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Personalized Digital Phenotype Score, Healthcare Management and Intervention Strategies using Knowledge Enabled Digital Health Framework for Pediatric Asthma

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Chapter

Personalized Digital Phenotype Score, Healthcare Management and Intervention Strategies using Knowledge Enabled Digital Health Framework for Pediatric Asthma

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Abstract

Asthma is a personalized, and multi-trigger respiratory condition which requires continuous monitoring and management of symptoms and medication adherence. We developed kHealth: Knowledge-enabled Digital Healthcare Framework to monitor and manage the asthma symptoms, medication adherence, lung function, daily activity, sleep quality, indoor, and outdoor environmental triggers of pediatric asthma patients. The kHealth framework collects up to 1852 data points per patient per day. It is practically impossible for the clinicians, parents, and the patient to analyze this vast amount of multimodal data collected from the kHealth framework. In this chapter, we describe the personalized scores, clinically relevant asthma categorization using digital phenotype score, actionable insights, and potential intervention strategies for better pediatric asthma management.

Keywords: Pediatric patients, Asthma management, Multimodal data, Personalization, Intervention, Digital phenotype, Actionable information, Self monitoring, Self management

1. Introduction

Asthma is a multi-trigger disease with or without co-morbities such as obstructive sleep apnea, increase in body mass index (BMI), rhinitis, sinusitis, gastroesophageal reflux disease, psychopathologies etc. [1]. 8.3% of children in United States suffer from asthma [2]. Pediatric asthma affects the child's quality of life with reduced activity, lack of concentration, growing up with missed school days, emergency room visits, etc. [3].

As per the current clinical practice, the clinician does not get the holistic view of the asthma patient's health condition during the clinic visit scheduled once in every one to two months for severe persistent and once in six months for mild persistent asthma patient [4]. However, with the advent of Internet of Things (IoTs) sensors and mobile applications for collecting Patient Generated Health Data (PGHD) it has become convenient for patients (parents in the case of children below age 12) to log their daily symptoms, medication intake, and daily activity. The multi-modal

PGHD is big data which suffers from challenges of velocity, volume, and variety [5]. The data is collected at different intervals for each sensor, is of different variety and volume. It is challenging to integrate this overwhelming data for analysis. It is impossible for the clinicians alone to analyze this data coming in with different velocity, variety, and volume along with their existing duties. It is challenging and practically impossible for the clinicians and the patients to generate actionable insights from this vast amount of data due to lack of time, resources, and data analysis skills [6].

In this chapter, we introduce a knowledge enabled healthcare framework, kHealth, which is being used by the pediatric asthma patients for self monitoring and by the clinicians to derive real time insights into patient's healthcare protocol. The technologies like kHealth are extremely useful especially during a pandemic when the in-person patient visits shifts to telemedicine appointments [7]. The clinicians can use kHealth framework during the telemedicine appointment to visually explores the PGHD along with the EMRs to better understand the patient's disease prognosis and suggest diagnoses. Also, a patient can use the kHealth framework to continuously monitor, appraise, and manage her chronic disease [8]. A detailed scenario for a pediatric asthma patient is given in [8, 9] [See Multimedia Appendix A].

The data collected from the kHealth framework is used to simulate Personalized Scores, and Digital Phenotype Score (DPS) which is a clinical equivalent for the Asthma Control Test (ACT) score. The DPS is used to categorize the asthma patients into their asthma control levels and recommend intervention strategies to the clinicians.

The chapter is divided into seven sections, Section 1 is introduction, Section 2 provides a brief overview of the kHealth framework and it's components, Section 3 explains the study methods, study design, and study protocol, Section 4 discusses the personalized scores followed by Section 5 on Digital Phenotype Score, Section 6 discusses actionable insights and causal intervention, and Section 7 concludes the chapter.

2. kHealth: knowledge-enabled healthcare

A knowledge-enabled healthcare framework, kHealth (**Figure 1**, Multimedia Appendix B), is a personalized framework for self monitoring of patient's symptoms, medication adherence, lung function, activity, etc. for pediatric asthma patients. The framework utilizes the existing medical knowledge along with the PGHD to assist the child, parent, and the clinician in better monitoring and

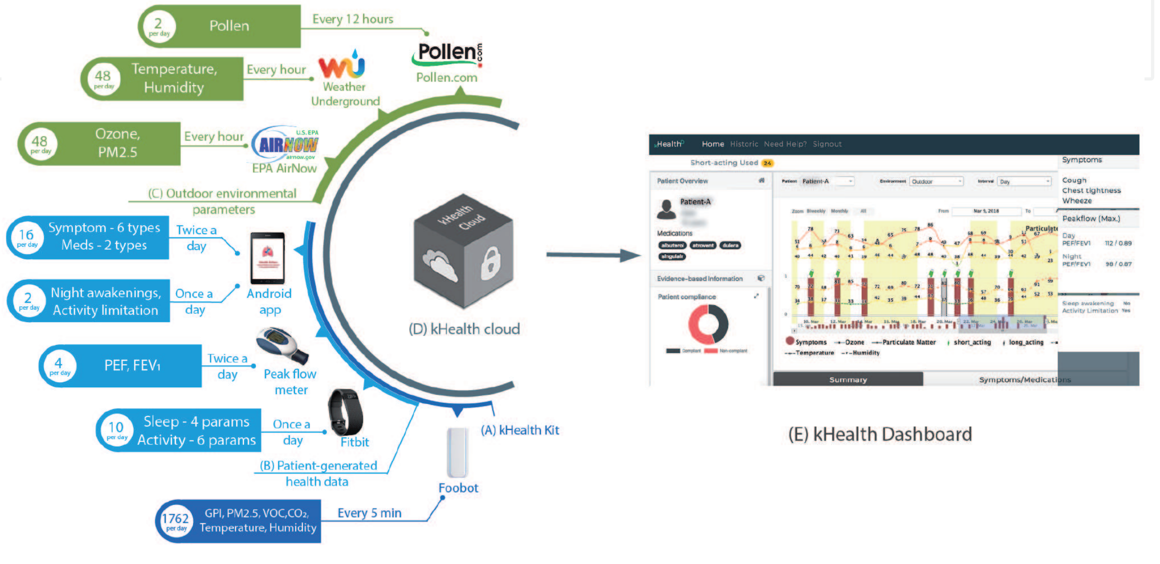

Figure 1.
kHealth architecture.

management of asthma. It provides an alternative to the traditional episodic clinician-centric health care by supporting real-time monitoring of a child's health condition. kHealth gathers empirical evidences to analyze and monitor disease progression and help in asthma management. It is a step towards exploring issues such as: What is the asthma control level of the child?, What is the medication compliance of the child?, What are the possible triggers for the child's asthma symptoms?, Can we understand the causal relationship between symptoms and possible triggers or factors responsible for the symptoms?, Can we predict asthma attacks based on the past data collected from the child?, etc. The kHealth framework consists of kHealth kit, kHealth cloud, and kHealth dashboard (described below).

2.1 kHealth kit

The kHealth kit consists of an android application (kHealth application) and a set of sensors (Foobot, Fitbit, and a Microlife Peak Flow Meter). Sections below provide a description of all the sensors and the type of data collected from them. kHealth framework uses the active and passive sensing techniques for data collection. Active sensing refers to the data collection where the child (or the parent) has to actively interact with the technology (e.g., answering questions in the kHealth application) [10]. Passive sensing refers to the data collected without active human interaction with the technology (e.g., Wearing Fitbit which automatically collects activity and sleep data) [10].

2.1.1 kHealth application

The kHealth application is built using the widely used Android platform. The application is designed in consultation with the clinician, tested with patients, and iteratively refined before reaching the current version used in the study [11]. The application asks questions similar to the ACT questionnaire (**Table 1**). The application captures symptoms, medication intake, and activity limitation because of asthma symptoms and nighttime awakenings using a questionnaire that the child is expected to answer twice a day. The application is personalized for every child,

kHealth application questions	Multiple-choice options
Are you currently experiencing any of the asthma-related symptoms below?	Cough, wheeze, chest tightness, hard and fast breathing, nose opens wide, cannot talk in full sentences, others
How many times did you take albuterol inhaler today because of asthma symptoms?	1, 2, 3, 4, 5, 6+
Have you had a wheeze, chest tightness, or asthma-related cough today?	Yes, No
How much did asthma or asthma symptoms limit your activity today?	None, a little, most of the day, at least half of the day
Did you take albuterol last night because of a cough or wheeze?	Yes, No
Did you wake up with a cough or wheeze last night?	Yes, No
Rescue medication question. For example, did you take albuterol today?	Yes, No
Controller medication question. For example, did you take Dulera today?	Yes, No

Table 1.
kHealth application questionnaire.

such as the medication (rescue and controller) information for every child is taken from the Electronic Medical Records (EMRs), and the medication intake questions are asked for the prescribed medications only. **Table 1** below shows the kHealth application questionnaire.

2.1.2 Fitbit

Fitbit is a wearable sensor which collects activity signals such daily step count, distance walked, floor climbed, sedentary minutes, lightly active minutes, fairly active minutes, very active minutes, and calories burned during the activities. The sleep signals includes minutes asleep at night, minutes awake, number of time the child woke up at night (number of awakenings), time spend in bed, minutes of REM (Rapid Eye Movement) sleep, minutes of light sleep, and minutes of deep sleep. The child is required to wear the Fitbit provided as part of the kHealth kit during the day and night.

2.1.3 Foobot

Foobot, is an indoor air quality sensor [12]. It is setup in the child's room or in the place in the house where the child spends majority of his/her time indoor. It connects to the home wifi, and records signal every 5-15 mins. The foobot records indoor temperature, humidity, carbon dioxide, volatile organic compound (VOC), and particulate matter 2.5 (PM2.5). The sensor turns red from green (healthy air quality) as an indicator of bad or unhealthy indoor air quality.

2.1.4 Microlife peak flow meter

Microlife Peak Flow Meter is used to record the child's lung function measures such as forced exhaled volume in 1 sec (FEV1) and peak expiratory flow (PEF). The peak flow meter has in-built memory to save upto 240 readings. Microlife has a free software available to the user to download their readings from the meter. The reading is taken by standing/sitting up straight, and blowing hard in the meter thrice. The device saves the highest of the three readings. As a backup, the child is also asked to input the reading in the kHealth application.

2.2 kHealth cloud

The data collected from the kHealth kit are synced in real time with Firebase, a Google cloud storage. Firebase provides active data listening for the client-side, which offers data persistence over a network failure and resyncs to the cloud when the network is restored. The kHealth application uses SQLite as the primary data storage and Firebase as the secondary data storage. Data from Firebase are available to Kno.e.sis researchers and clinicians for real-time analysis. Firebase provides a set of real-time database rules and user authentication that allow data access control on a per-user basis. It is built on the Google Cloud Platform, sharing the same level of data security [13].

2.3 kHealth Dashboard

kHealth Dashboard (**Figure 2**, Multimedia Appendix C) is a cloud-based platform that integrates and visualizes multi-modal PGHD data from the kHealth kit. kHealth Dashboard visually explores the correlations between the child's readings about their asthma symptoms, lung function, medication usage, and

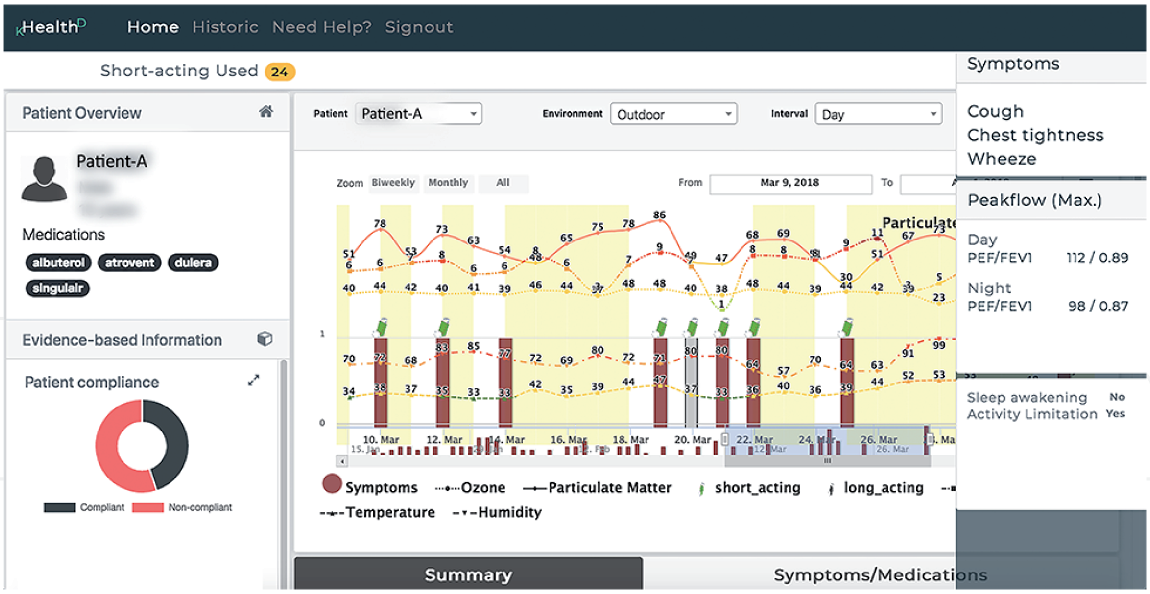

Figure 2.
kHealth dashboard.

environmental data [14] In the **Figure 2**, the patient in consideration is prescribed Albuterol, Atrovent, Singulair and Dulera by the clinician, had 24 intakes of rescue medication (short-acting) during the course of the study, had symptoms of cough, chest tightness and wheeze, had activity limitations, and had maximum PEF/FEV1 values of 112/0.89 and 98/0.87 in the day and night respectively during the course of the study. The patient took rescue medications on 10th March when the outdoor environment condition was: ozone 44 (good), pollen 6 (medium), and particulate matter 78 (moderate). The next section describes the study procedure such as study design, study recruitment, etc.

3. Methods

The section describes the kHealth study design and study recruitment process.

3.1 Study design

kHealth is an observational longitudinal study involving collaboration among researchers from the Artificial Intelligence Institute at the University of South Carolina, Kno.e.sis—an Ohio Center of Excellence for BioHealth Innovations at Wright State University, and Dayton Children's Hospital (DCH), the latter consisting of a clinician and a nurse coordinator. The study was approved by the DCH institutional review board (IRB). The study uses off the shelf sensors and widely used technologies. The study comprises of 30 kits which allows parallel participation of up to 30 children at a time. The kHealth framework does not save any patient identified information such as name, date of birth, etc. The kHealth participant is given a kHealth ID such as KH001, KH002 to anonymize the data. The information to anonymize and de-anonymize is stored only at the DCH and is not shared with the researchers [15]. The information never leave the DCH servers.

3.2 Study recruitment

The study participants were recruited from Dayton Children's Hospital (DCH) under the guidance of a pediatric pulmonologist. The participants were children within the age group of 5-17 years diagnosed with asthma. The study coordinator approached the parents of the children seeking asthma treatment at the DCH. The parent, along with the child, consent to participate in the study. The parent provides consent, and the child assent by signing a consent form to participate in the study and giving permission to obtain the medical details from the EMRs. The participant recruitment was random, with asthma diagnoses as the only prerequisite. The type of asthma, such as persistent, non persistent, exercise induced, and non exercise-induced asthma was not taken into consideration for the study recruitment. The participant were given an option to participate in either one month or three month study period. The consented participant were given a brief demonstration of all the kHealth components. The participants also had access to a user guide, tutorial video in the application to make it more accessible. The contact information of the study coordinator, and the kHealth team were saved in the user guide to reach out in case of any technical difficulties. The technical difficulties were resolved by the kHealth team while keeping the participant identity anonymized.

The PGHD collected from the pediatric patients using the kHealth framework is used to generate personalized insights into one's healthcare protocol. The next section describes the personalization in chronic diseases like asthma and how does the PGHD can be used for better disease management, and self appraisal.

4. Personalization

Asthma is a personalized disease. An asthma patient differs from another patient with respect to their asthma symptoms, possible triggers, medication adherence, and asthma control levels. The below observation comes from preliminary analysis and anecdotal evidence from the data. For example, Patients A and B, both in the same asthma control, and severity level category and have fall pollen allergies. However, Patient A does not show symptoms until the pollen crosses the threshold 6 (pollen: medium [16]) whereas Patient B starts showing symptoms as soon as the pollen levels goes beyond 3 (pollen: low-medium [16]). Personalization in the kHealth framework is able to capture these granularities (symptoms, medication intake, difficulty sleeping and reduced activity due to the outdoor environmental conditions) at a given point in time. We also observe patients in one asthma control level category are more proactive towards their health and medication adherence resulting into fewer We define personalized scores such as Symptom Score, Medication (Rescue, Controller) compliance Scores, Activity Score, etc. to get a real time insight into the patient's health condition unlike the irregular ACT administered during the clinic visits. The personalized scores helps in real time categorization of the patient into their asthma control levels.

4.1 Symptom score

Symptom score for a child is defined by the number of symptoms experienced by the child during the course of deployment period. The symptom severity (Chest Tightness being more severe than wheeze and cough, etc) is ignored for the symptom score estimation.

$$SS = \frac{Total\,symptoms\;experienced\;by\;the\,child}{Study\,Period} \tag{1}$$

4.2 Activity score

Activity Score of a child is the number of days the child had restricted activity during the study duration. The kHealth application asks a multiple-choice question: How much did asthma symptoms limit your activity today? with four options: none, a little, half of the day, and most of the day. The options are weighted on a scale of 0-3, respectively.

$$AcS = \frac{Number\ of\ days\ of\ activity\ restriction\left(weighted\ option\right)}{Study\ Period} \tag{2}$$

4.3 Awakening score

The Awakening Score (AwS) is the measure of number of nights the child woke up because of asthma symptoms during the study period. The kHealth application asks a multiple-choice question: Did you wake up with wheeze, cough, or any asthma-related symptoms?

$$AwS = \frac{Number\ of\ days\ child\ woke\ up\ due\ to\ asthma}{Study\ Period} \tag{3}$$

4.4 Rescue compliance score

The kHealth application collects data on the intake of the rescue medication (short-acting bronchodilators) by asking questions such as Did you take albuterol today? Rescue Compliance Score (RCS) is defined as the number of times the child took the rescue medication during the study period. The rescue medication is taken to mitigate or prevent the symptoms.

$$RCS = \frac{Total\ Resuce\ medication\ intake\ by\ the\ child}{Study\ Period} \tag{4}$$

4.5 Controller compliance score

The kHealth application asks questions (eg, Did you take Dulera today?) about the intake of the controller medication (long-term control medication). An asthmatic patient is prescribed a controller medication, which is supposed to take at least once a day depending on the asthma control levels. The Controller Compliance Score (CCS) is defined as the fraction of the number of days the child took the controller medication during the study period.

$$CCS = \frac{Total\ Controller\ medication\ intake\ by\ the\ child}{Study\ Period} \tag{5}$$

The threshold for Controller Compliance Score is defined as Highly Compliant for score greater than and equal to 0.70, Well Compliant for score greater than and equal to 0.30 and less than 0.70, and Poorly Compliant for score less than 0.30.

Let us take an example scenario to better understand the personalized scores and generate actionable insights into their asthma management. Alice is ten yrs. old and clinically (using the ACT score) categorized into Not Well Controlled asthma control level. She and her parents agreed to participate in the one month kHealth study period. According to the data collected using the kHealth framework, Alice had ten incidents of cough, ten incidents of wheeze, five chest tightness, no incidents of hard and fast breathing, and no incidents of cannot talk in full sentences. She woke up during the night due to asthma symptoms on ten nights and had asthma symptom related activity limitation for five days. She had her controller medication for twenty days and had five rescue medication during her study period. Alice had a Symptom Score of 0.83 (=25/30; 10 cough +10 wheeze +5 chest tightness = 25 symptoms), Awakening Score of 0.33 (=10/33), Activity Score of 0.16 (=5/30), Rescue Compliance Score of 0.16 (=5/30), and Controller Compliance Score of 0.66 (=20/30). Alice is Well Compliant for her controller medications. The next section utilizes the above personalized scores for real time categorization of the child into their asthma control levels.

5. Digital phenotype score: Asthma categorization

The child (or the parent) is given an Asthma Control Test (ACT) at the regular checkup appointment. The ACT asks questions about the asthma symptoms, school days missed, night time awakenings, inhaler intakes etc. in the past four weeks. The child is categorized into one of the three asthma control levels of Well Controlled, Not Well Controlled, and Very Poorly Controlled asthma based on the scores obtained in the test. The ACT is used to analyze the asthma management of the child in between the visits, and also as a measure of Does the therapy helps the child's asthma management?, or Is there a need for intervention and change in therapy/treatment protocol? The ACT is administered during the infrequent clinic visit and asks questions about past four weeks, it is highly unlikely the child or the parent will remember all the relevant asthma episodes which leads to incorrect asthma control level classification [17, 18].

Digital Phenotype Score (DPS) defined using the kHealth data and National Heart, Lung, and Blood Institute (NHLBI) guidelines to categorize the child into their asthma control level overcomes the limitations of the ACT scores [19–22]. The child/parent and the clinician do not have to wait for the clinic visits to get an analysis of the current asthma management of the child. The clinician can use the DPS for early and timely intervention to recognize any barriers to the current therapy. The DPS is a quantified measure of the symptom score, activity score, awakening score, and rescue compliance score. The DPS of greater than and equal to one is classified as Very Poorly Controlled asthma, greater than equal to 0.28 and less than one is classified as Not Well Controlled asthma, and less than 0.28 is classified as Well Controlled asthma. In the case of Alice, the DPS is 1.48 (=0.83 + 0.16 + 0.33 + 0.16). According to the thresholds defined her asthma is classified as Very Poorly Controlled.

6. Causal intervention and actionable insights

The Personalized scores along with Digital Phenotype Score related categorization can be used to generate actionable insights into a patient's healthcare protocol [21, 23]. These insights in future can also be used by the clinician to design a perfect intervention strategies/policies (**Figure 3**) for better health outcome and improving the quality of life of the patient [24, 25]. Let us take an example scenario, A child categorized as having Very Poorly Controlled asthma using the DPS, suffering with

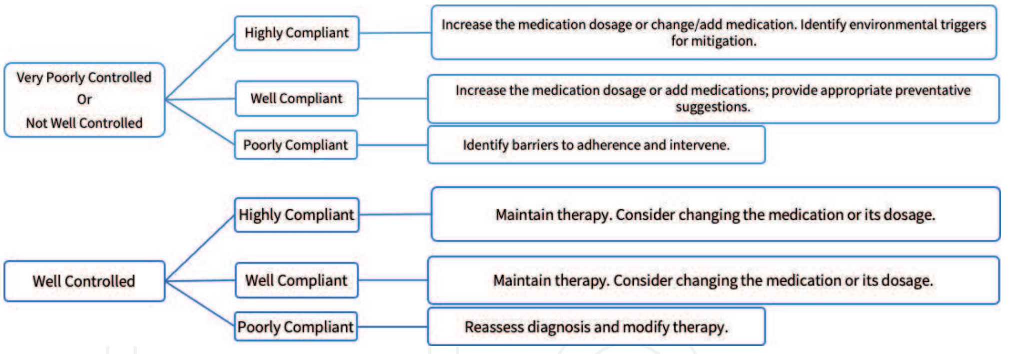

Figure 3.
Root cause analysis techniques can be used to access the path specific policy update for intervention strategies.

a high symptom score and Highly Compliant for the controller medication. The CCS and the DPS sheds light on an important aspect of the child's asthma management that although the child is highly compliant towards the controller medication but still suffers from high symptom score. This is an opportunity for the clinician to intervene with either increasing the medication dosage, or change or add a medication, and identify the environment triggers for mitigation. On the other hand a child with Very Poorly Controlled asthma and poorly compliant with the controller medication is in the worst health condition and requires immediate attention from the clinician and support from the parent/caregiver. The intervention strategy would be to identify the barriers to medication adherence and suggest mitigation/alternative efforts. A child with well controlled asthma and highly compliant with the medication is a use case when the child/parent are proactive towards the asthma management. In this scenario the clinician can choose to intervene with either maintaining the therapy or considering changing the medication or lowering the dosage.

In the case of Alice, she is well compliant with her controller medication and as per the DPS has very poorly controlled asthma. The clinician can intervene in her asthma management protocol with either increasing the medication dosage or adding a new medication since her current medications are unable to control her asthma, and also provide appropriate preventive suggestions to reduce future asthma exacerbation.

7. Conclusions

The digital healthcare technologies such as IoTs, self-reporting applications, wearables can be used to improve the quality of life of the pediatric asthma patients. The kHealth framework has moved the current healthcare approach from clinician-centric to patient-centric. The child/parent feels empowered to take control of their health management. The clinician can include the framework like kHealth in their current protocol which is especially useful during the pandemic when the care has shifted from in-person clinic visit to tele-medicine appointment. The asthma patients are prescribed Longacting combination inhalers, Long-acting inhaled steroids or Oral Steroids depending on how controlled is a patient's asthma condition. The long term use of steroids leads to a growth suppression, adrenal gland suppression, osteoporosis, increase a risk of high blood pressure, heart attack, increase in appetite leading to weight gain and eventually increase in body mass index [26]. The early and timely intervention strategies discussed can be used to avoid overuse of the steroid medications, and can eliminate the vicious cycle of asthma affecting obesity or obesity affects asthma.

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Conflict of interest

The authors declare no conflict of interest.

Abbreviations

PGHD	Patient Generated Health Data
IoTs	Internet of Things
DCH	Dayton Children's Hospital
ACT	Asthma Control Test
DPS	Digital Phenotype Score
IRB	Institutional Revenue Board
EMR	Electronic Medical Record
NHLBI	National Heart, Lung, and Blood Institute
CT	Chest Tightness
HFB	Hard and Fast Breathing
CTFS	Cannot talk in full sentences
PM2.5	Particulate Matter 2.5
VOC	Volatile Organic Compounds
SS	Symptom Score
AcS	Activity Score
AwS	Awakening Score
RCS	Rescue Compliance Score
CCS	Controller Compliance Score

Multimedia Appendix A

Augmented health with personalized data and AI, TEDx2020, The University of South Carolina, Oct 21, 2020, Accessible at: https://bit.ly/3ahJEhy

Multimedia Appendix B

The kHealth project webpage: https://bit.ly/3aX4Ng0

Multimedia Appendix C

kHealth Dashboard video: https://bit.ly/2ZfeSj8

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