Monitoring and Improving Compliance and Asthma Control: Mapping Inhaler Use for Feedback to Patients, Physicians and Payers

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KEYWORDS: electronic monitoring, asthma management, inhaler sensor, wireless health, mobile health, device design, compliance

SUMMARY

Increasing emphasis on the assessment of asthma control and risk has renewed interest in the ability of technology to capture patient-reported outcomes and real-time histories of symptoms and medication use. Ambulatory monitoring of physiological parameters and medication use, together with online interfaces and applications which allow patients to complete composite questionnaires of asthma control and report quality of life indicators, are expanding opportunities for individual and population management of asthma. A robust, accurate and timely picture of asthma control can be developed and used to improve asthma management and outcomes.

This article describes the technical development and operation of a medication monitoring system, Asthmapolis, and accompanying smartphone and web interfaces to help patients and physicians manage asthma. The potential utility of this technology to influence day-to-day medication taking and disease management is reviewed including results from a published pilot study designed to evaluate whether asthma control can be improved. Disease management tools provided for physicians and public health to help address the burden and management of asthma are also described.

INTRODUCTION

In the United States, asthma is responsible for an estimated 1.75 million emergency department visits and 456,000 hospitalizations each year [1, 2], with overall costs of $55 billion [3]. Many asthma exacerbations could be prevented with appropriate treatment, but the majority of patients do not have their disease under control [4]. Clinical practice guidelines recommend physicians
monitor whether treatment is controlling symptoms and improving quality of life [5], but physicians lack tools to objectively and reliably assess the frequency and severity of symptoms, and generally overestimate disease control [5].

Patients and caregivers are expected to monitor their asthma using daily diaries, in which they record symptoms, medication use, and measurements of lung function, and also to follow the guidance of asthma action plans when adjusting medication or seeking medical care [5]. Unfortunately, patients have low expectations for their own disease control and may be unaware that more can be done to prevent attacks and day-to-day symptoms [4]. Many patients do not feel confident in their understanding of their health status and are uncertain whether their asthma is under control and what their triggers are. Others fail to voice concerns or report troublesome symptoms. In short, patients need tools that help them recognize when they need help, and better methods to convey this information to their doctors.

Asthma control questionnaires have become popular tools to help monitor patients and determine their level of control [6]. Questionnaires require patients to recall and report the frequency of symptoms, activity level and restriction, and inhaler usage, over a specified period of time. Evidence that the frequency of symptoms and inhaled bronchodilator use are important indicators of disease management, and valuable early warnings of worsening disease, form the basis of these assessments [7]. However, there are a number of limitations because questionnaires do not offer real-time indications of disease management and control and they also require the patient to expend additional effort managing their disease. Questionnaires are also subject to recall bias and different interpretations of symptoms and ideas about control.

Increased adoption and ownership of smartphones has enabled the development of connected medical devices and specialized software applications focused on health monitoring and disease management. Asthmapolis, from Madison, WI based Reciprocal Labs Corporation, combines inhaler sensors and smartphone applications to create a data-driven and patient-centered approach to asthma management, focused on the passive collection of information about the day-to-day burden and management of asthma.

**THE ASTHMAPOLIS SENSOR**

Figure 1 illustrates the electronic sensor designed to passively and objectively track the use of most metered dose inhalers (MDIs). The sensor mounts to the end of the MDI canister by means of a small adapter cap. This cap adapts different canister diameters to the sensor and allows for simple and secure attachment and detachment, permitting the sensor to be switched from canister to canister upon refill. Some MDIs with atypical housings or dose counters integrated on the end of the canister do not permit mounting of the Asthmapolis sensor.

An actuation detection assembly in the Asthmapolis sensor automatically determines when the inhaler has been fired. This mechanism is tuned and bench tested to match the forces required to actuate the range of adaptable MDIs and designed to optimize accuracy and reliability. Following American Thoracic
Society / European Respiratory Society guidance [7], inhalations occurring within a two minute time period are displayed together as a single medication use event by the system, although the individual inhalations are retained as discrete records in the database. The current version of the sensor is not able to determine whether the medication has been inhaled by the patient and can only sense the most basic aspects of technique, such as the elapsed time between inhalations. In addition, the patient must manually record priming of the inhaler using the smartphone or web applications.

The sensor uses a secure, low-power, wireless radio protocol to transmit collected data to a cooperating mobile phone (or base station), which then determines the location of the event and communicates event information to the system servers. If an individual does not own a smartphone, a fully integrated base station designed to securely capture information from the Asthmapolis sensor can also be used. The base station automatically downloads new events from the sensor whenever it is in range (30-100m) and securely uploads this information to the servers over the Qualcomm wireless network. This setup requires minimal participation by the patient and eliminates the need for internet access or technology ownership of any kind.

If a transmitting device is unavailable when an event occurs, the sensor stores the details in local non-volatile memory (which can hold approximately 3,900 events) and transmits the information at a later time. The sensor contains a real-time clock and operating system which timestamps the event whenever it occurs. Each sensor is identified by a unique serial number that allows the system to determine with which patient and medication the sensor is associated. Patients who use multiple medications have separate sensors for each product.

A simple interface provides the user with basic information relating to remaining battery life, pairing status and airplane mode. A secondary button controls various functions of the sensor, such as initiating pairing and entering and exiting airplane mode. The device has an approximately 40 day battery life under normal use and a battery that is recharged through a standard USB connector.

The sensor also periodically sends “heartbeat” messages describing its functional status, allowing the system to create a thorough operational record and proactively alert an individual if any issues are detected or if the sensor needs to be recharged. This approach permits the system to know both when an event occurred and when it did not; no longer is the absence of an event marked by significant uncertainty as it is with tools that rely on manual self-report.

**MOBILE AND ONLINE INTERFACES:**

**DISEASE MANAGEMENT TOOLS**

A comprehensive platform of mobile applications and websites for both patients and health care providers can be used in conjunction with the Asthmapolis sensor. Smartphone applications, designed for Android and iOS devices, serve to transmit the data from the sensor and also provide an interface to the collected data and disease management tools. For patients, the goal of these applications, which are available in English and Spanish, is to encourage and support optimal self-management by providing an informative and data-driven assessment of their level of asthma control and adherence, an overview of the burden of asthma in their community, and personalized educational guidance and support based on their observed morbidity and management (Figure 2). For health care providers the tools are designed to support proactive and informed management of their patients.
One aim of the feedback is to foster a greater awareness and understanding of an individual’s own level of control, impairment and risk. Simple summaries and periodic email reports and text messaging offer an easy-to-understand assessment of asthma control, derived from National Asthma Education and Prevention Program (NAEPP) guidelines, that encourages continued attention and efforts, and confirms and reinforces behaviors when the person gains control. The applications also aim to increase awareness and understanding of asthma triggers, in part by providing individuals with the ability to review historical trends and explore the circumstances behind when, and where, they experience symptoms. Maps of rescue inhaler use and reports of trends and patterns in these locations (Figure 3) highlight the areas and environments that frequently lead to exacerbations, often resulting in the discovery of particular exposures, whether at home, school, work or in the community, responsible for the development of symptoms.

Patients and family members can use the applications to monitor and encourage adherence to daily controller therapy and support appropriate preventive behaviors, such as the mitigation and avoidance of environmental triggers. Trends and charts illustrate the difficult-to-discern relationship between controller medication adherence and symptom-free days, helping to dispel a common misperception that controller medication may be unnecessary. Moreover, medication reminders via email or text messaging can be sent when the user fails to take a prescribed dose of medication.
Figure 3. Asthmapolis web interface provides an assessment of the level of control and guidance and education to support self-management (fictional patient shown).

By arming patients and families with an accurate record of their management and ongoing impact of asthma, the system is also designed to improve communication during clinical consultations about level of control, health and medication-taking behaviors, and the environments and exposures that lead to the development of symptoms. Individuals may authorize their health care providers to view their collected data and summary reports, so that clinical decisions can be informed by the collected data.
Figure 4. Health care provider dashboard summarizes key metrics, such as level of control and adherence, facilitating identification of patients with worsening symptoms (fictional patients shown).

A variety of interfaces are also available to healthcare providers to remotely monitor the level of control and adherence of their patients. Physicians and other authorized healthcare providers receive access to online summaries of management and control, including notifications of excessive rescue inhaler use or insufficient adherence to controller medications (Figure 4). The system routinely evaluates medication use against physician-established thresholds and national guidelines, allowing patients in need of additional review to be quickly identified. Fully customizable alerts and notifications about individuals and populations can be defined and delivered to physicians, nurses and care managers. Electronic medical record integration is under development.

Asthmapolis has also been designed to enable a bottom-up and data-driven approach to public health surveillance. Asthma is unique in that an important medication is often used at the time and place of exposure that causes symptoms. But identifying locations that may pose a particular risk has been a challenge for public health experts, who have been limited to retrospectively analyzing the small proportion of attacks that led to emergency room visits and hospitalizations.
These events typically indicate where the patient lives but do not provide information about where the symptoms began. Yet, evidence suggests that there are differences in the prevalence of asthma and respiratory symptoms among groups living in small geographic areas and significant variation across time, unexplained by known personal and environmental risk factors [8]. In addition, previous investigations have shown that tracking where and when symptoms begin could help to identify clusters of asthma exacerbations, evaluate public health interventions to reduce asthma morbidity, and offer clues about the causes of attacks, even revealing previously unknown risk factors [9, 10].

REGULATORY APPROVAL

The Asthmapolis System is considered an electronic MDI Accessory according to the Code of Federal Regulations (21 CFR 868.5630), and requires a 510(k) clearance reviewed by the Center for Devices and Radiological Health (CDRH) at Food and Drug Administration (FDA). Non-clinical performance testing of sensor actuation and data capture established appropriate functionality. In addition, third-party testing for compliance to IEC 60601 series standards [11] for general electrical safety and electromagnetic compatibility and ISO 10993 series standards [12] for biocompatibility were completed by accredited laboratories prior to regulatory submission. Accredited laboratories validated cleaning instructions, and testing in appropriate environments for wireless interference was completed to support safety and efficacy demands. Software and Firmware for the Asthmapolis System were designed and developed according to a robust software development process aligned, verified and validated with CDRH guidance documents [13-16]. The Asthmapolis System successfully completed performance (bench) testing according to applicable standards and testing, including FCC licensing and wireless/Bluetooth technology in accordance with both design specifications and regulatory guidance [17]. In July 2012, the sensor, smartphone applications and web interfaces received 510(k) clearance from the FDA.

CLINICAL EXPERIENCE WITH ASTHMAPOLIS

The Asthmapolis system has been used for both intervention and outcome measures in a variety of studies ranging from examinations of technology as a tool in self-management, clinical care and treatment, to population health and epidemiological studies designed to investigate the respiratory health effects of a variety of environmental exposures. These efforts have spanned clinic and community populations and involved individuals across age groups and socioeconomic strata. Below we highlight and summarize results from an initial study that assessed the utility of sensor-derived feedback as an intervention to guide self-management and designed to improve asthma control [18].

In a pilot study, a total of 30 patients were enrolled from clinics and community locations in the Madison, WI area and provided with an earlier version of the sensor for monitoring use of their prescribed short-acting bronchodilator [18]. The study was designed to evaluate whether capturing information about the time, frequency and use of rescue medication, and providing feedback on asthma management, would result in measurable improvements in asthma control, as assessed by composite questionnaires of control and self-reported frequency of symptoms. Participants completed entry questionnaires including the Asthma Control Test (ACT) [19] at entry and monthly thereafter. They were monitored for one month without receiving any feedback from the system. At the end of the first month, participants began to receive weekly email reports from the system providing them with an assessment of their level of control along with personalized guidance and education about how they might improve their management (drawn from NAEPP guidelines).
There was no statistically significant difference between the mean ACT scores at entry and at the end of the first month, [18] when there was no intervention (ACT Score at Entry = 17.6 ± 3.35; ACT Score after first month = 18.4 ± 3.60; p=0.66). Each month of participation following the availability of inhaler usage data through the online interface and weekly email reports resulted in a further improvement in ACT score (ACT score at second month = 20.1 ± 3.66; ACT Score after third month = 21.2 ± 3.36) [18]. At the conclusion of the study period, 75% of participants had controlled asthma (an ACT score > 19) compared with 38% at entry [18]. Receipt of weekly e-mail reports and online access to asthma event history was also associated with a significant decrease in number of days and nights with symptoms. In exit surveys and interviews, participants reported that remote monitoring and feedback had been a practical aid in supporting self-management.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No Intervention</th>
<th>Intervention</th>
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<tbody>
<tr>
<td></td>
<td>Entry Mean</td>
<td>1st Month</td>
</tr>
<tr>
<td>Days with Symptoms</td>
<td>4.84 ± 4.13</td>
<td>4.95 ± 4.43</td>
</tr>
<tr>
<td>Nights with Symptoms</td>
<td>2.03 ± 3.35</td>
<td>1.85 ± 2.10</td>
</tr>
<tr>
<td>ACT Score</td>
<td>17.6 ± 3.35</td>
<td>18.4 ± 3.60</td>
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In subsequent, collaborative projects with the US Centers for Disease Control and Prevention and other organizations, Asthmapolis has provided a practical means to collect timely and geographically specific information about asthma morbidity and management. By offering views of aggregated and de-identified patterns of inhaler use, epidemiologists and public health groups can strengthen their ongoing asthma surveillance activities, improve scientific understanding of disease triggers and progression in the community, and target and evaluate interventions. Currently, municipalities, including the city of Louisville, are using Asthmapolis to assess the real-time burden of disease in their communities, and exploring how comprehensive health information networks can bridge clinical, environmental and public health data systems. Public health dashboards provide an integrated view of the burden of asthma, including relevant environment and health care utilization information, as well as tools to explore views of environmental exposures and risks mapped to local jurisdictions to help focus and evaluate public health efforts (Figure 5).
DISCUSSION AND CONCLUSIONS

Evidence supports integrated approaches to asthma management, and the most recent clinical guidelines emphasize patient education, self-management, and control and avoidance of aggravating environmental factors in the daily management of asthma [5]. Unfortunately, asthma patients continue to lack the tools and information needed to effectively manage their disease. Despite traditional reliance on asthma action plans as an important tool for conveying and reinforcing information about early warning signs, medications and trigger avoidance, in some populations, less than a third of persons with asthma report receiving a written asthma action plan from their provider [1, 2]. In higher-risk populations, as few as 10 percent report having an asthma action plan, fewer than 20 percent know their personal asthma triggers, and only 10 percent report knowing what to do to avoid or reduce their exposure to triggers [20].
The combination of inhaler sensors with mobile and web applications in an integrated and evidence-based system offers a promising tool to support patients in everyday self-management, to improve their expectations about achieving asthma control, and to provide them and their physicians with a clear, timely picture of their asthma and health status. Additional research in controlled studies over longer durations is needed to reveal the utility and cost-effectiveness of the system in the management of asthma and characterize the impact on clinical decision-making and care and treatment. A randomized trial involving approximately 440 individuals in two arms is enrolling participants at two hospital systems in California. While this study will measure symptoms, medication use and asthma control, the primary analytical endpoints are changes in asthma-related health care utilization assessed using claims data from participating health plans. The results of this effort may enable the development of technology that supports and augments individual and clinical management, maximizes collective public health, and advances our understanding of the origins of the disease.

ACKNOWLEDGEMENT

MAB is a Robert Wood Johnson Foundation Health & Society Scholar at the University of California (UC) San Francisco and UC Berkeley.
REFERENCES


18. Van Sickle, D, Magzamen, S, Truelove, S, Morrison, T: Remote monitoring of inhaled bronchodilator use and weekly feedback about asthma management: An open-group short-term pilot study of the impact on asthma control, PLOS ONE 2013, 8(2).
