Pulmonary Monitoring Using Smartphones

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Abstract Pulmonary assessment is widely employed by medical professionals and has become an important marker of health. It is used for screening, diagnostics, and management of chronic pulmonary diseases like asthma, chronic bronchitis, and chronic obstructive pulmonary disease. However, pulmonary assessment has mostly been restricted to self-report and routine monitoring at a physicians office. Smartphones have disrupted this practice, enabling daily collection of self-reported symptoms and airway testing from a patient's home. This chapter outlines how various markers of pulmonary health are collected from mobile phones. In particular, discussing the importance of disease specific monitoring and highlighting research studies that employ mobile phones for pulmonary data collection.

1 Introduction to Pulmonary Sensing

Respiratory diseases are among the leading causes of death worldwide. According to a 2008 WHO survey, pulmonary infections (such as pneumonia), lung cancer, and chronic obstructive pulmonary disease (COPD) account for more than one-sixth of fatalities globally [39]. This fatality rate can be mitigated through two mecha-

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nisms: (1) finding pulmonary diseases early through diagnosing and screening, and (2) managing these lung diseases to keep them from exacerbating.

In particular, early stage diagnosis is critical for preventing complications but has proven to be difficult. Chronic obstructive pulmonary disease, for example, is vastly under-diagnosed, with an estimated 50% of sufferers unaware they have the condition [53]. Factors like high cost, access to clinics and doctors, and limited awareness often hinder effective early diagnosis. However, even when lung diseases are found early, diagnosis is not the only challenge. Many diseases are chronic, requiring patients to manage triggers and symptoms over a lifetime. While effective management has shown improved outcomes, reduced healthcare costs, and more rapid recovery, it is often impeded by factors like access to medication, limited awareness, and non-compliance to treatment regimens.

The adoption of mobile phones, especially smartphones, promises to disrupt current practices of management and diagnosis for pulmonary diseases. In developed countries, access to mobile phones is all-but-guaranteed and developing countries are adopting these phones at breathtaking rates [20]. Hence, incorporating phones into the diagnosis and daily management of chronic pulmonary ailments promises to save lives and increase quality-of-life.

Moreover, phones have advantages over dedicated medical devices such as low-cost and ubiquity, as well as computing and communication capabilities. Mobile phones can also help to facilitate communication between patients and care providers. Yun *et al.*, for example, demonstrated how using the phone's messaging capabilities can increase awareness of asthma progression and symptom triggers [74]. Furthermore, mobile phones can also help automate symptom logging where self-report is notoriously unreliable. In this chapter, we discuss many such systems and how each promises to improve diagnosis and management of pulmonary diseases. We also argue that current mobile monitoring practices have not reached their full potential because a holistic system that incorporates knowledge from diverse sources has not yet come to fruition.

Section 2 discusses the physiology of chronic pulmonary diseases and how these diseases can benefit from automated mobile monitoring. Section 3 surveys the landscape of symptom diaries and discusses challenges of current systems. Section 4 provides an overview of how automated, continuous monitoring systems can improve health outcomes. Section 5 discusses how mobile phones are making mobile airway sensing more accessible. Section 6 concludes with a discussion of the technical challenges that lay ahead.

2 Pulmonary Ailments where Mobile Monitoring May be Beneficial

There is no gold standard measurement for monitoring the lungs in general. Rather, each pulmonary disease has an accepted means for measuring wellness. In mobile monitoring, most research focuses on diseases that chronically affect the air-

way. Chronic lung diseases are the third most common cause of death in the world [1, 13, 30]. In fact, COPD is the fourth leading cause of death and is rapidly becoming more deadly than infectious lung diseases, like pneumonia and influenza combined [42]. Chronic lung diseases have no cure, but instead must be diagnosed and monitored for the duration of a patient's life. Because these diagnoses are life-long, it is especially important to diagnose individuals with these diseases as early as possible, in order to mitigate the irreversible complications caused by the illness going untreated. The problem is twofold, (1) finding and diagnosing individuals with lung disorders and (2) monitoring and managing the condition properly [73].

The most common chronic lung diseases are those that affect the airways and are further classified as *obstructive* or *restrictive*. Obstructive diseases affect the flow of air from the bronchi and bronchioles through collapsed or inflamed airways. Asthma and COPD are classified as obstructive diseases. Common symptoms include shortness of breath, coughing, and wheezing. Restrictive lung diseases are characterized by reduced lung expansion. There are varied reasons for restriction but the most severe is typically from pulmonary fibrosis, which restricts lung volume through scarring of the lung tissue. Cystic fibrosis is also considered to be a restrictive disease, characterized by an increased amount of mucus in the lungs. Chronic coughing and shortness of breath are common symptoms associated with restrictive diseases.

The standard of care for diagnosis of chronic lung diseases is based upon collecting information about symptoms, meeting with a physician regularly, and seeking measures from a medical device known as a spirometer [39, 73]. This device measures the velocity and amount of air a patient can exhale from their lungs. Physicians will take repeated spirometer measures and consult with a patient several times before diagnosing a chronic condition.

As with many other chronic conditions, physicians have begun to explore mobile health technology as a means of collecting information more efficiently. This includes the use of electronic asthma symptom journals [8, 14], telemedicine [19, 47, 57], and mobile spirometry [64]. These mobile sensing methods have been employed successfully for screening, diagnosis, and continued management tools. Even so, mobile technologies have not yet disrupted current screening practices. Mobile technologies that focus on low-cost screening could radically increase diagnostic rates—which are currently estimated to be below 50% [53]. This is especially true for mobile spirometry because it has become standard for screening obstructive ailments.

Beyond screening, mobile technologies can be effective for long term monitoring, especially in evaluating treatment. Treatment regimens for chronic pulmonary ailments are highly personalized and dynamic over a patient's lifetime [36, 43]. Careful monitoring of patient perceptions, symptom frequency, and lung function can considerably increase quality-of-life. However, current practices are too burdensome to make such data collection practical. Mobile management tools can help reduce this barrier, paving the way to efficient, data-centered pulmonary management.

3 Monitoring Through Daily Symptom Diaries

Daily symptom diaries have been used for patients suffering from a wide variety of conditions. Traditionally, symptom diaries are paper journals given to a patient during a clinic visit. The patient is asked to enter data in the diary on a daily basis with the intent of reviewing during a follow-up visit. These diaries consist of questions pertaining to a specific disease or condition—the answers to which may provide useful information about the patient's treatment, symptoms, and quality-of-life. As the mobile health industry has progressed, daily symptom diaries have evolved to take advantage of readily available technology such as text messaging [51] and smartphone apps [9]. They have been used in studies of patients with upper respiratory conditions, such as COPD [29] and asthma [25], with heart conditions [48], as well as psoriasis [68], cancer [2, 22, 67], and cystic fibrosis [16].

3.1 Applications

The use of daily symptom diaries is associated with many significant positive outcomes for both adults and children [60]. For example, data from symptom diaries can be utilized to determine the effectiveness of treatment options [16] and for effective symptom management [2]. Furthermore, compliance with symptom diaries is associated with increased survival rates and quality-of-life [49]. Diaries help to fill in the gaps that traditional testing misses. Data from spirometry measures, for example, are not able to capture symptom severity or variability [34]. Furthermore, diaries help to contextualize data gathered via traditional medical devices, providing patient's perception of their illness.

Asthma and COPD have been the center of several studies involving the efficacy of daily symptom diaries. One such study conducted by Leidy *et al.* evaluated the reliability of a daily symptom diary for use with COPD patients [34]. During the study, many participants with "stable" COPD found significant symptom variability, indicating further treatment management was necessary. Moreover, results of the study indicate that "numerical scoring" from the tested diary was appropriate for quantitative measures across patients (an important finding for using symptom diaries in clinical trials).

3.2 Existing Research

The validity and reliability of symptom diaries and patient compliance have been the focus of many studies. Several studies focused on evaluating symptom diaries in the context of alternative methods such as Retrospective Questionnaires. Symptom diaries have also been custom-tailored for use with monitoring and managing certain conditions (*i.e.,* Asthma Symptom Diaries). As the mobile health industry has

evolved, the development of electronic symptom diaries has spurred trials focused on evaluating their validity and reliability. Moreover, studies have investigated how utilizing native smartphone applications [9] and Short Messaging Service (SMS) [51, 75] can augment traditional diaries.

3.2.1 Symptom Diaries and Retrospective Questionnaires

Traditional symptom diaries require patients to answer questions using pen and paper. These face a number of issues affecting patient compliance and data reliability such as (1) forgetting to enter or intentionally disregarding data, (2) omitting questions, (3) fabricating responses, (4) writing illegibly, and (5) losing the diary altogether [25]. Furthermore, additional issues arise when considering the data entry process in which a patient's data is recorded, such as the potential for transcription errors, difficulty with statistical analysis of the data, and the cost associated with the data entry itself [25].

To evaluate reliability of symptom diaries, Juniper *et al.* [25] and Okupa *et al.* [46] conducted studies comparing symptom diaries against Retrospective Questionnaires in the context of asthma management. Retrospective Questionnaires take place during a clinic visit and patients are asked to recall symptoms for a given period of time. Given the nature of recall-based questions and the length of the recall period (often 1-4 weeks) reliability varies [46]. Although the burdensome nature of symptom diaries introduces several inherent issues, the two studies determined that symptom diaries and retrospective questionnaires are both valid methods of monitoring asthma [25, 46], but Okupa *et al.* determined that symptom diaries may yield more precise data for managing treatment [46].

3.2.2 Asthma Symptom Diaries (ASD)

While the monitoring and management of asthma can benefit from data derived from spirometry measures it is becoming more apparent that this data is not, on its own, an adequate measure of asthma's impact upon patient quality-of-life [56]. As a result, several studies have focused on developing and evaluating symptom diaries specifically for patients with asthma.

Globe *et al.* reviewed symptom diaries developed for use with asthma patients [14]. While several diaries were effective for garnering additional information about asthma sufferers, many required additional validity evaluations. Globe went on to unify the content and structure of these diaries into what is known today as the Asthma Symptom Diary (ASD). Globe also conducted studies to determine its acceptability as an end-point for asthma clinical trials. The study, which included adults and children who had an asthma diagnosis for at least one year, began with an enrollment process in which each subject completed a version of the Asthma Control Questionnaire (ACQ-7) and the Asthma Quality of Life Questionnaire (AQLQ). Both tests focus on gathering information about the impact of asthma, specifically in

terms of items such as nighttime awakening, activity limitation, emotional function, use of fast-acting inhalers, and spirometry measures [14].

The next phase of the study consisted of subjects participating in 60 minute, semi-structured concept elicitation interviews. During each private interview, subjects were asked to describe their personal experience with asthma and how their symptoms impacted them on a typical day. The results of these interviews were used to identify the key components of the disease which affect overall patient experience. With this qualitative data gathered, a panel of clinical experts in the treatment of asthma, patient-reported outcome development experts, and members of the sponsor's team revised the previously developed ASD. The updated ASD consisted of two sections, morning and evening, having 6 items and 5 items respectively. With FDA guidance, the end result of this study was a revised, 11-item ASD which addresses the four most relevant symptoms for asthma patients—shortness of breath, chest tightness, coughing, and wheezing [14].

3.2.3 Electronic Symptom Diaries

As access to electronic devices and smartphones has become more widespread, electronic symptom diaries have been developed and studied for use with a wide variety of conditions. Some of these studies have focused on the validity of electronic symptom diaries in relation to their paper counterparts while others have focused on the impact of electronic diaries upon overall compliance.

In a randomized crossover study conducted by Ireland *et al.*, the reliability of electronic symptom diaries was evaluated within a body of subjects diagnosed with asthma [24]. Participants in both groups of the trial completed the asthma symptom diary twice daily and either transitioned from a paper-and-pencil diary to an electronic diary, or vice versa. Over the course of the study, the electronic version of the diary had adequate test-retest reliability as well as measurement equivalence with the pencil-and-paper version. Furthermore, the test-retest reliability for Rescue-Free Days (RFD) for the electronic version of the diary met or exceeded reproducibility standards while the pencil-and-paper version did not, suggesting the electronic version may be more reliable [24].

Electronic symptom diaries have also been studied in the context of smartphones. One such study performed by Choe *et al.* evaluated the impact of a native smartphone app upon compliance [9]. The study investigated diary adherence by developing an Android widget to accompany the app itself. Applications for Android devices can be developed to include "Widgets" which are essentially application views that can be embedded within other components of the operating system, including the lock screen and the home screen. The widget developed for this study was designed to reduce user burden by allowing participants to provide time-stamped, self-reflection feedback with just a single tap, such as logging when the participant consumed a caffeinated drink. Furthermore, widgets also provide users with shortcuts for accessing certain components of the application itself. For example, users could quickly open the widget and navigate to the "Daily Sleep Diary" with a single

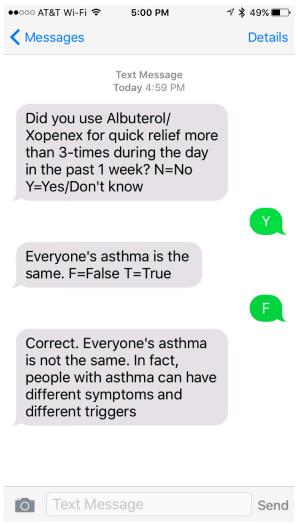

Fig. 1 Example text messages from Yun *et al.* (left: query-based message, center: knowledge-based question, right: response to knowledge-based question) [75]

tap on a specific region of the widget. Throughout the 4-week study, the participant group which utilized the widget had a 92% compliance rate whereas compliance dropped to 73% without the widget [9].

As an alternative to more traditional electronic symptom diaries, which are often web-based, Yun *et al.* utilized the Short Messaging Service (SMS) as a method of educating and surveying children with asthma during periods between physician visits [75]. The study focused on modifying Asthma Therapy Assessment Questionnaire (ATAQ) questions in order to make them age-appropriate for children and then dividing the study participants into three study groups. Children who participated were placed in the ”Query” group received fifteen yes/no questions regarding their asthma symptoms and management every other day. Children in the ”Query and Knowledge” group received fifteen questions each day which alternated between the query questions and true/false educational questions. The true/false questions were accompanied by responses indicating whether the submitted answer was correct or incorrect. Finally, children in the control group received no SMS questions at all. As evidenced by a response rate of 84% for a period of 3-4 months, Yun *et al.* determined that SMS is a feasible method of obtaining symptom data from patients and can be embedded into clinical practice [75].

In a study at Mount Sinai, Chan *et al.* used electronic symptom diaries in an app powered by Apple’s ResearchKit^{TM} to allow asthma sufferers to participate in ongoing asthma research [8]. The app allows users to track symptoms, view trends, and receive feedback on progress. The app also provides reminders to take prescribed medications. The focus of the study is to help patients reduce asthma-related limitations and decrease distress through better symptom control, reduced medical visits, and a generally improved quality-of-life [8].

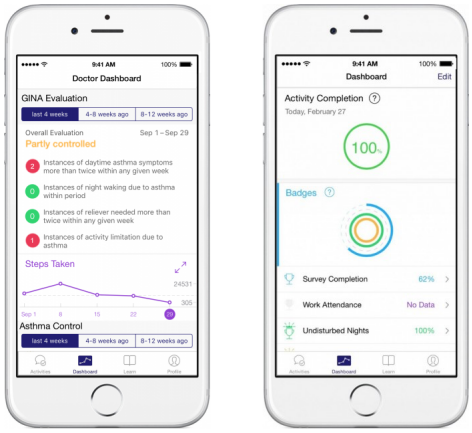

Fig. 2 Screen shots from the Asthma Mobile Health study being conducted by Chan *et al.* at Mount Sinai [8]. (Left: a dashboard highlighting GINA evaluation results, Right: a general dashboard indicating how the user has performed today)

3.3 Areas for Further Investigation

Over the last decade, dozens of studies have investigated the validity and reliability of daily symptom diaries, evaluated their impact on specific conditions, and studied their evolution from paper diaries to electronic instruments. Despite this vast amount of research, there are still areas are under explored.

One area for further investigation is the evaluation of an electronic symptom diary in conjunction with daily, out-of-clinic patient testing. Many upper respiratory conditions that benefit from spirometry measurement also benefit from daily symptom diary data [34]. More studies are required to determine if symptom diaries and spirometry measurements could dynamically interplay, providing richer context and more actionable management information. Furthermore, clinicians and researchers may benefit substantially from the ongoing pairing of spirometry data and symptom data recorded across several weeks or months. For instance, symptom diaries could be mined to ascertain when spirometry testing might be most useful. Similarly, spirometry testing might help patients contextualize their perceptions of symptom severity in survey responses.

4 Continuous Symptom Monitoring

Symptom monitoring for pulmonary ailments typically refers to the logging of coughs and wheezes. Coughs and wheezes are the most common symptoms of chronic respiratory conditions and have significant impact on a patient's quality-of-life [40, 59, 61, 65]. Logging the frequency of these symptoms can provide valuable insights for disease management, but reliable collection is difficult. This difficulty stems from discerning symptoms from other bodily functions (*e.g.*, cough versus throat-clearing) and is influenced by the ambient context of the sensing: nocturnal

versus ambulatory. Nocturnal collection of symptoms is easier to collect than ambulatory collection because hardware can be less compact and there are typically fewer noise sources to account for in a sleeping environment. This is especially true for audio based data collection methods—noises in a bedroom are far less diverse than noises encountered while a user is active during the day.

However, nocturnal symptom monitoring and ambulatory monitoring provide clinically distinct measures. While sleeping, coughing is mostly a reflex of the body. In this way, symptom logging while a patient sleeps might be linked with perception of sleep quality or related to sleep apnea [11]. On the other hand, coughing while active is typically not based solely on reflex—tickles in the throat or perceptions of breathing may prompt someone to cough or clear their throat more often. Ambulatory monitoring, then, may be linked with perceptions of cough severity or daytime triggers (like allergies) [23]. From this perspective, both nocturnal and ambulatory monitoring should be collected as well as the context around ambulatory activities (such as running, driving, walking, stationary) in order to help infer why the coughing was triggered.

4.1 A Primer on Medical Practices for Symptom Assessment

Because wheezing is difficult to detect continuously, it is typically assessed from breathing exercises. A patient sits in a quiet room and an audio recording of the breathing is made. Severity of the wheeze is then assessed by a specialist that looks at the amplitude and spectra of the wheeze and also listens to the recording. With proper visualization, specialists can reach an agreement about the severity of the wheeze [17, 35, 50, 69]. Some automatic measures of wheeze in nocturnal settings have been attempted, but are not routine medical practices. As such, most automatic wheeze measurement is in the form of spot checks that measure the number of detected wheezes over a short duration of breathing (*i.e.,* 30 seconds) [66]. Clinical efficacy of this marker is still early on, but may provide usable information about managing emergency visits or used to predict when a lung function test might be appropriate [66].

In case of cough, the most common technique for estimating severity is to have patients self-report using numeric (0-5) or visual scoring [52]. These self-reported values are most often part of a symptom diary, quality-of-life questionnaire, or illness control survey. However, the number of coughs a patient self-reports is more related to their perception of severity than actual symptom occurrence [11, 26, 44, 63]. Moreover, patients cannot accurately track trends in their cough frequency from hour to hour or while sleeping. Therefore, a number of systems have been created to quantify severity of cough automatically and objectively.

According to the European Respiratory Society [41], coughing can be quantified in a number of different ways, but the most preferred method is to report the frequency of explosive individual cough sounds (known as cough frequency). Studies have shown that the number of coughs per hour can allow early detection of res-

piratory exacerbation in patients with chronic respiratory diseases such as asthma, cystic fibrosis, and chronic obstructive pulmonary disease. Early intervention has been shown to decrease hospitalization rates and improve long-term outcomes, including survival [40, 59, 61, 65] While a number of research studies have been carried out investigating objective measurement, they are not currently part of routine practice for assessing illness severity. The reasons for this are straightforward: patient compliance is low and the technology costs prohibitively high. In the remainder of this section, we enumerate the difficulties with symptom data collection, introduce a number of existing technologies, and postulate future research avenues. Ambient audio monitoring has become a popular means of assessment because of its low cost and reliability, but early systems employed a number of different sensing mechanisms that attach to the chest or throat. As such, this section dichotomizes current methods into (1) early devices and (2) ambient audio based systems.

4.2 Early Systems for Ambulatory Monitoring

There is a large body of work in automated symptom sensing. Dating back to the 1950s, researchers developed methods of measuring airflow from the mouth in order to obtain unbiased measures of cough frequency [4]. This type of research has had limited utility in medical practice as airflow during coughing fits has not shown any consistent relationship for diagnostic or screening use. Instead, the detection and counting of cough fits is of primary importance.

A number of different methods have been proposed that use wearable technology to monitor the chest during a cough. For instance, Kraman *et al.* created an accelerometer-based system that placed an accelerometer at the participant's chest wall [28]. Sensor traces were saved to a flash drive and researchers manually counted coughs based on the visualization of the accelerometer data. However, automated discovery methods were never investigated.

The VivoMetrics Lifeshirt [10] was a commercial product that incorporated various physiological sensors to monitor breathing rate, heart rate, activity, posture, and skin temperature. For cough sensing, the system used a combination of a throat microphone and respiratory inductance plethysmograph (RIP). RIP is measured using two inductive coils attached to the rib cage and abdomen. Changes in inductance are proportional to expansion and contraction of the body. VivoMetrics was able to combine the RIP and microphone sensors for cough detection by time aligning the sensor streams and visualizing for human review. During ambulatory conditions the reported true positive rate was about 80% and the false positive rate was less than 1%. Methods for automatic detection are documented in the patent [10] but were never evaluated. The company was, however, liquidated a few years after the release of the LifeShirt.

Contact microphones also offer a compelling method for assessing cough sounds. Contact microphones use piezoelectric sensors that adhere to the chest wall, neck, or abdomen. VitaloJAK [38] is a commercial product that uses a piezoelectric sen-

sor attached to the chest wall to detect coughs. Barry *et al.* created a system called the Hull Automated Cough Counter (HACC) [3], using a lapel microphone and wearable recording device. The feature set used was motivated by speech recognition; namely, mel-frequency and linear predictive cepstral coefficients (MFCCs and LPCCs) fed into a Neural Network classifier. They achieved about 80% true positive rate and 4% false positive rate — however, the recorded audio was collected in an outpatient clinic for one hour per person, which is a relatively controlled and noise-reduced environment.

4.3 Why Use Ambient Audio Sensing?

The various sensing methods that can be used for cough detection prompted a study by Drugman *et al.* to compare different sensing techniques [12]. In this work, Drugman collected data in controlled environments, but added noise sources during data collection and asked users to sit, walk, and climb a ladder while coughing. They collected data using a number of different sensors including electrocardiograms, thermistors, piezoelectric chest belts, chest-worn accelerometers, contact microphones, and ambient microphones. They used a number of different features including spectral characteristics and moving windows of aggregated statistics from the sensor streams. A neural network was then trained to identify cough sounds. Their results clearly delineated ambient audio sensing and contact microphones as superior methods, with nearly 20% higher sensitivity than the other sensors. Ambient microphones slightly edged out the performance of contact microphones, with sensitivity of about 95% and fewer false alarms. They conclude that ambient audio sensing is more practical than contact microphones because it is less bulky to wear and maintain. They also investigated hybrid sensing approaches, but none clearly outperformed the ambient audio method.

In the same study, Drugman compared the performance of the different sensors to a commercial product from iSonea (previously named KarmelSonix). The iSonea system, named PulmoTrack-CC, uses ambient audio sensing combined with contact microphones and a piezoelectric belt to count coughs, but had a far lower specificity of about 65% (compared to 95% with Drugman's method). Previous reports of the iSonea system had sensitivities in the range of 91% [70]. This highlights the need for more formalized evaluation of ambulatory monitoring—the location and other noise sources can dramatically change the performance of the evaluated systems.

Drugman's study highlights that ambient audio sensing might be the most reliable method for sensing cough symptoms. Furthermore, dedicated wearable sensors pose usability issues because they are bulky and require patients to actively participate in maintaining them. Another advantage of ambient audio sensing is that it can leverage existing sensors from a mobile phone, potentially reducing patient costs and increasing usability.

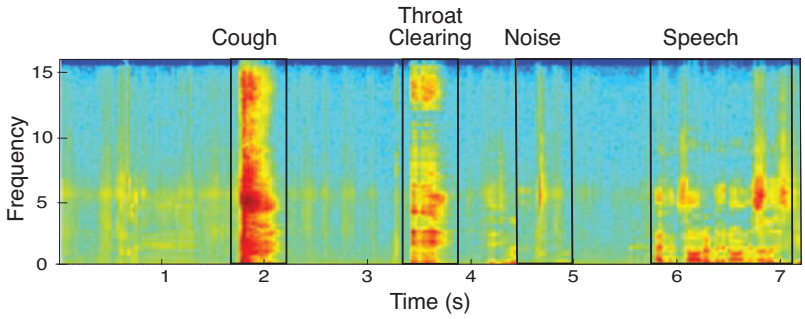

Fig. 3 A spectrogram of ambient noises from a lapel microphone. The cough sound has distinct spectral characteristics from the surrounding noises.

4.4 Ambient Audio Techniques for Cough Detection

A number of different studies have investigated the use of mobile phone microphones as cough sensors. We discuss several methods here, dichotomized by (1) frame-by-frame analyzers and (2) Markov chain based methods. Both methods use windows over time series data to extract features for each frame. However, frame methods classify fixed durations of audio as cough or non-cough and Markov chain methods classify cough sounds using a sequence of dynamically sized frames.

4.4.1 Frame-by-frame Analyzers

Larson *et al.* evaluated an audio system using in-the-wild recordings of users coughing [33]. The recordings were made using microphones from smartphones placed on a tether around users necks (practically, similar to how a lapel microphone would be worn). Coughs were annotated manually by teams of reviewers. They extracted spectral features such as the mean decibel energy of the entire spectrum, the mean decibel energy of the spectrum above 16 kHz, and below 16 kHz. They also employed principal component analysis of the magnitude spectrum from cough sound spectra. Larson showed that these components may be used to reasonably reconstruct the magnitude spectrum of a cough sound but are poor at reconstructing spectra for other sounds, especially speech. An example spectrogram of cough audio and various other ambient sounds is shown in Figure 3.

For classification, incoming audio data was converted to a magnitude spectrum and projected onto the principal components. Larson found that 10 components for each 150ms segment was sufficient for classification, greatly reducing the computational requirements of the classification algorithm. They employed a two-stage classification system: The first stage used a shallow decision tree (*i.e.*, a decision tree with only three nodes) and was effective at screening for cough sounds, albeit with a high false positive rate. The second classification stage used random forests

to classify the frames as cough or non-cough. They reported good results with high sensitivity (about 90%) and only a few false alarms per hour.

Larson's system also had the added benefit of compressing the audio spectrogram of the coughs—the principal components of classified coughs can be transmitted quickly and used to reconstruct the sound using only a fraction of the samples. They tested this approach with subjective listeners and showed that coughs were rated as having good fidelity, but other audio such as speech were unintelligible to listeners, helping to preserve a patients audio privacy.

Drugman *et al.* [12] evaluated an audio-based system that recorded audio from a lapel microphone as described previously. Drugman used a number of features of the audio data including spectral and statistical aggregations of time series windows. Spectrally, their method used a combination of mel-frequency cepstral coefficients (MFCCs), bandpass filters magnitudes spaced linearly over the frequency spectra and spaced using the Bark scale (used in MFCCs), and chroma features (widely employed in music applications). Chroma features break up the frequency spectrum in logarithmically increasing bandwidths that coincide with the twelve semitones of the musical octave. There are few theoretical underpinnings for what the most effective spectral characteristics should be for discerning cough sounds—therefore a variety of aggregations were investigated. Statistics of the spectra were also investigated such as spectral spread, centroid, variation and flux. Drugman determined through feature selection algorithms that the most useful features for classification were (1) the total loudness of the microphone, (2) the derivative of total loudness, and (3) the derivative of the Bark scaled energy from 3.7kHz to 5kHz. The feature selection chosen by Drugman was based upon mutual information, looking at the monotonicity between features.

These features are then fed into a three layer neural network. Drugman concatenated frames over contiguous periods of time to classify every 150ms of data. A median filter was then applied to the classifier output over time to smooth the classifications and eliminate spuriously positive frames. The system requires no user specific calibration (*i.e.*, it is trained to work on a user's audio data it has never seen) and the results show good sensitivity and specificity near 95%.

4.4.2 Markov Chain Analyzers

Matos *et al.* created a system called the Leicester Cough Monitor (LCM) [37], which uses a lapel microphone with a portable audio recorder. They used MFCCs (with derivatives) as features to a Hidden-Markov Model (HMM). The HMMs required audio calibration data from each participant. Matos collected data in ambulatory settings. Their average true positive rate was high at 71% and a false alarm rate of 13 cough events per hour. After applying an energy threshold to discard low intensity coughs, the average true positive rate for LCM could be boosted to 82% and false alarms reduced to 2.5 events per hour. However, the tradeoff was to discard on average 29% (6-72%) of the cough events for each subject. The HMM approach is very much inline with classical speech recognition techniques and therefore developers

can benefit from many of the standard toolkits available. In follow-up studies, LCM has reported a true positive rate of 91% and false positive rate less than 1% [5].

Rhee *et al.* also employed the use of HMMs with standard speech recognition tools [55]. Their system, coined the Automated Device for Asthma Monitoring or ADAM, uses a variety of tools to monitor asthma symptoms including questionnaires and sound monitoring from a smartphone. They use MFCCs and average loudness, like Matos *et al.*, but their evaluation includes more than just an investigation into the algorithms. Rhee *et al.* evaluated the system while running on a smartphone—that is, an online evaluation of the system running in real time. With such an evaluation, implications on battery life and user reaction to wearing a lapel microphone could be investigated. Rhee *et al.* found that users were open to using the lapel microphone, but battery life was a significant drawback with only a few hours of usablility between charging. Rhee *et al.* report high sensitivity and specificity in their trials, with about 70% sensitivity and a few false alarms per hour.

In subsequent studies Rhee *et al.* recruited a number of teens and young adults to use the ADAM system and monitored cough counts along with a variety of other data including accelerometer data, self-reported symptom severity, symptom diaries, and spirometry measures like FEV_1 [54]. Their analyses reveal some interesting correlations between cough frequency and poor spirometry measures, as well as predicting the use of different health care services. Higher activity from accelerometer data was also correlated with cough frequency. Exit interviews with teens using the device (for a period of about a week) revealed that the lapel microphone was an acceptable wearable and the general attitude towards using a smartphone was positive. Although longer deployments of the device are needed to assess long-term compliance, these findings are encouraging.

4.5 Areas for Further Investigation

4.5.1 Difficulties with Data Collection

Methods for collecting symptom data in the literature are varied and there is no standard. Perhaps the most realistic method is to collect data in actual conditions—users are shown how to use the sensors and then asked to go back to their daily routines. After use, equipment is collected from the user and a long annotation process begins with multiple reviewers pouring over the data streams, annotating the data with symptom labels. While cumbersome, this type of data collection ensures that rich evaluation of an algorithm can take place with sensitivity and false alarms per hour easily calculable. Even so, this process is extremely time consuming and expensive. In many studies, the annotation process for 24 hours of collected data might take 3-5 days of annotation. As such, many studies opt to collect a small amount of pilot data using this approach, but then abandon the annotation of the data for larger groups. Data that is not manually annotated can be run through automated systems and then the output of the system can be reviewed. This is a far more scalable approach in

terms of time and cost, where review of 24 hours of recorded data takes 10-15 minutes. The relative ease in review comes at the expense of evaluation—sensitivity cannot be measured but many evaluation criteria such as specificity and false alarms can still be estimated from the system outputs.

4.5.2 Mixed Hardware and Algorithmic Designs

Despite the numerous research studies in the area, no technology has become standard for automated symptom monitoring. Audio based methods that leverage smartphones appear to be more practical for patients to use, but the processing speed, battery life, and data storage are still unsolved problems. For example, compressed audio for a typical day might take up a few gigabytes of storage on a phone and decrease the battery life to six or seven hours.

As an alternative, it is also possible to process the incoming audio in real time to save on storage and facilitate real time interventions of feedback. However, the processing will further reduce battery life. Future studies, then, could leverage a combined software and hardware solution that can process audio in near real time with sustained battery life. For instance, audio co-processors in phones may provide a means of tracking audio using specially designed, low-power signal processing hardware and heterogeneous computing. These systems would be similar to the motion co-processors in modern smartphones that allow continuous accelerometer and gyroscope monitoring for periods greater than 24 hours. To some degree, these audio coprocessors already exist: for instance, smartphones that employ Qualcomm‘s snapdragon chip have built-in natural language processing and Apple’s M9 coprocessor has built-in low power audio listening capability. Research studies have already begun to exploit them for ”always-on” audio sensing applications [31].

Hybrid methods may also play a potential role. For instance, smart watch microphones might help to record and process symptom audio when the phone is put away, potentially also adding arm motion towards mouth as a predictor of coughing. Such hybrid systems would require an audio coprocessor in each device. Finally, wheeze detection from ambient audio methods is significantly lacking behind cough detection. Further research is required to determine if wheezes can reliably be detected in ambulatory settings.

5 Mobile Spirometry

As described in section 2, lung ailments are diagnosed in a number of ways. Airway tests are one of the most prolific diagnostic measures because of their ability to detect airway obstruction severity and restriction. The most widely accepted objective airway measurement is known as Spirometry. Spirometry involves analysis of flow and volume of expelled air, usually through a patient exhaling into a device that directly measures the airflow. Measurements provided by such sensing include

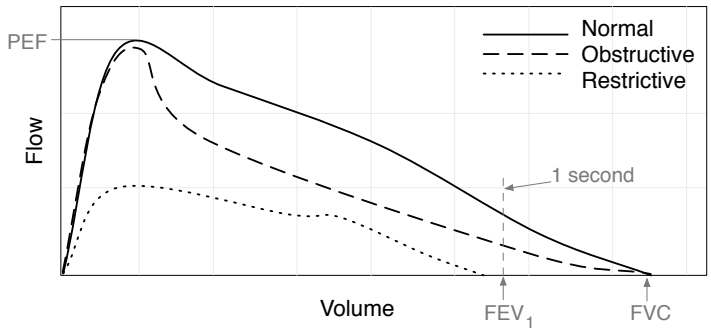

Fig. 4 Example flow/volume curves showing typical behavior of normal, obstructive, and restrictive subjects.

peak flow rate (PEF), total volume of air exhaled (FVC), total volume of air exhaled within the first second (FEV_1), and percentage of total volume exhaled within the first second (sometimes abbreviated as $FEV_1\%$ or FEV_1/FVC). As part of the diagnostic process these measures are compared against predicted norms for patients on the basis of age, height, and gender. Measures that deviate from the norms typically reflect an obstructive or restrictive pulmonary disease [39]. For obstructive diseases, the magnitude of the deviation from normal can help diagnose severity.

In addition to comparing predicted norms, spirometers also generate *flow vs. volume* and *volume vs. time* plots. Health care professionals visually inspect the shape and curvature of these graphs for evaluating validity of the spirometry efforts as well making a diagnosis. For example, Figure 4 shows different flow vs. volume curves for different patients. For a healthy individual, once the air flowrate reaches its maximum (*i.e.*, peak flow or PEF), the flow starts decreasing linearly in relation to volume. When the flowrate is plotted against cumulative volume this results in an almost straight descending limb. In contrast, when the airflow is obstructed, the flowrate decreases more rapidly after reaching peak flow. Therefore, it attains a curved or scooped slope. This is because the smaller airways become obstructed and cannot sustain their maximum flowrate. For an individual suffering from a restrictive lung disease, such as cystic fibrosis, the entire curve is smaller than predicted norms.

Spirometry is more than just a *diagnostic* tool—measurement of spirometry at home allows patients and physicians to regularly monitor trends and changes in lung function. Regular spirometry testing can result in earlier treatment of exacerbations, more rapid recovery, reduced health care costs, and improved quality-of-life [27, 40, 61, 62]. However, traditional spirometers are notoriously expensive,

require calibration, and may not be approved for use outside of a clinical setting. As such, spirometry solutions that use the computing power of smartphones have grown in popularity. This section explores three methods for leveraging the power of a smartphone, categorized by the sensing method: direct sensing, indirect sensing, and hybrid sensing.

5.1 Direct Sensing

Direct sensing techniques rely on directly sensing the primary physical phenomena: airflow. Traditional spirometers operate by directly estimating the amount of flow exiting a user's mouth, such as with a mouth piece that directs all flow into a chamber or tube for sensing. Direct sensing approaches employ various methods including mechanical turbines and using ultrasonic waves to estimate airflow. Mobile spirometers also use these direct sensing techniques. One such mobile device, called MobiSpiro [58] directs the exhaled air past a hot film anemometer, cooling the hot film according to the fundamental thermodynamic properties of air, allowing for an accurate estimate of flow rate. Once the flow is measured over short time intervals, all other measures (*e.g.*, volume) can be calculated and a full diagnostic report can be generated. While this approach is accurate, low-cost implementations are limited by the cost of the sensors, manufacturing, and quality control. Furthermore, anemometers require repeated calibration, limiting their long term reliability in a patient's home.

Differential pressure-based methods that leverage a smartphone have also started to gain popularity. Researchers at Rice University created such a device, called mobileSpiro [18, 45]. Carspecken *et al.* created a similar device called TeleSpiro [7]. These devices measure the pressure drop across a tube of known dimensions. The difference in pressure is monotonically related to the flowrate. The cost of manufacturing these types of devices in bulk is estimated to be less than $20 USD. To reach such a low cost-point, the sensor outputs are directed through low-cost microcontrollers and sent over USB to a smartphone or tablet. The phone then interprets and conditions the signal before calculating measures from the sampled flowrate. While more research is required to determine long-term reliability and calibration requirements, these designs could be low-cost sensing solutions for many pulmonary sufferers. Even so, because the devices must be tethered to the phone (and must be carried with a cable), their usability and long term patient compliance may be decreased.

Other devices such as the EasyOne mobile spirometer and Cohero Health wireless spirometer guide the user's exhalation through a tube with ultrasonic transducers positioned on either side of the tube [72]. Ultrasonic waves are transmitted through the turbulent flow of the user's exhalation, disrupting the generated acoustic signal before it reaches the receiving transducer. Analysis of the received waveform yields flow rate with a high accuracy thanks to the highly controlled environment through which the user's airflow can travel. While these devices can be integrated

with smartphones, they employ custom hardware for analysis and therefore are more costly compared to other designs.

5.2 Indirect Sensing

Indirect sensing techniques rely on side effects of the primary physical phenomenon, such as the reverberant sound created by the vocal tract as a patient forcibly expels air during a spirometry effort. This sound is created by the turbulent flow of air as the patient's lungs force air through the various resonating cavities that make up the vocal tract. Larson and Goel *et al.* [15, 32] developed a system to estimate the flow exiting a patient's mouth using the microphone on a smartphone and later adapted the algorithm to function through the GSM network (*i.e.*, during a phone call), requiring no custom hardware or software for the patient.

The authors used three signal processing techniques for flow rate estimation. The first technique uses spectral analysis, finding features in the frequency domain corresponding to resonances in the patient's vocal tract. These resonances change as the vocal tract flexes in response to flow rate through it. The second method uses temporal envelope analysis. That is, measuring localized energy in the audio signal. The final method is linear predictive coding, which models the vocal tract as a filter excited by a white noise source. By estimating the energy in the white noise source over time, they could estimate the magnitude of airflow from the lungs. All energy estimates must account for energy lost through dispersion (parameterized by the distance between microphone and mouth and the diameter of the patient's head). Without accounting for dispersion losses, changes in distance between the microphone and mouth can have drastic effects on the aforementioned features. The author's reported accuracy based upon 50 patients, was within 5% of a traditional spirometer. The authors report that this value is within the normal range for comparing spirometers, but warn that there are some worrying outliers in the data.

These indirect sensing methods often have a strong machine learning component, requiring large datasets to build a reliable mapping between the captured features and the desired diagnostic information. As new phones are created, this mapping becomes more complicated and must account for differences in sensors, microphone placement, and firmware. Performing clinical trials and comparing against ground truth spirometry is therefore an integral part of developing these techniques, as it is otherwise impossible to build a perfect model of the air escaping from the user's vocal tract through purely indirect sensing. Utilizing secondary physical phenomena to perform airway sensing yields an inherent dichotomy; sensing phenomena such as the sound of turbulent air escaping the user's throat is cheaper to sense, but also requires extensive signal processing and machine learning efforts to generate a useful end result.

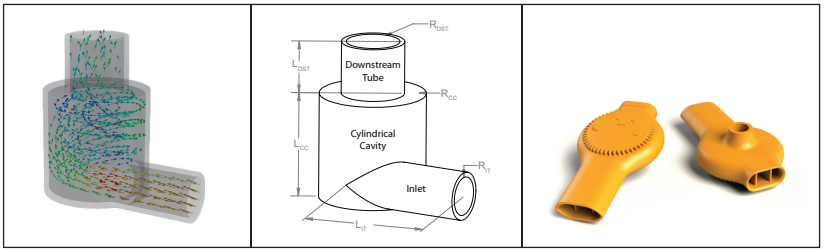

Fig. 5 Left; The vortex whistle directs incoming air flow into vortex within a resonating chamber, creating a frequency proportional to the amount of incoming flow. Center; Sato's [21] design has many parameters that alter the performance of the whistle. Right; DigiDoc Technologies whistle.

5.3 Hybrid Sensing

Hybrid sensing techniques find a middle ground between directly capturing exhaled air and inferring flow from the vocal tract. In hybrid approaches, a custom transducer is used as a mouthpiece to alter the sound of the flow as it escapes the mouth. An important example transducer is the vortex whistle first introduced by Vonnegut in 1954 [71]. The vortex whistle (shown in Figure 5) resonates at a frequency that is directly proportional to the input air flow rate, thereby transforming the indirect sensing problem into a frequency tracking problem—which is well-understood in the digital signal processing literature. In 1999, Sato *et al.* [21] performed pilot experiments using the vortex whistle for spirometry measurements. By tracking the frequency over time and applying a simple regression, the flow rate over time was determined. A similar study was performed by Brimer *et al.* using a slightly different vortex whistle design [6]. However, no formal evaluation of performance was published.

More recently, Goel *et al.* combined frequency tracking with certain problem-specific constraints (such as the fact that flow rate will rise to a peak value, and then fall monotonically) to create a simple yet robust flowrate estimate using a mobile phone microphone [15]. Goel *et al.* performed a study of the system with 50 participants resulting in an error rate of less than 8% for the $FEV_1\%$ measure when compared with a ground-truth spirometer (the authors note that when comparing two ground-truth spirometers, disagreement between the two averaged at 5%). This hybrid sensing modality has a number of trade-offs with direct and indirect sensing approaches. First, it eliminates the need to analyze secondary physical phenomena, thus reducing the complexity of the signal processing and machine learning effort. However, this advantage is at the cost of needing a physical whistle. In contrast to direct sensing approaches, the whistle has no moving parts or electronics, meaning manufacturing costs are extremely low. Companies have already started to manufacture ultra-low cost injection-molded vortex whistles, such as the design by DigiDoc Technologies shown in Figure 5.

5.4 Areas for Further Research

One of the main challenges in performing accurate spirometry is coaching a patient to exhale properly over repeated tests. A valid spirometry effort requires considerable concentration and effort—failing to exert oneself can result in erroneous results. This problem is currently mitigated by physical presence—trained health care professionals coach patients through each effort. However, for a mobile application, future research needs to determine proper coaching methodologies when a patient is unsupervised.

Indirect and hybrid sensing approaches face many challenges from the nature of their sensing approach. Analyzing the sound of an exhalation or a whistle requires that the signal be reliably received, which depends largely on the environment around the user. Additionally, patient pose and hardware variations between mobile devices can cause variance in received signals. Therefore, direct sensing approaches like mouthpieces or other custom hardware that isolate exhalation gain an inherent advantage in uncontrollable environments. However, for patients where the cost or inconvenience of custom hardware reduces access or compliance, steps must be taken to ensure that the environmental factors do not decrease the signal-to-noise ratio necessary for an indirect or hybrid system to function.

Mobile airway sensing is still an area of active research, especially with regards to patients with extremely low lung function. Indirect and hybrid sensing techniques rely on sufficient airflow to excite detectable sounds—a condition which is not fulfilled in some cases of severe obstruction or restriction. Patient airflow must exceed a certain threshold to create the turbulent flow that generates the sound detected by the indirect sensing methods; similarly, vortex whistles have a minimum flow rate that must be achieved to start resonating. This minimum frequency is a function of the design parameters of the whistle itself. However, more research is required to understand how different whistle shapes might be used for detecting lower airflows from more severely obstructed individuals.

6 Conclusion

From a global perspective, respiratory diseases contribute to a staggering number of fatalities each year, possibly due to the diagnosis process and difficulties associated with managing diseases. There is no standardized method of obtaining information about general lung health, each disease or illness has its own accepted means of measuring wellness. The development and evolution of digital methods of pulmonary monitoring present new opportunities for presenting clinicians with otherwise unobtainable or unreliable data.

Studies involving daily symptom diaries have shown there is significant potential for self-reported symptom data to have a serious impact upon the monitoring and management of upper respiratory conditions and diseases. The use of electronic symptom diaries through digital mediums such as native smartphone apps and SMS

have also shown improved compliance over traditional daily symptom diaries. Although the potential for benefit is high, more research most be done to investigate the implications of their use within new digital devices and mediums. With the evolution of electronic symptom diaries comes promising research of how data from these diaries could be paired with at-home testing performed by patients to further impact disease monitoring and management.

Smartphones are also being increasingly used to as a method of detecting symptoms. In the future, these solutions will begin to exploit always-on audio capabilities of smartphones to track trends. The most exciting part of this analysis is the potential to gather context information from the smartphone which could be used to help identify symptom triggers or effective management —pairing symptom data with activity, location, and previous history may be the key to having personalized medicine without requiring extensive data analysis or over-utilizing self-reported data.

As the capabilities of smartphones have improved, spirometery research has quickly taken advantage of these changes. Traditional spirometers are typically only utilized in a clinical setting due to their high cost, the challenges of patient coaching, and required calibration. Indirect sensing methods have been evaluated as a potential low-cost method of gathering reliable spirometry measures, however, this approach requires an extensive machine learning component. Mobile spirometry still faces the challenge of appropriately coaching patients through the measure, however, native smartphone applications may yield reliable methods of coaching patients at home.

Pulmonary monitoring using smartphones has already made a significant impact to respiratory research and many of the discoveries are already being utilized to increase the quality-of-life of those suffering from respiratory diseases. As researchers continue to investigate new avenues of improving data retrieval and patient compliance, mobile devices promise to further shape the future of pulmonary health.

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