Smart cough monitoring: an innovation milestone for global respiratory health

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Abstract
Each year, respiratory diseases such as tuberculosis, COPD, lung cancer, asthma, and now COVID-19 take millions of lives and disrupt or disable hundreds of millions more. The global burden of these diseases is expected to increase as developing nations industrialize, and the need to track and respond to that spread grows evermore urgent. These diseases share a common syndrome, coughing, the characteristics of which allow physicians to diagnose and monitor the course of respiratory illnesses. The medical value of cough tracking has long been recognized as a critically important tool in patient care and public health, but until recently technology has lagged behind the need for effective cough monitoring solutions. Now, with the parallel rise of smartphone use and machine learning analytics, half the world's population is already carrying the device that can fundamentally change our approach to the global crisis in respiratory health. Smartphones offer the ideal platform for a scalable, effective, and smart cough monitoring tool.

Keywords
respiratory disease — cough tracking — mobile health — machine learning — TB — COVID-19

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Respiratory disease: a global burden

Respiratory diseases account for one-quarter of all deaths worldwide [1]. They are the leading cause of death in developing nations [1]. The most lethal of these – lung cancers, tuberculosis (TB), chronic obstructive pulmonary disease (COPD), and pneumonia – take more than 10 million lives each year [2]. In developing countries, these four illnesses result in a combined death toll nearly matching that caused by heart disease, HIV/AIDS, and diarrheal diseases combined (20.3% vs. 22%) [2].

In addition to this staggering loss of life, **hundreds of millions endure chronic respiratory conditions** that disrupt livelihoods, undermine mental health, and abbreviate lifespans [1]. Chronic respiratory diseases such as COPD, chronic cough, asthma and allergies reduce the life expectancy of hundreds of millions and result in four million premature deaths each year [3]. Upper respiratory infections may lead to relatively few deaths worldwide (e.g., 3,000 per year attributable to the common cold)[4], but they are the leading cause of disability and disease harm with an estimated 17.2 billion cases annually [5]. Their prevalence is more than seven-fold that of the second leading cause, diarrheal diseases (2.39 billion cases) [5].

To add to these long-standing threats, **many novel and re-emerging pathogens tend to target our respiratory tract.** Examples include anthrax (2002), SARS-CoV (2003), H1N1 (2009), pertussis (2012), MERS-CoV (2012), and SARS-CoV-2 (2019 - current). Such outbreaks involve our respiratory system because (i) airborne particles provide an efficient pathway for zoonosis, (ii) the respiratory tract offers an ideal culture site for infection, and (iii) iterative air exchange serves as a highly effective means of transmission to new hosts [6]. These novel respiratory illnesses have claimed millions of lives, including 1.84 million in a single year by SARS-CoV-2 alone, and they have induced global economic recessions and disrupted access to health services worldwide [7, 8].

Respiratory diseases drain resources, depress economies, and perpetuate social inequalities that exacerbate cycles of global poverty [1]. For COPD alone, the costs of treatment, morbidity and lost earnings are counted in the tens of billions ($24 billion in 1993)[17]. The economic burden of seasonal flu is also in the tens of billions in the United States alone [18]. In Asia, for example, the average annual impact for a worker with chronic respiratory disease is $4,191 US and a 36% reduction in productivity [19]. In the case of the ongoing SARS-CoV-2 outbreak, $3.5 trillion in lost income occurred in just three months (April – June, 2020) [20]. These costs disproportionately impact the lives of minorities, women, and marginalized families, which is why respiratory illnesses are referred to as diseases of poverty [21].

While certain illnesses such as TB are currently in decline [9], **many respiratory diseases are on the rise**, particularly in industrialized nations. These include COPD [22], lung cancer [23], asthma [24], and allergenic conditions such as hay fever [25]. All of these diseases are projected to proliferate as the world population ages and developing nations continue to concentrate people and pollution within urban centers [22, 21]. Many diseases are driven by four common drivers, all of which

Box 1. Prevalent respiratory diseases

Tuberculosis (TB) is among the top ten causes of death worldwide, and the leading cause of death from a single infectious agent (outside of pandemic years) [9]. It causes approx. 10 million illnesses annually [5, 9], of which 1.5 million result in death [9]. 10 to 15% of cases occur in children [1]. TB is most lethal in sub-Saharan Africa and southeast Asia, where susceptibility is increased through comorbidity with HIV/AIDS. 8.6% of cases occur in people living with HIV/AIDS, but 20.9% of deaths occur among HIV-positive patients [9].

TB is transmitted via airborne respiratory droplets. Symptoms of tuberculosis disease of the lung include coughing, chest pain, and bloody sputum, among other symptoms [10].

Acute respiratory infections, such as pneumonia, result in 4 million deaths in a non-pandemic year [11]. These infections, which are caused by bacterial, viral, or fungal pathogens, are often among the top five causes of death globally and are the leading cause of death in children under five [2]. The majority of deaths (3 million) occur in children under five, meaning pneumonia kills far more children than HIV/AIDS or malaria [12, 13].

Each year the epidemic of seasonal influenza A results in 90 million cases worldwide [14], of which 3 – 5 million are severe and 290,000 – 650,000 result in death [15]. 99% of these deaths occur in developing countries, and 28,000 – 111,500 of deaths occur in children under 5 [14].

Compared to seasonal flu, zoonotic influenzas like avian and swine flu typically have an aggressive clinical course [16]. These, and other zoonoses like SARS-CoV-2, include coughing as a common symptom. They spread primarily via respiratory droplets, and have been responsible for recent global outbreaks such as the ongoing COVID-19 pandemic [15, 7]. In 2020, SARS-CoV-2 and its variants infected 85 million people, 1.8 million of whom perished [7].

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are on the rise in developing urban centers: (a) tobacco use or exposure, (b) indoor pollution, (c) outdoor air pollution, and (d) occupational exposure to toxins and irritants (Schluger and Koppaka 2014). Likewise, novel outbreaks of zoonotic respiratory diseases are predicted to increase alongside factory farming, the trade in wild game, and the encroachment of population centers into wild areas [6]. These trends indicate that respiratory disease is on track to become increasingly prevalent and increasingly deadly in the decades to come.

Coughing: a keystone symptom

Respiratory pathogens hijack our respiratory tract, including defense mechanisms such as coughing. Infections trigger mucus production, restrict airways and irritate the upper respiratory tract, and thus induce reflexive behaviors such as coughing and sneezing – ironically, the very mechanisms we have evolved for keeping foreign bodies out. These robust actions propel the pathogen's next generation through the air in search of its next host [26]. Mucus production, inflammation, and tracheal irritation also occur as a result of non-communicable respiratory diseases, such as lung cancer and asthma, which is why coughs and sneezes are common symptoms of most prevalent respiratory illnesses (see Box 1).

However, despite the role they can serve in transmission, **coughs and sneezes can also be invaluable assets in the fight against respiratory disease.** As with any disease, respiratory illnesses cannot be treated properly without timely diagnosis and close patient monitoring [1, 9]. In the case of highly contagious diseases such as TB, COVID-19 and influenza, the successful containment of outbreaks hinges upon rapid identification of cases and strategic resource allocation [16]. These mitigation measures are all facilitated by syndromic surveillance of symptoms such as coughing, which are relatively prevalent and easy to monitor.

Coughing is a conspicuous and easily tracked indicator of health [27]. The noise associated with coughing can be observed without specialized equipment, and it is widely recognized as a potential indicator of illness by people without medical training [28, 29]. The coughing sound contains important diagnostic information, as do patterns in the frequency and severity of cough production [27], that are of great value to doctors and public health officials [29].

In the last century, **cough counting has emerged as an increasingly important tool** for screening, diagnostics and monitoring [30, 31, 32, 33, 27, 34]. Cough counts are now primary endpoints in antitussive therapies [35, 36], and cough frequency has been used to detect and monitor a variety of prevalent illnesses including TB [37], COPD [38], chronic cough [35], and others listed in Box 1 [39, 27].

Digital cough monitoring: established value

While the potential value of cough tracking is difficult to overstate, the limiting factor has been technology. Early on in the use of coughing as a diagnostic tool, when patient surveys and doctor visits were the primary means of screening, health care providers quickly recognized the need for cough tracking systems that are objective, quantitative, and long-term [45, 27]. Such systems could produce continuous records of cough activity, which would prove invaluable in diagnostics and patient monitoring. The variety of instrumentation developed over the last century reflects the profound importance of technological innovation to cough monitoring

Box 1 *continued*. Prevalent respiratory diseases

Lung cancer and other respiratory cancers match the TB death toll of 1.5 million deaths annually [40] and are also among the top ten causes of death worldwide [2]. Lung cancer is the leading cause of cancer in males, comprising 17% of new cancer cases and 23% of total cancer deaths, and the second-leading cause of cancer deaths in females [23]. Half of cases occur in developing countries [22], but case rates are two- to five-fold higher in developed countries, where it is the third most common cause of death overall [23].

Like COPD, lung cancer is a non-communicable disease whose prevalence is increased by smoking, exposure to secondhand smoke, and air pollution [22]. Symptoms of lung cancer commonly include chronic cough, coughing up blood, chest pain, shortness of breath, and wheezing [30].

Pertussis, or whooping cough, has been rare in the United States and Europe since the development of a vaccine in the 1940s, but it remains prevalent in developing nations [41]. About 24 million cases occur annually in children under 5, leading to 160,700 deaths [42, 41]. 33% of cases and 58% of deaths were reported from African nations [42].

Pertussis is caused by a bacterial pathogen that is transmitted through respiratory droplets [41]. Its infection leads to death when it causes secondary bacterial pneumonia [41]. Pneumonia occurs in 13% of all pertussis cases, with higher incidence in children under 6 months [41].

Chronic cough, which is defined as cough that persists for at least 8 weeks, affects 9.6% of the world population [43]. It is most prevalent in developed countries [43]. This is a non-communicable illness that is caused by smoking, exposure to cigarette smoke and other environmental pollutants [43]). It is associated with other diseases such as COPD, bronchitis and asthma, as well as postnasal drip syndrome and pulmonary fibrosis [43]. Patients with chronic cough account for up to 38% of respiratory outpatient care in the United States [28, 44, 29].

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[46, 47, 48, 49, 50, 32].

The acoustic signature of a cough has allowed for creative monitoring and analysis solutions. Tools for acoustic cough monitoring were first developed in the 1950s [45], and the first attempts to automate acoustic counts were begun in the 1980s [51]. Ambulatory versions of such devices were developed in the 1990s and 2000s [52, 53], examples of which include the Lifeshirt system [54], the RBC-7 [55], LR100 [56, 57], LR102 [47], Pulmotrack-CC [58], Hull Automatic Cough Counter [59], and Caytano Cough Monitor [60].

In the last decade, **two cough counting systems have been widely adopted for research.** The Leicester Cough Monitor, which archives continuous recordings on a commercially available digital recorder using a lapel microphone [61, 62, 63, 64, 65, 37], and the VitaloJAK, which receives sounds on a lapel microphone and a contact microphone on the sternum, then records instances exceeding a noise threshold to a special recording device carried in a belt bag [66, 67]. Similar systems employing lapel microphones and customized mobile recorders have recently been developed (e.g., MobiCough [68]).

Recent tools for cough counting, though valuable, share common limitations, namely (1) they are not a scalable solution, since they require custom instrumentation available only through research collaborations; (2) their use of auxiliary microphones increases cost, complicates use, and introduces opportunities for malfunction; (3) they archive sounds locally, which creates opportunities for data corruption and loss; and (4), for the products that record sounds continuously, patient privacy cannot be ensured, which erodes rates of patient participation [27]. The limited adoption of these tools has constrained researchers' efforts to cross-validate results, correlate measurements with clinical data, and integrate the tools into clinical care [67]. Nevertheless, even with their limited use, these tools have proven the concept and provided essential guidance on acoustic cough monitoring within clinical [69, 70, 71, 49].

Smart cough monitoring: an emerging opportunity

In their comprehensive review, Hall and colleagues [27] outlined ten criteria for the "ideal" cough monitoring tool:

1. Be easily portable, compact, and minimally-intrusive.
2. Provide continuous, passive monitoring that targets non-elicited coughs as patients go about their lives.
3. Operate on a 24-hour basis to account for diurnal variations in cough.
4. Perform well in the patient's own environment.
5. Function across a range of subjects and types of cough.
6. Reliably and consistently detect all coughs (i.e., high sensitivity).
7. Reliably and consistently distinguish coughs from non-cough sounds (i.e., high specificity).
8. Distinguish between the patients' own cough and those produced by others.
9. Detect coughs in real-time and avoid continuous recording (i.e., privacy assurance).
10. Provide a fully automated analysis of collected data (i.e., consistency and scalability).

Box 1 *continued*. Prevalent respiratory diseases

Asthma is attributed with 180,000 – 200,000 deaths each year [24, 3, 22]. Although it is most prevalent in developed countries [24], 80% of deaths occurr in low- and middle-income countries [72, 73].

Despite this death toll, asthma's greatest burden is actually in its morbidity and the disruption of life it causes [3]. Approximately 300 million people suffer from asthma [24, 74], and it is the most common chronic disease among children [75]. In North America, asthma affects 10% of the population [24] and accounts for 30% of pediatric hospitalizations [3, 1]. In Western nations, the financial burden on asthma patients ranges from $300 to 1$,300 per patient per year [24].

The prevalence of asthma is increasing by 50% every decade [24], in correspondence with the proportion of the world's population living in urban areas [22]. Asthma has high comorbidity with allergic rhinitis, or hay fever, which afflicts 400 million people globally [25]. Rates of allergic rhinitis are also on the rise [25]. Asthma symptoms include wheezing and shortness of breath as well as cough, particularly in children under 5 [75].

Croup is a prevalent upper respiratory infection that affects about 3% of children a year, usually in ages under three [76]. Symptoms typically resolve on their own, but severe infection can possibly lead to pneumonia, respiratory failure, and death. The mortality rate is lower than 0.5% in children treated with intubation. Croup is usually caused by infection by a parainfluenza virus that is transmitted through respiratory droplets [76].

Note that **air pollution** is strongly correlated with COPD, lung-cancer, chronic cough, asthma, and hay fever (Schluger and Koppaka 2014). Air pollution has also been found to be related to rates of seasonal flu [77] and COVID-19 [78]. Air pollution causes 5% of lung cancer deaths 1% of deaths from acute respiratory infections [79].

This study concluded that, though these characteristics "should not seem beyond expectations," no such system "is currently freely or commercially available" [27]. Moreover, "there has been very little financial investment in counting tools to date" [27].

These authors conclude by proposing that **the proliferation of smartphones is the key to effective cough monitoring.** Smartphones are devices with built-in microphones, data storage, software platforms, and accessory sensors such as GPS and accelerometers, all of which removes the need for custom instrumentation to monitor coughs. These devices also carry the ability to download software and upload data to satellite-linked cloud-based data servers. In principal, these features would allow for the rapid distribution of a cough counting app, as well as immediate cough classification and timely upload of detections to secure data centers (Hall et al. 2020). In turn, these features establish the potential for real-time supervision of patient health by researchers and primary care providers.

Most importantly, **smartphones are already in the hands of over 3 billion people.** As of early 2020, 45% of the world population owned a smartphone [80]. In Western developed nations, smartphone penetration is well over 80% [80]. If cough monitoring tools were distributed as smartphone apps, the potential contribution to patient care and public health would be unprecedented in the extreme. In turn, the volume of data produced by the widespread distribution of 'smart cough monitoring' would enhance the accuracy of cough classification algorithms, the versatility of the monitoring tool, and its application to problems of resource allocation and disease control.

As smartphones proliferate, **machine learning tools are advancing the automated analysis of enormous volumes of data.** As more and more cough data are collected, AI-based algorithms will become increasingly proficient at (1) distinguishing coughs from other percussive sounds, (2) associating certain cough attributes with particular diseases, and (3) identifying individual-level characteristics in a patient's cough [27]. These tools enable real-time syndromic monitoring for remote patients and even entire populations, and have the potential to fundamentally change our approach to patient care, public health, and emergency response [81, 27, 82]. The parallel rise of smartphone and machine learning technologies has brought 'smart cough monitoring' within reach.

Altogether, smartphones offer the ideal platform for a scalable, effective, and smart cough monitoring tool that could change the nature of our approach to global respiratory health.

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