CHEST

Smart Devices Are Poised to Revolutionize the Usefulness of Respiratory Sounds

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The association between breathing sounds and respiratory health or disease has been exceptionally useful in the practice of medicine since the advent of the stethoscope. Remote patient monitoring technology and artificial intelligence offer the potential to develop practical means of assessing respiratory function or dysfunction through continuous assessment of breathing sounds when patients are at home, at work, or even asleep. Automated reports such as cough counts or the percentage of the breathing cycles containing wheezes can be delivered to a practitioner via secure electronic means or returned to the clinical office at the first opportunity. This has not previously been possible. The four respiratory sounds that most lend themselves to this technology are wheezes, to detect breakthrough asthma at night and even occupational asthma when a patient is at work; snoring as an indicator of OSA or adequacy of CPAP settings; cough in which long-term recording can objectively assess treatment adequacy; and crackles, which, although subtle and often overlooked, can contain important clinical information when appearing in a home recording. In recent years, a flurry of publications in the engineering literature described construction, usage, and testing outcomes of such devices. Little of this has appeared in the medical literature. The potential value of this technology for pulmonary medicine is compelling. We expect that these tiny, smart devices soon will allow us to address clinical questions that occur away from the clinic. CHEST 2023; 163(6):1519-1528

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In 1816 with the invention of the stethoscope, Laennec[1] began naming lung sounds and sound patterns and noting their associations with anatomic abnormalities and diseases revealed in postmortem examinations. During the last half of the 20th century, researchers building on the work of Laennec and others began to investigate the anatomy, physiology, and pathology associated with lung sounds, exploring the acoustic properties of the respiratory system, naming lung sounds according to acoustic principles rather than presumed sites and manner of production, and improving the technology used to record and analyze lung sounds.[2]

Historically, “lung sounds” fall into several classes: The normal ("vesicular") lung sound and its variations (tracheal and bronchial in appropriate locations), musical sounds (wheeze, rhonchi, and stridor), and

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discontinuous sounds (fine and coarse crackles, friction rubs, and squawks). All are recognized as useful physical findings indicating either health or illness in which the sounds help narrow the differential diagnosis.[3] Chest auscultation offers the clinician the ability to quickly, cheaply, and efficiently assess the respiratory system.[4]

In recent years, investigators began exploiting the development of microelectronics and machine learning to assess respiratory sounds in ways previously impossible or impractical.[5] Miniature acoustic sensors, computers, and wirelessly connected devices such as smartphones[6] have provided a framework to overcome technical obstacles. Such capabilities have propelled research and development of novel devices to monitor respiratory sounds (Fig 1). Resulting publications reflect the impact of artificial intelligence, particularly in recent years (Fig 2). These have appeared mostly within the engineering literature, even though such capabilities would be of great interest to pulmonologists, pediatricians, and primary care practitioners.

We believe that this technology holds the most promise when focused on four sounds that are associated with common and clinically important conditions. This requires a broadening of the previously mentioned definition of "lung sound," so henceforth we refer to "respiratory sounds" (Fig 3).[7] These four sounds are wheeze, snoring, cough, and crackles. When present, adventitious sounds and cough can be objectively assessed in the clinic, but outside of that, clinicians rely on subjective reports from the patient or family. Snoring is almost exclusively reported by bed partners. Crackles are clinic-only sounds. Machine learning algorithms that can run on small-scale instruments are opening up the possibility of developing stand-alone, even wearable devices that may permit convenient, long-term assessment of these conditions, using acoustic analysis outside of the clinic or hospital when doing so is deemed necessary or desirable. Until recently, such equipment was unwieldy, complicated, and incapable of timely automatic interpretation.[8,9] This review is intended to make pulmonary specialists, internists, pediatricians, and general practitioners aware of these developments.

Literature Search

We carried out a PubMed advanced search on ([lung sounds] OR [respiratory sounds]) AND ([computer] OR [spectral] OR [waveform] OR [artificial intelligence] OR [deep learning] OR [machine learning]). We excluded case reports and publications without relation to the recording and analysis of human respiratory sounds. We considered full-length papers in peer-reviewed journals and in the English language. We selected recent review

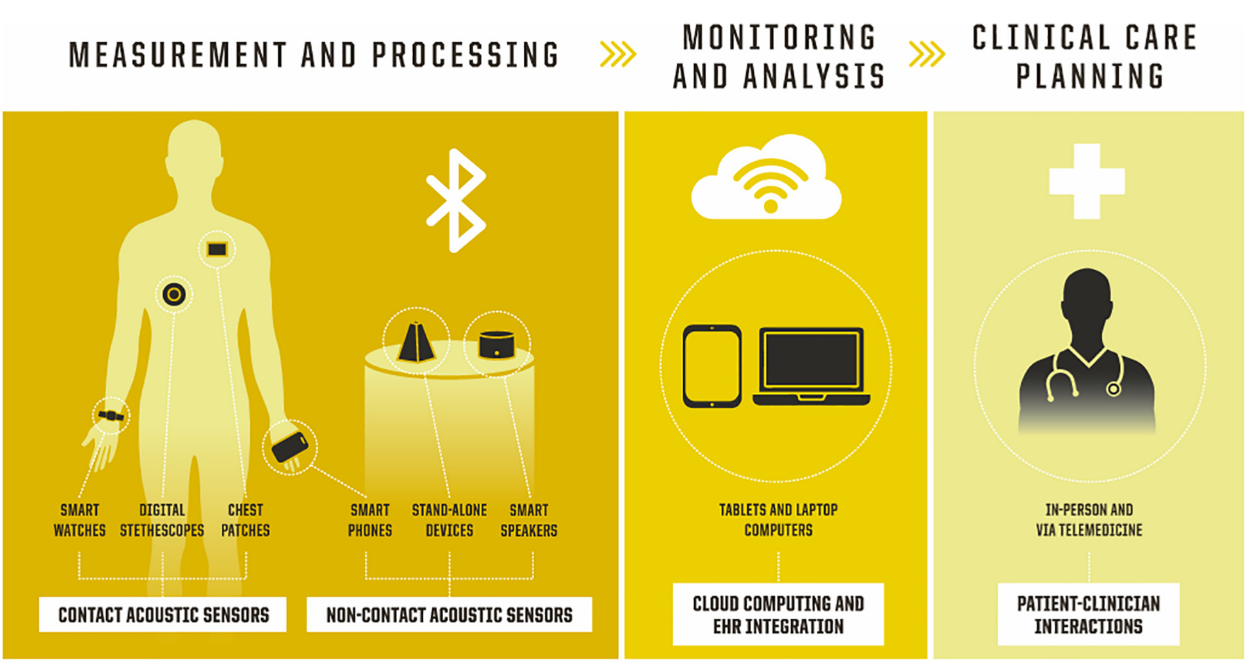

Figure 1 – *Technologic advances with relevance to respiratory sounds. EHR = electronic health record; cloud computing = network of remote servers on the internet to store, manage, and process data.*

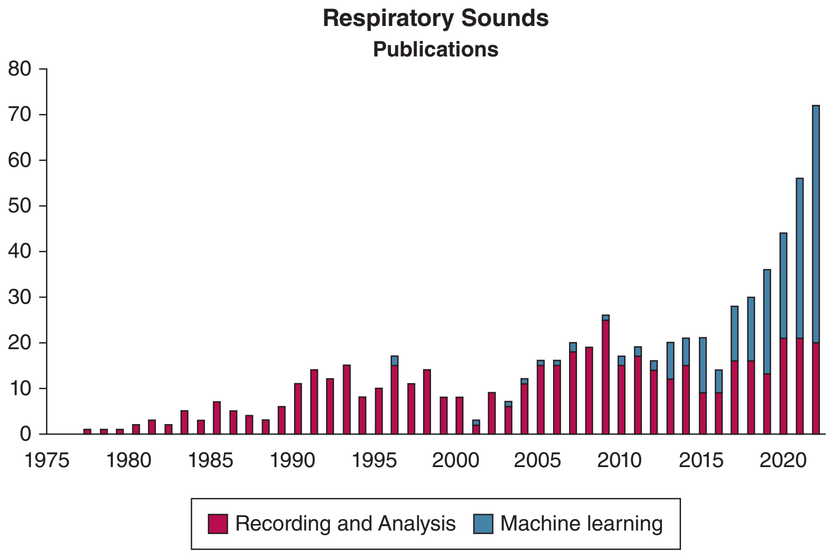

Figure 2 – *Reports of the acquisition and processing of respiratory sounds have greatly increased during the past decade. Most of these publications are directed toward biomedical engineers and involve machine learning (artificial intelligence, deep learning).*

articles, reports of new technologies, and existing clinical applications as well as perspectives on current developments and future potential.

Evidence Review

Wheeze

Wheezing is an audible hallmark of airway obstruction.[10-12] Clinically, the correlation of wheeze severity, defined as the average proportion of wheeze per breath,[13] with the severity of obstruction has been widely used in automated methods of acoustic monitoring. However, whereas the presence of wheeze reliably signals airway obstruction, the absence of wheeze does not assure absence of obstruction, eg, shallow spontaneous breathing with mild obstruction or very severe airway obstruction.

Wheeze is a frequently measured and analyzed respiratory sound because of its clinical utility as well as its distinct acoustic characteristics.[10] Its tonal nature relative to the noisy sounds of breathing lends itself well to spectral analysis, yielding easily interpretable estimates of severity in the context of respiratory phase and chest location. To further exploit the presence of wheeze for patient diagnosis or monitoring, investigators have applied machine learning approaches[14] with high detection sensitivity and specificity in clinical environments.[15]

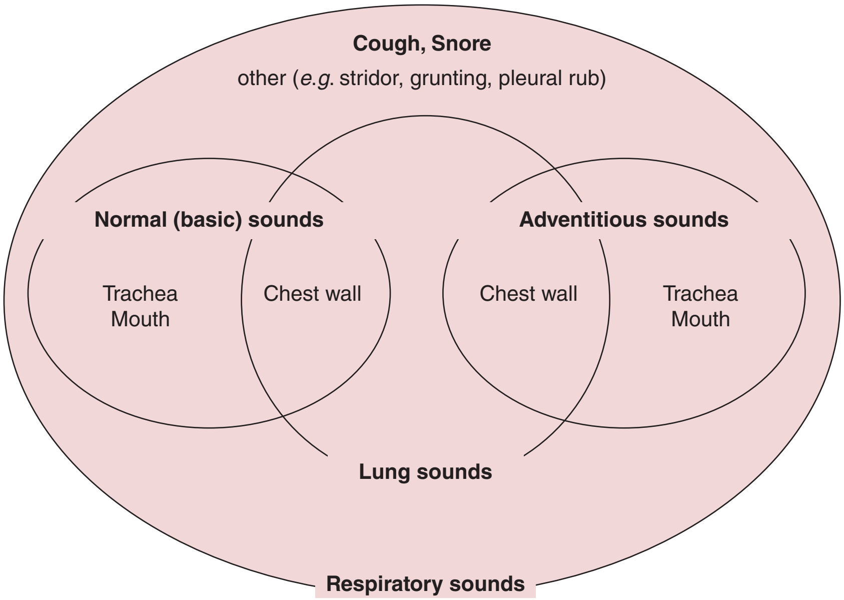

Figure 3 – *Categories of respiratory sounds (modified from Pasterkamp et al[7]).*

Although wheezes appear in several conditions, their recognition in adults is potentially of importance in the detection of breakthrough bronchospasm when the clinician is unavailable, and especially during sleep. Another potential use for ambulatory wheeze monitoring is in the assessment of occupational asthma, an often difficult and time-consuming process attributable primarily to symptoms that may occur only when the patient is at work or at home after work combined with "the forensic nature of attempting to establish a causal association between exposure and disease."[16] The opportunity to use a wearable device that would provide an objective detection of the presence, timing, and severity of wheeze throughout a work week would be transformative.

In children, wheezing is common, particularly during their first years of life, and almost one in five young children may experience recurrent wheezing. Most of their obstructive airway diseases are caused by respiratory viral infections. Clinically, a resulting increase in respiratory secretions and mucosal edema, a.k.a. "snotty lungs,"[17] can lead to different types of "wheeze" than that predominantly caused by bronchospasm. These different wheezes, also referred to as "ruttles" in the United Kingdom,[18] are particularly common in very young children. The automated characterization of wheezing in young children has focused predominantly on readily distinguishable whistling sounds, whereas the mix of rhonchi and coarse crackles have not been adequately addressed by current approaches to automated wheeze detection. Analysis of respiratory sounds in infants with viral bronchiolitis shows repetitive complex sound waves that are unlike the sinusoidal waves of whistling sounds.[19] Observations in a small group of wheezy infants suggest that such respiratory sound characteristics may relate to their response to bronchodilator inhalation.[20] Progression of recurrent wheezing during the first years of life to an established diagnosis of asthma later on occurs in only a minority of children.[21] The occurrence of wheezing episodes during early childhood, or "wheeze trajectories," can predict asthma in adolescence,[22] and their objective documentation by parents and caregivers is now becoming feasible with digital stethoscopes and wheeze detectors.[23,24] Also, in the absence of spirometry in young children outside of specialized centers, wheeze is often viewed as a quantifiable measure of airway obstruction. In fact, wheezing is an explicit parameter in almost all clinical scores of asthma severity in children.[10] New possibilities of recording with digital stethoscopes at the point of care, cloud storage of vast numbers of annotated sound clips, and the application of machine learning techniques offer great hope for a more reliable use of wheezing as a clinical sign in children.

As a foundation, numerous annotated databases of respiratory sounds (including wheeze) as measured in a myriad of settings have recently been created.[25] The most translational progress in device development has been made via partnerships between academic engineering with its novel technologies, medical centers for guidance and patient access, and companies for product development and manufacturing. One such is StethoMe, which markets in the European Union a handheld electronic stethoscope for home asthma monitoring with embedded machine learning algorithms for adventitious sounds detection and cloud-based connections to health care providers.[26] StethoMe also offers access to its algorithms to clinical investigators worldwide to accelerate efforts to relate measurements made with other electronic stethoscopes to pathophysiology and, in turn, clinical care. Another example is Strados in the United States through its development and marketing of a Bluetooth-enabled acoustic sensor patch that is placed on a patient's chest. This wearable device connects via communication techniques to electronic health records and provides a 24-h recording and summary akin to a Holter monitor.[27] In addition, to overcome the corruption of respiratory sounds measurements caused by noisy environments, Sonavi Labs in the United States has developed and markets a handheld stethoscope with a microphone array and embedded noise-canceling algorithms that allow high-fidelity recordings in field clinics within low-resource settings.[28] Hybrid devices are rapidly emerging as well, with Omron in Japan evaluating a handheld unit that combines a spectral analysis approach to wheeze detection with a machine learning one for ambient noise cancellation.[29] The widespread adoption of these and other rapidly emerging technologies will require engineering-medicine-industry partnerships that inform and shape these innovations in the most clinically relevant ways.

Cough

Cough, and especially chronic cough, are two of the most frequent problems encountered by pulmonologists.[30] The recording and analysis of cough sounds shares much of the technology that is in use for respiratory sounds, and in itself, cough is closely related to pulmonary conditions that also generate adventitious respiratory sounds. The sound of a cough is caused by vibration of the large airways and laryngeal structures during turbulent flow in expiration and is said to be individualized, akin to individualized voice.[31] A characteristic cough sound waveform has an explosive, an intermediary and a voiced phase (Fig 4), although the latter is absent in approximately one third of subjects.[32]

Although the most common causes of chronic cough—asthma, postnasal drip, gastroesophageal reflux syndrome, and side effects of angiotensin-converting enzyme inhibitors—are often revealed by history, physical examination, and therapeutic trial, some chronic coughs are frustratingly resistant to all diagnostic attempts and can last for years or decades. The recent development of orally administered selective P2X3 receptor antagonists[33] promises to offer relief to patients with chronic cough regardless of cause. However, the effectiveness of any cough suppressant, especially during sleep, is difficult to determine by subjective cough assessment. This is where wearable or free-standing AI-enabled cough counters could be most useful. Because cough is easily measured at a distance, software running on a smart phone could be useful if appropriately validated.

In children, cough is a common symptom leading to visits to general practitioners. It is typically caused by viral respiratory tract infections and resolves in most cases within 2 weeks.[34] Prolonged acute cough (extending past 3 weeks) and chronic cough (beyond 8 weeks) often lead to further investigations. Physicians have to be aware that the cause of chronic cough in children differs from that in adults.[35] Objective documentation of recorded cough in children by manual counting of events was first reported in 1966.[36] Cough counting systems remain a niche research tool, but recent technological advances are driving the development of real-time fully automated ambulatory cough frequency monitoring.[37] Given the frequency of respiratory viral infections in children, objective documentation by recordings of cough, particularly at night, could resolve the question of recurrence vs persistence and allow for automated characterization. Subjective cough quality descriptors, eg, productive and wet sounding vs dry or barking, correlate well with observations on bronchoscopy,[38] but their specificity is not high enough to accurately distinguish between common acute respiratory illnesses in children.[39] Furthermore, parental characterization of their children's cough can differ significantly from the classification by physicians,[40] and their reporting of cough severity can be biased.[41] Considering the pace of current developments, wearable sensors and contact-free techniques to record cough in children, reliably count cough events, and acoustically characterize these in relation to annotated circumstances and medical diagnoses should overcome such limitations.

Stand-alone cough-counting devices such as the Leicester Cough Monitor from the United Kingdom and the VitaloJAK (joint US/UK)[37] have exhibited in controlled conditions high accuracy in cough counting in a range of pulmonary disorders. More recently, however, smartphone-based cough counters and classifiers using machine learning techniques offer the ability to create large databases of cough sounds arising in various diseases and under a range of measurement environments and conditions.[42] Working with an array of engineering and medical partners in Australia, ResApp Health's app-based system has exhibited utility through a pair of clinical studies in both detecting

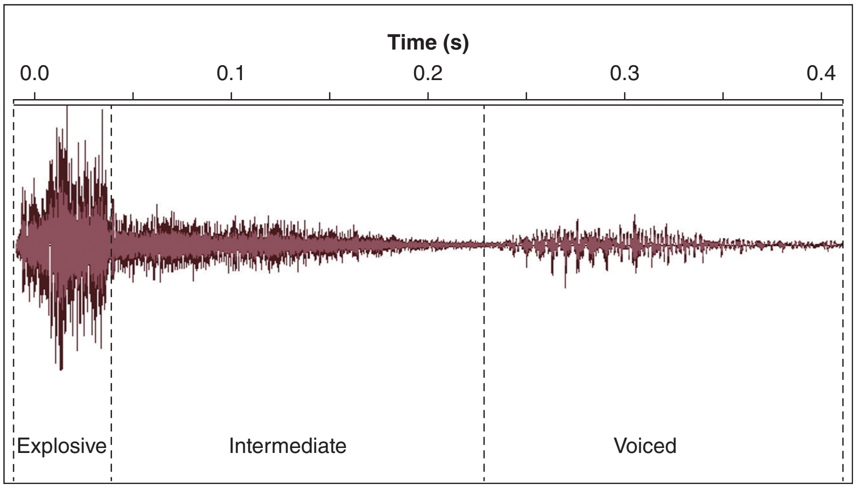

Figure 4 – *Typical cough waveform.*

COPD exacerbations[43] and diagnosing pneumonia. In addition, Hyfe in the United States is creating a large cough sounds database from patients with infections as a foundation for early detection of such diseases as TB and COVID-19.[44] These automated, efficient, connected technologies have the potential to impact a wide variety of patients by bringing accurate information to the clinician on cough rate and acoustic quality as it relates to disease state. A current example is a free smartphone application (Coughtracker), developed by Hyfe and released by Merck & Co to the general public, making it simple for anyone to count their coughs day and night.

Snore

The snoring sound is the result of vibrations of the soft tissues of the pharynx, soft palate, and uvula in addition to variable degrees of airway collapsibility.[45-47] Endoscopic evaluation of upper airway structures during snoring has revealed flutter of the soft palate, which may be combined with noise generation by vibration of other structures, such as tonsils, tongue base, and epiglottis.[47] In children, the functional anatomy of the upper airway is significantly different from that of adults, and snoring sounds may arise from different anatomical sites. Although the soft palate is predominantly involved in adult snoring, only a minority of children have palatal snoring.[48]

Snoring is an important indicator of the presence and severity of OSA/hypopnea,[49] with poor sleep, daytime hypersomnolence, disturbance of bed partners, and association with all-cause mortality.[50] Testing for sleep apnea usually follows the discovery of certain symptoms, such as snoring, daytime sleepiness, failure to wake up in the morning refreshed, and so forth. However, polysomnographic testing in a sleep laboratory is inconvenient, expensive, and sometimes inaccurate if the patient is unable to sleep normally. Home tests are cheaper and often effective; however, unlike the tests done in a sleep laboratory, they measure breathing only, not sleep stage, and are not attended, so a device malfunction or the patient turning face down cannot be corrected.

In children, snoring may occur when their upper airways become congested during viral respiratory infections. Habitual snoring, however, that is, snoring loudly at least 3 nights per week,[51] is often a sign of sleep-disordered breathing. Acoustical analysis of snoring in children shows a greater likelihood of OSA/hypopnea in those who have a greater snore index (average snores/h) and louder snoring.[52] The impact of sleep-disordered breathing on cardiovascular long-term morbidity is more clearly documented in adults than in children,[53] but strong evidence suggests that childhood sleep-disordered breathing is associated with deficits in neurobehavioral functioning, and clinical symptoms such as chronic snoring remain the best predictors of morbidity.[54] While estimating the severity of snoring in young children relies on parental recall, which can be biased and often leads to underreporting,[55] contactless nocturnal recordings of snoring in children, eg, with sensors embedded in a mat that is placed on the mattress,[56] offers objective documentation. Observations over longer periods should become more widely available with novel wearable sensors and wireless transmission of data.

Numerous recently developed smartphone-based apps, such as SnoreLab[57] in the United Kingdom, record and analyze snoring to both determine its prevalence and assess its relation to various body position changes. A growing number of therapeutic devices are aimed at decreasing upper airway vibration. More sophisticated technologies, such as that under development by ResMed[58] in the European Union, integrate advanced acoustic techniques, including echo ranging to assess body position and movement as well as noise-canceling to reduce bed partner and other extraneous room sounds. These approaches offer the potential to augment or eventually replace at-home sleep studies. As these smart devices[59,60] and applications become widely available, they will also be adopted by members of the public and used to obtain information about their own health, much as they are already doing with fitness trackers, smart watches, and oxygen saturation-heart rate monitors. Such novel devices are changing the relationship between patients and health care providers.

Crackles

Relative to wheeze, crackles are a challenge to record on the chest surface because of the potentially confounding effects of similar noises generated by transducer motion or the rubbing of clothing.[61] Thus, the increasing number of devices that contain crackle detection and characterization algorithms typically employ some form of noise cancellation that is either passive (sound damping materials or a flexible sensor that conforms to the skin surface),[62,63] active (with multiple transducer elements some of which measure the noise),[28] or computational (containing advanced analytics to separate crackles from noise based on subtle discriminating features).[64] Such devices include the aforementioned Strados, Sonavi Labs, and

StethoMe systems, amongst others that are commercially available, as well as numerous in translation from academic laboratories toward production. These crackle analysis systems are targeted for use in home or work settings with respiratory sound identification capabilities comparable to those of trained experts.[64] Such focused applications have spurred the creation of new annotated databases specific to crackles. For example, eKuore, in collaboration with pharmaceutical companies in the European Union, developed a system to discriminate fine crackles heard in patients with pulmonary fibrosis[65] from the coarse crackles heard in patients with other respiratory diseases such as bronchitis. The integration of these disease-specific advances is collectively eliciting a trend toward devices with comprehensive analysis platforms that detect and simultaneously analyze in a holistic manner, complex recording that may contain multiple respiratory sounds such as wheeze and crackles.

Future Directions

These technologies have unveiled new ways in which respiratory sounds can be used to inform and enhance patient care, particularly for those patients with chronic conditions that are prone to exacerbation. Wheeze, cough, and snore are exemplar sounds in this regard because they readily reflect pathophysiologic changes and have well-recognized and easily accessible acoustic characteristics.

The development of the next generation of technologies that exploit the information inherent in respiratory sounds can be broken down into three overlapping stages, each of which is bolstered by machine learning approaches as already anticipated in 2014.[66] The first stage, which is already upon us, is the ability to accurately detect the occurrence of these respiratory sounds in an ergonomically friendly way in uncontrolled environments such as home or work, and during both day and nighttime. Miniature microphone arrays containing embedded noise reduction functions are already appearing on the market in both digital stethoscopes and wearable patches. Similar technologies could readily be introduced into smartphones and smart speakers and used for cough and snore detection. Machine learning algorithms that differentiate the sounds of interest from background noises are entering the market as stand-alone devices or software. This trend toward preventive monitoring has begun to alter the care paradigm available for such patients.

The second stage of technology development, which is emerging already in some devices and is heavily reliant on machine learning approaches, is reflected in the capability not only to detect and count respiratory sounds but also to analyze and place them into

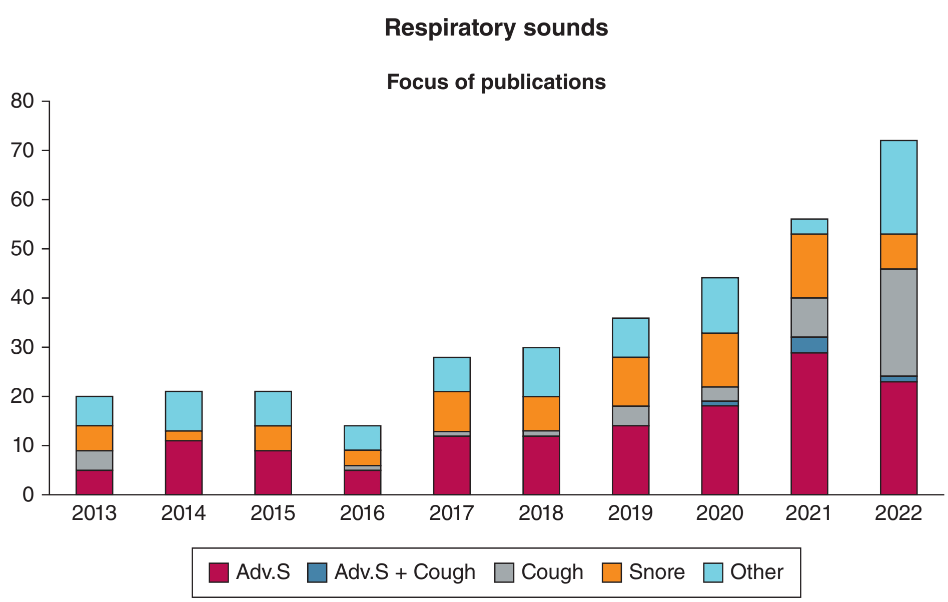

Figure 5 – *The rapid increase of publications that are focused on adventitious sounds (Adv.S.), and cough predates the years of the COVID-19 pandemic and has greatly increased since 2020 because of the need for contact-free monitoring. "Other" includes studies on normal (basic) respiratory sounds and unspecified "breath sounds."*

clinically useful categories. Distinguishing between wheeze arising from bronchospasm and other wheeze-like sounds in children, differentiating unproductive "dry" from productive "wet" coughs, and identifying the anatomical upper airway site where a snore arises serve as examples. The incorporation of these and other such capabilities into devices and applications is occurring rapidly, fueled by the ever-growing number of databases of respiratory sounds that are annotated by experts and used to train the embedded machine learning algorithms. Features that allow for automatic respiratory sound characterization will become available within the next few years. How useful they become will ultimately depend on the quality and completeness of the clinical information in respiratory sound databases. High utility will be achieved only through significant clinical knowledge being infused into the device design process throughout its software development.

The third development stage, which has just begun, accelerated by the need for patient assessment at a distance during the COVID-19 pandemic (Fig 5), will take some years and even more clinical input to complete. It focuses on how to coalesce respiratory sounds information with other clinical signs, symptoms, and tests to optimize their additive value to patient outcomes. This data integration goes well beyond the simple inclusion of respiration sound information in electronic medical records and will elucidate which patient groups benefit most from these noninvasive monitoring systems. Although this remains a challenge, when machines learn respiratory sounds based on the "ground truth" of human experts and enhanced by clinical "meta-data,"[67] we can expect significant progress in diagnostic utility in the next decade from sounds measured in the home or afield.

Summary

The growing interest in respiratory sounds as noninvasive indicators of disease squarely rests on more than two centuries of research that started with Laennec[1] and links what is heard to underlying anatomical and pathophysiologic changes via acoustic principles. However, what has catalyzed its resurgence in the last few years are a myriad of technical advances that allow for the ready measurement of these sounds in nonclinical settings and subsequent rapid analysis that matches or even exceeds that of a trained professional (Fig 1). We anticipate that this is only the beginning of the rise of the respiratory sound machines.

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