Breathing Counts
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I. **Hypotheses and Specific Aims**:

Adherence to asthma medications has been associated with good asthma control in children[1], however adherence to asthma medications is poor.[2] Children who are hospitalized due to their asthma are at a significantly high risk of re-hospitalization[3], and represent a particularly high risk group. Successful control of asthma in a high-risk population requires a network of care providers who communicate relevant up-to-date information and support asthma control. Additionally, lay health worker interventions have been shown in some cases to decrease missed school days and parental work days.[4] We propose to evaluate the efficacy of an asthma navigator program in a high-risk population of patients at Children's Hospital Colorado. We will evaluate the ability of the program to improve health outcomes of children who have asthma and who are at high-risk of re-hospitalization. The project will also evaluate the ability of the navigator program to increase the number of stakeholder communications amongst school nurses, program navigators, physicians, caregivers and children.

Specific Aim 1: Evaluate whether or not the addition of an asthma navigator to the current clinical standard of care will lead to sustainably increased levels of adherence compared to historical rates.

Hypothesis: By providing up to date adherence rates to the patient's medical care team and by addressing patient identified barriers, we hypothesize that the addition of an asthma navigator to the standard of care at Children's Hospital will increase asthma medication adherence rates, and that these adherences rates will be sustained over the 3-6 month monitoring period.

Specific Aim 2 Evaluate whether or not the addition of an asthma navigator results in increased levels of communication between PCPs, specialty providers and school nurses.

Hypothesis: The addition of an asthma navigator will result in increased emails and general communication between various providers in a patient's care team.

Specific Aim 3 Evaluate whether or not other asthma related outcomes (measures of asthma control, asthma related quality of life, presence of a school asthma action plan, among others) are altered with the addition of an asthma navigator to a patient's care team.

Hypothesis: The addition of an asthma navigator will improve other markers of asthma control and quality of life. We anticipate an increase in asthma control and increase in the number of patients with a school asthma action plan.

II. **Background and Significance**:

Adherence to asthma medications is poor

Adherence to asthma medications is poor, especially in high-risk populations,[5] and even with monitoring studies show adherence worsens over time.[6] The large Childhood Asthma Management Program study found that 75% of children studied had adherence levels of less than 80% when measured objectively.[7] In fact, one review of previous attempts to measure adherence to asthma medications utilizing electronic monitoring devices showed adherence rates between 28-73%, with only one study showing an adherence rate above 90%.[8]

Asthma morbidity is a significant public health problem.

Over eight percent of children in the US carried a diagnosis of asthma in 2013, and 58% of those children had an asthma exacerbation in that year.[9] Asthma exacerbations/hospitalizations remain a significant source of healthcare expenditures[10]

Inhaled corticosteroids have been shown to significantly improve asthma control

The use of low-dose ICS in asthmatic children and adults has been shown to significantly decrease the rate of asthma-related hospitalization[11] and asthma related death.[12] Additionally, chronic use of inhaled corticosteroids has been shown to improve asthma control.[13]

Adherence has been correlated with some improved asthma outcomes.

Previous evaluations of adherence using electronic monitoring devices have shown lower adherence rates to be correlated with higher levels of healthcare utilization,[14] and worsened levels of asthma control[15,16] A small study of Australian children showed a trend toward improvements in lung function with greater adherence, however this failed to reach statistical significance.[17] The correlation of adherence to other asthma outcomes including exacerbations and various markers of lung function/inflammation in high risk children has not yet been studied.

Non-adherence disproportionately affects a high-risk population of children with asthma.

High-risk children are disproportionately of color, have low household levels of education and income, attend poorer performing schools, come from lower socio-economic background.[18] Poorly controlled asthma contributes to poor school performance by disrupting sleep and causing missed days of school[19,20], and associations between poor asthma control and missed school are higher among minority children.[21] Researchers have suggested possible determinants of non-adherence including concerns about medication adverse effects, belief that asthma is not a serious problem, belief that medications are not helping, and preference for a non-pharmacological approach, among others.[22] In order to address both the persistent high levels of morbidity associated with asthma and increasing disparities, new approaches to asthma management are needed to more effectively deliver evidence-based preventive treatments and identify children who need a more intensive, stepped up treatment plan. While some interventions based in schools, in the home, or in the community have shown promise,[23-25] important limitations have included lack of coordination with community health care providers (HCPs), lack of involvement of schools and the community, inability to monitor medication adherence and lack of sustainability. In short, we aim to reduce health disparities with this program by targeting the highest risk asthma patients, those admitted to the hospital inpatient or emergency department with an asthma exacerbation, which tend to be disproportionately minority patients, and utilize new and innovative technology to improve care for these patients.

III. Preliminary Studies/Progress Report:

We have been conducting a pilot study evaluating the use of electronic adherence monitoring devices in the pediatric asthma population. We have collected preliminary data on the usability of these devices in our population of children aged 6-17. Preliminary evaluation of this data has shown that the devices are largely well tolerated, and data from the devices is accessed often by providers. Most patients feel comfortable utilizing smartphone applications, and the majority of patients found the devices easy to use.

IV. Research Methods

A. Outcome Measure(s):

A table of outcomes to be collected during the study time period is give below (table 1). A detailed description of the outcome follows.

	Outcome Measure	Visit 1 (admission visit)	Visit 2 (2 months)	Visit 3 (4 months or end of study)	Visit 4 (6 months or end of

					study)
Aim 1	Adherence (continually monitored during trial)		X	X	X
Aim 2	Communication among providers	X			X
Aim 3	Asthma Related Health outcomes	X	X	X	X

a. Adherence- measured on adherence monitoring devices. The rate of daily prescribed controller medication use will be monitored. For example, if an individual is prescribed two doses per day and the monitoring device records one doses, then the daily adherence measure will be 1/2 or 50%. The outcome measure will be continuously gathered via the Propeller Health monitoring device ® (Madison, WI). Rate of monthly adherence will be calculated between study visits,
b. Communication between providers. Communication between providers will be measured in a number of ways. Providers include nurses, parents, physicians and patients. In order to measure any change in communication the following communication metrics will be monitored.
    i. Number of emails sent between providers will be assessed if email is used as the primary means of communication.
    ii. A subset of provider teams will possibly be enrolled in asynchronous communication monitoring. This is a method of HIPAA compliant messaging, which involves providers utilizing an application or website, and communicating securely within that platform. We plan to utilize the Stich platform, which is marketed as HIPAA compliant (https://www.teamstitch.com). We are currently on a waiting list to possibly test the technology.
    iii. Providers will be surveyed before and after the intervention to determine if they felt that the navigators adequately improved communication regarding specific patient related issues.
c. Other asthma related outcomes including asthma control test, symptom assessments, asthma related readmissions or revisits, missed school days, and provider satisfaction.
    i. Asthma Control Test, a self (or in the case of this study, phone administered)-administered questionnaire with 5 questions which summarizes asthma control, will be used to record asthma control in children 12 or older.
    ii. Childhood Asthma Control Test (or in the case of this study, phone administered), a parent and child administered questionnaire, will be used to record asthma control for children 6-11 years of age.
    iii. Pediatric Inhaler Adherence Questionnaire, a self (or in the case of this study, phone administered) survey of barriers to medication adherence
    iv. Parent attitudes towards medications and barriers to adherence.
    v. Changes in adherence barriers and behaviors to improve adherence over time
    vi. The number of asthma related readmissions or revisits between study visits will be self-reported.

vii. The number of missed school days between visits will be self-reported.
viii. Provider satisfaction will be recorded using the pre-post surveys

B. Description of Population to be Enrolled:

a. Children admitted to Children's Hospital Colorado inpatient or emergency department with a primary diagnosis of asthma exacerbation.
   i. Inclusion criteria-patients
      1. Age 6-17 years
      2. On a controller medication at baseline
   ii. Inclusion criteria-providers
      1. Aged 18-70
      2. Caring for a patient that is enrolled in the study
   iii. Exclusion criteria
      1. Primary language other than English or Spanish (smartphone application only available in these languages)
      2. Homeschooled or not in school
      3. Significant developmental delay, cystic fibrosis, interstitial lung disease, tracheostomy/ventilator dependence
      4. Following up with a pulmonary or allergy provider outside of the CHCO system

C. Study Design and Research Methods

The proposed study is a single center trial at Children's Hospital of Colorado, designed to evaluate the effects of a navigator program on medication adherence, provider communication and other asthma related health outcomes. Participants will be recruited from the population of patients between the age of 6 and 17 years admitted to Children's Hospital Colorado inpatient or emergency department with a primary diagnosis of asthma exacerbation. Investigators plan on a one-year enrollment period and will follow each study participant for 3-6 months.

Recruitment

Upon admission hospital staff will identify potential participants based on the admission medical record. Patients will be approached by research staff and asked if they would like to participant in the study. A member of the research team (principally, the research coordinator) will do the recruiting. The research coordinator will explain the study and enroll subjects. Estimated duration is 45-60 minutes depending upon the patient.

Consent/Assent

We will obtain a signed parental permission form and an age-appropriate assent form for participants younger than 18 years. Consent will be obtained by a member of the research team (principally, the research coordinator or a research assistant). It will be made clear to patients that the research team is not part of the treatment team.

Study Design

We plan to enroll a total of 100 patients. and up to 400 providers. Patients enrolled will be provided and trained on using the adherence monitoring prior to discharge (sensors will be placed on discharge controller and quick-relief medication). Participants will also be enrolled in the smartphone application that will give them feedback about their medication usage. Once enrolled in the application, patients will receive push notification reminders to use their medications, as well as be able to access their adherence information in real time. Caretakers will also be given the

option to have access to their child's adherence information. The smartphone application also has portions dedicated to education about asthma triggers. Patients will be set up with a pulmonary or allergy follow up within 2-4 weeks of discharge. Patient's pulmonary or allergy providers will also be enrolled in the propeller health system, with access to the propeller health dashboard. Once providers receive access, they will be able to log-in and view all of their patients in list format. They will be able to see up to the minute data on patient adherence at any time that they choose to log-in to the dashboard. Providers will also receive email notifications if their patient has not used their controller medications for 7 days, or if their patient has had a significant increase in quick-relief medication use, indicating a worsening of asthma status (see figure 1 below). Patients will be monitored for a total of 3-6 months. The asthma navigator will contact the families at 2, 4 and 6 months post-enrollment, and discuss the patient's recorded adherence with the families. If a patient is enrolled for 4-5 months, we will discuss adherence at 2 and 4/5 months. If a patient is only enrolled for 3 months, we will discuss adherence at 2 and 3 months. Additionally, they will discuss any barriers to adherence that the family may be experiencing, and make referrals to social work as necessary, as well as attempt to brainstorm ways to improve adherence with the families. Additionally, the asthma navigator will collect each patients' adherence data and create an adherence report, which will be distributed on a monthly basis to the patient's primary care provider, pulmonary/allergy provider, and school nurse via email. The asthma navigator will be monitoring communications between the providers and marking the numbers of communications.

At the time of enrollment, patients will be asked for permission to contact the child's primary care provider and school nurse. If these providers agree to participate in the study, surveys will be sent to all providers of patients (PCPs, school nurses and specialists) to determine if they found the navigator to be helpful, and to see if communication increased due to the intervention. Additionally, the research coordinator will be monitoring the provider portal to ensure that patients' devices are regularly syncing with their phone's Bluetooth, and contact any patients whose devices are not syncing normally. At the study's conclusion, we will plan to have the families return the devices to the research coordinator via US mail. After the conclusion of the study, families will be contacted by the research coordinator to ask if they would be willing to evaluate the navigator via the PSN-I navigator assessment tool. The navigator assessment tool will be used to evaluate utility of the navigator themselves. This is a tool that has been utilized previously in this context to evaluate efficacy of navigator programs. This will only be evaluated at the end of the study. There will be no reimbursement for time for this last survey.

If a patient is having difficulties with syncing their sensors to their phone, we will provide them with a hub to collect the sensor data.

D. Description, Risks and Justification of Procedures and Data Collection Tools:
There will be no medical procedures done during this study. The data collection will occur via surveys, and data collected from the adherence devices. Risks of data collection include accidental disclosure of information, though steps will be taken to prevent this. Also, there is a GPS capability of the devices, so there is a risk of disclosure of patient's location patterns.

E. Potential Scientific Problems:
We are aware that we are underpowered to fully evaluate some of the outcomes that we are interested in obtaining. Additionally, we are limited to single group analysis by request of the funding agency (rather than also having a control group), so we are limited in our ability to make full comparisons. However we would like to undertake this study as a pilot evaluation for the use of the asthma navigator in this population, utilizing adherence monitoring technology to better understand the influence of these evaluations.

F. Data Analysis Plan:

Analysis plan

Demographic information including age, sex, race, and other baseline clinical information upon recruitment including duration of asthma, C-ACT score, ACT score, asthma symptoms, lung function, prescribed medication, and asthma related health care use in the previous year will be obtained at enrollment. The distributions of outcomes will be examined for normality using the Anderson-Darling Test. Dependent upon the distribution we will use the Wilcoxon rank-sum test, Mann-Whitney U test or paired T-test to test for significant changes in outcomes during the study period. Longitudinal patterns of adherence will be examined graphically.

Monthly rates of adherence, asthma symptoms, asthma control scores and monthly missed number of school days and number of hospitalizations will be calculated by study arm. Survey information from patients, caregivers, physicians and navigators on the navigator intervention will be reviewed by study staff and summarized qualitatively. Number of rehospitalizations will be obtained via chart review at 1 month, 6 months and 12 months post hospitalization.

The cost-effectiveness of the navigator intervention will be summarized based on medical resource utilization (direct) and loss of productivity (indirect). Medical resources utilization will include medical care resource utilization, asthma medication variables, navigator time and salary, while loss of productivity will be measured using the number of hours caretaker missed work due to participant's asthma, number of hours dependent participant missed school due to his/her asthma, and number of hours independent participant missed work due to his/her asthma. Unit costs will be applied to healthcare resources and loss of productivity and summed to obtain total costs for each subject. Average costs for the study group will be presented.

Power and Sample Size

The study is limited by time frame and funding for a one year recruitment period. The primary goal of the study is to provide preliminary information on the effect of a navigator program on the patient and caregiver response to asthma disease control. As a pilot and feasibility study, investigators have chosen to enroll a total of 100 patients and up to 400 providers. Through past clinical experience, we know that some months of the year are higher risk for asthma exacerbations, so we expect to screen more patients during the fall and winter than summer or spring. Considering the variable clinical case load Investigators plan on enrolling an average of 10 participants per month. Anticipating an enrollment rate of approximately 20% (in 2015, there were >600 asthma related admissions at Children's Hospital Colorado), investigators state they should be able to enroll up to 100 patients within one year. We plan to enroll up to 4 providers per patient with a simple pre-post survey as well.

The primary hypothesis of interest is to test whether change in adherence rates are different from zero. The smallest detectible difference was based on a paired sample t-test between pre and post adherence scores with a Type I error rate of 0.05 and 90% power. Based on previous studies[8], investigators assumed a mean adherence rate of 50% with a standard deviation of 22%.

Table X:	
N	**Δ**
100	8%
65	10%
30	15%

Table X lists the smallest detectable difference (Δ) for by sample size. For the primary aim investigators will be able to detect a change of 8% or more in percent adherence during the study period with the available 100 patients.

F. Summarize Knowledge to be Gained:

a. **Utility of an asthma navigator in addition to electronic adherence monitoring in improving adherence to asthma medications**

b. **Utility of an asthma navigator in improving communication amongst all of a patient's medical providers**

c. **Utility of an asthma navigator in improving other asthma control related outcomes.**

Asthma Control Classification

Control is computed based on taking the entry with the worst outcome in the following age-based tables:

Asthma Control Classification (Age 5-10)

(Age 5-11)	Asthma	Control	Classification
	Well controlled	**Not well controlled**	**Very poorly controlled**
Symptoms (manually entered)	≤ 2 days/week but not more than once on each day	> 2 days/week or multiple times on ≤ 2 days/week	Every day in previous week
Nighttime awakenings (rescue inhaler usage at night)	≤i1x/month	≥x2x/month	≥x2x/week
Rescue inhaler usage	≤ 2 days/week	> 2 days/week	Every day in previous week

Asthma Control Classification (Age 12 or older and adults)

(Age 12 and older and adults)	Asthma	Control	Classification
	Well controlled	**Not well controlled**	**Very poorly controlled**
Symptoms (manually entered)	≤ 2 days/week	> 2 days/week	Every day in previous week
Nighttime awakenings (rescue inhaler usage at night)	≤i2x/month	1-3x/week	≥-4x/week
Rescue inhaler usage	≤ 2 days/week	> 2 days/week	Every day in previous week

Figure 1

H. References:

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