Social Support	The Social Support Questionnaire (SSQ)[66] is a 27-item, validated, adolescent-report measure of social support.	II, AB, UT
Problem Solving	The Social Problem Solving Inventory-Revised: Short Form (SPSI-R:S)[67] is a 25-item, validated, adolescent-report measure that assesses problem solving orientation and skills in everyday life.	II, AB, UT
Asthma-Related Quality of Life	The Pediatric Asthma Quality of Life Questionnaire (PAQLQ)[68] is a 23-item, validated, adolescent-report questionnaire that measures extent of asthma impairment in quality of life.	II, AB, UT
Acceptability	The ReAct Satisfaction Questionnaire is an 8-item modification of the Client Satisfaction Questionnaire[57] that assesses overall participant satisfaction with the ReACT intervention. Semi-structured interviews assess what	UT

	adolescents like and do not like about ReACT, its relevance, and its perceived helpfulness with medication adherence.	
Usability	The Health Information Technology Usability Evaluation Scale[58] is a 20-item, validated questionnaire that assesses perceived usefulness, impact on disease, perceived ease of use, and user control. Think aloud testing gathers stream of consciousness data regarding thoughts and feelings of users as they complete specified tasks. Semi-structured interviews assess the the look and feel of ReACT, ease of navigation, and experience accessing intervention content.	UT

*II = Design Phase I Individual Interviews, AB = Advisory Boards, UT = User Testing

Figure Legend:

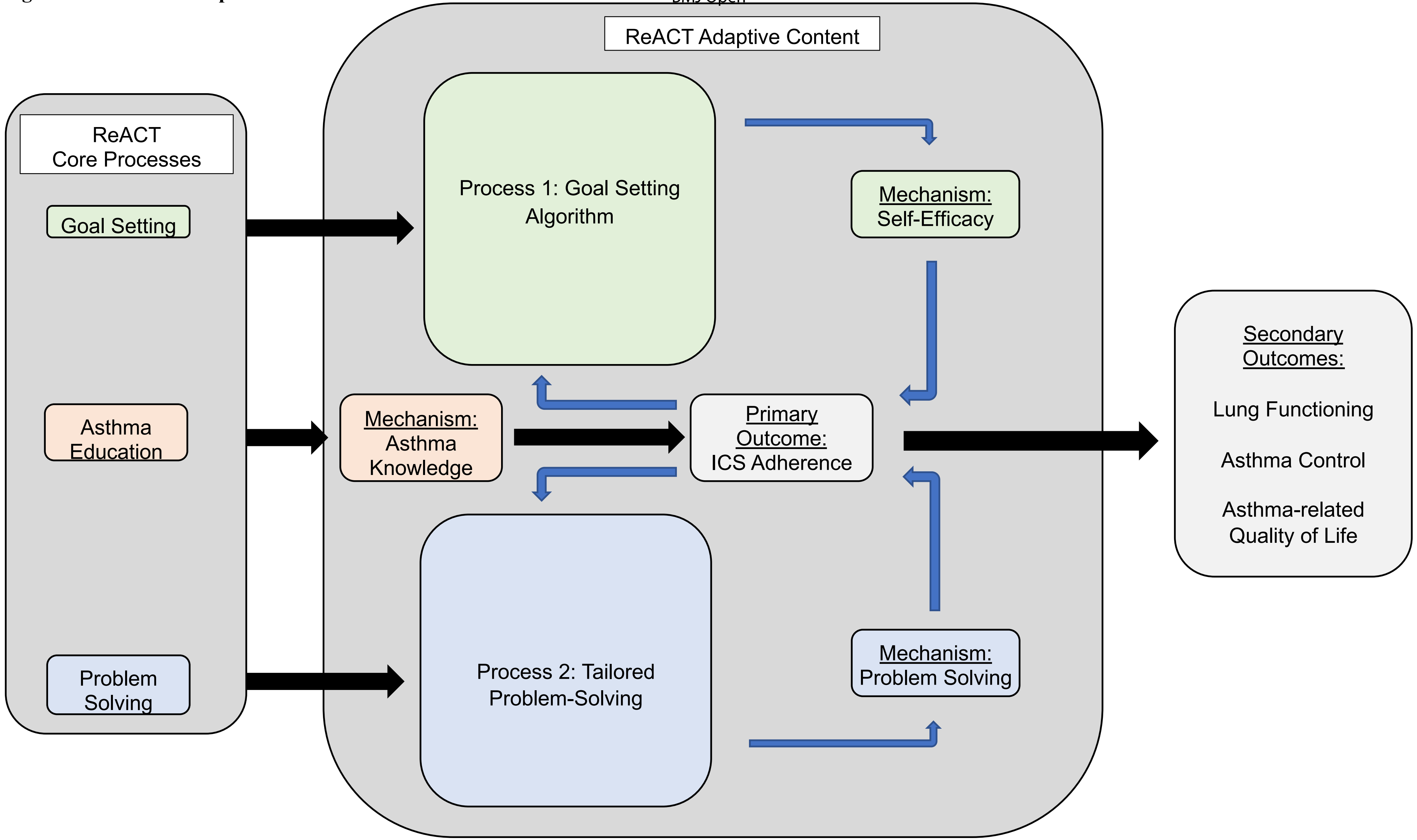
Figure 1. ReACT Conceptual Model, Note: Black arrows represent mechanistic processes occurring during the ReACT intervention period. Blue arrows indicate recursive processes happening repeatedly during the intervention period. ICS adherence = Adherence to inhaled corticosteroids.

Figure 2. Study Timeline.

Figure 3. React Participant Flow. Note: Diamonds indicate intervention decision rules. ICS = inhaled corticosteroids, SABA = short-acting beta-agonist.

Figure 4. ReACT Flow of Formative Work.

Figure 1. ReACT Conceptual Model



Note: Black arrows represent mechanistic processes occurring during the ReACT intervention period. Blue arrows indicate recursive processes happening repeatedly during the intervention period. ICS Adherence = Adherence to inhaled to corticosteroids.

Figure 2. Study Timeline

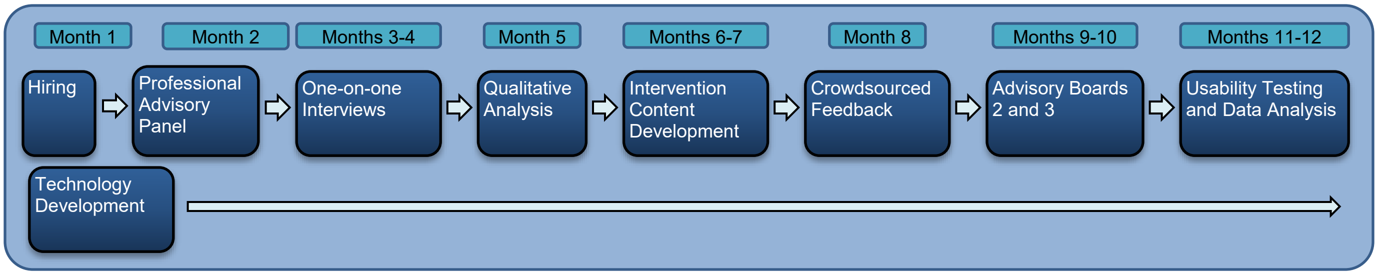
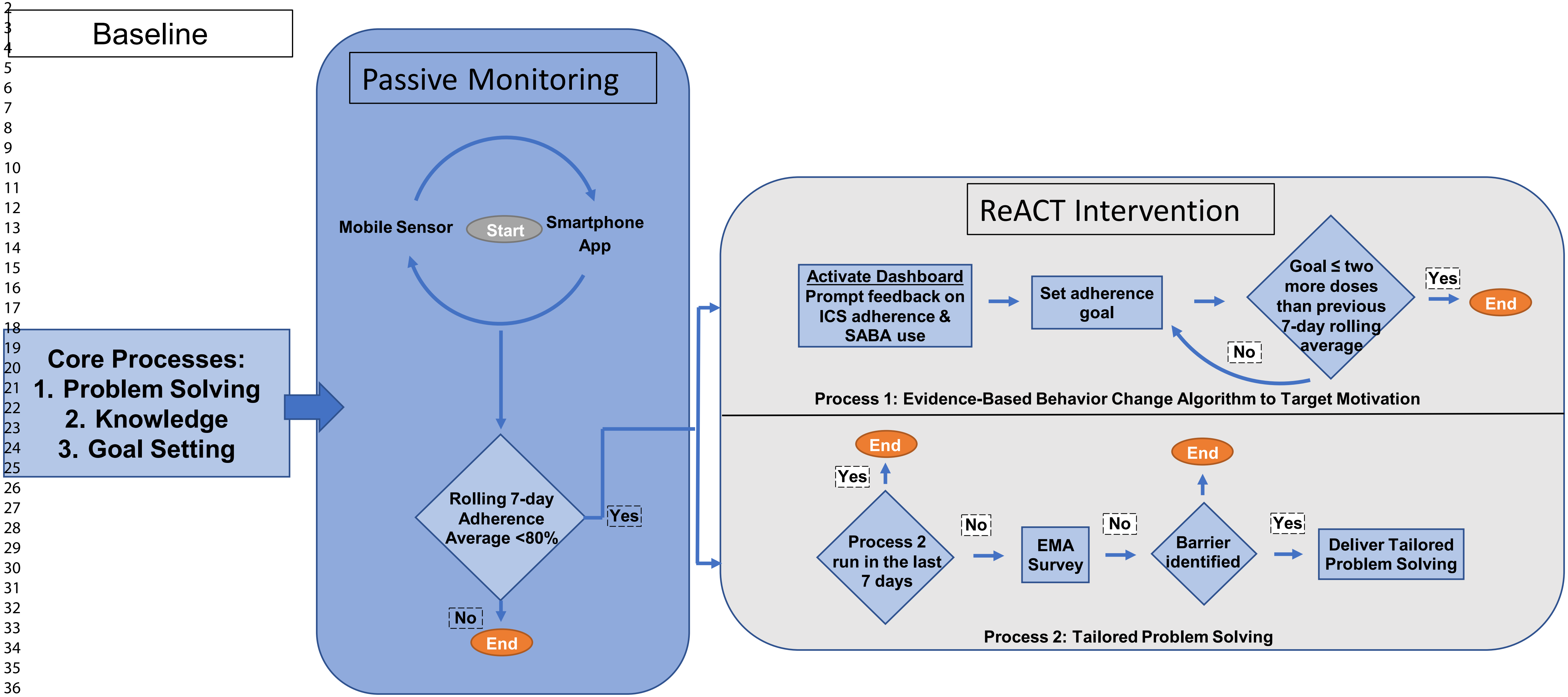


Figure 3. ReACT Participant Flow



Note: Diamonds indicate intervention decision rules. ICS = inhaled corticosteroids, SABA = short-acting beta-agonist.

Figure 4. ReACT Flow of Formative Work