INTRODUCTION

Air pollution poses tremendous threats to human health.1,2 In 2015, global deaths and disability-adjusted life-years attributable to air pollution were 6.485 million and 167.3 million, respectively.3 Recently, an increasing number of studies have documented the adverse impacts of environmental exposures on human health.2 These investigations have furthered the understanding of associations between environmental conditions and human health. Although global efforts toward climate change have improved air pollution in some regions, there is still a need for strategies to minimize its adverse effects and protect people from the same.4 Many recent studies have focused on incorporating the precision medical approach into efforts to reduce the effects of environmental exposure on human health using digital healthcare technology.

Major environmental health issues are chronic airway diseases, especially asthma and chronic obstructive pulmonary disease (COPD), as the lungs are the first bodily destinations for any inhaled environmental particulates. These particulates directly induce pulmonary inflammation, increase susceptibility to respiratory tract infections, and narrow the airways.4 Acute exacerbation of chronic airway diseases accelerates disease progression, worsens quality of life, and increases mortality risk. Environmental exposure and response analyses have suggested that air pollution increases the risk of acute exacerbation of chronic airway diseases.5 Several studies have attempt-
ed to develop prediction models for acute exacerbation. However, their integrated environmental exposure data have been obtained from open public sources; as a result, the immediate consequences of environmental exposure have not been adequately evaluated. This limitation has made it difficult to apply real-time prediction models to patients. Real-time prediction models can provide patients with early self-detection and allow immediate self-management of acute exacerbation of chronic airway diseases. In order to develop a real-time precision medical approach toward human health in response to environmental exposure, particulate measurements and physiological signs should be collected individually and in real-time.

In light of these motivations, we have first discussed the application of digital health technologies in general environmental healthcare and chronic airway disease management. Moreover, we have reviewed and suggested how digital health technologies can be applied to reduce the adverse effects of environmental exposure in chronic airway diseases, based on personal exposure-response modeling.

SECTION 1: AIR POLLUTION AND DIGITAL HEALTH TECHNOLOGIES

Scientific research on air pollution exposure can be divided into two categories: modeling exposures in large populations, and measuring exposures in individuals. Large scale approaches include measuring air pollution level with new sources and high-tech/low cost sensors, and predicting ambient pollution with new models to provide higher resolution. Elaborating personal exposure to air pollution include tracking individual chronological position and matching it with air pollution map, measuring personal exposure itself with portable sensors, or both. With recent advances in computational modeling and personal mobile devices, researchers have been enabled to combine all technologies and begin to estimate personal, chronological exposures to air pollution. This section focuses on how new technologies are developing the personal exposome research field (Table 1).

| Method                      | Example                     | Advances                                                                 |
|-----------------------------|-----------------------------|--------------------------------------------------------------------------|
| Modelling ambient pollution | SHEDS, AERMOD, RLINE        | - Incorporate new variables: pollution emissions data, topography, meteorological data, satellite data, personal behavior/time activity, and micro-environmental characteristics |
| ML-based prediction         | Di, et al., 2019; Huang, et al., 2021 | - Provide 100× higher resolution from satellite-based measurements by applying mixed-effect models with ML algorithms |
| Air pollution measurement   | Özkaynak, et al., 2013; van Donkelaar, et al., 2015 | - Measure aerosol optical depth in global scale with 1×1 km resolution and 10-year timelines |
| World Air Quality Index project | Rodriguez-Urrego, et al., 2020 | - Combine global air pollution station measurement and produce real-time data |
| Citizen science initiatives  | iSPEX; xAire; CuriezeNeuzen | - Produce air pollution measurement data from citizen volunteers with very high spatio-temporal resolution |
| Low cost sensors            | Barkjohn, et al., 2021; Feinberg, et al., 2019 | - Increase resolution and accuracy of government monitoring stations |
| Portable sensors            | PAM; AirBeam | - Gold standard for personal air pollution exposure assessment |
| Personal time-activity tracking | mHealth based GPS records | - Differentiate personal exposures by combining high-resolution air quality prediction model with individual time-matched travel records |

SHEDS, Stochastic Human Exposure and Dose Simulation; AERMOD, American Meteorological Society/Environmental Protection Agency Regulatory Model; RLINE, Research-LINE; ML, machine learning; PAM, personal air monitor; mHealth, mobile health; GPS, global positioning system.

Ambient air pollution prediction

Conventional measurements from government or central-site monitors lack the spatiotemporal resolution to assess complex personal air pollution exposure data. Stationary monitoring sensors are known to represent concentrations of their immediate surroundings. However, recently developed models (e.g., Stochastic Human Exposure and Dose Simulation, SHEDS; American Meteorological Society/Environmental Protection Agency Regulatory Model, AERMOD; Research-LINE, RLINE) incorporate other variables, including pollution emissions data, topography, meteorological data, satellite data, and micro-environmental characteristics, and offer higher resolution in ambient concentrations. Nowadays, efforts are being introduced to further enhance the accuracy and resolution of estimated...
concentrations with new data sources discussed below.

Remote sensing by satellite-based sensors is one of the most valuable data sources in estimating global air pollution.\textsuperscript{6-11} Measuring aerosol optical depth (AOD), the amount of light extinction in the given atmospheric column due to aerosols, gives estimates of particulate matter (PM\textsubscript{2.5}) at a 1×1 km resolution all over the Earth. These records can span timelines as long as a decade.\textsuperscript{13} Sentinel-5 and Sentinel-5P, which were launched in 2017 by the European Space Agency, are expected to further enhance this technology with their own high-resolution capacities.

Another novel approach is densifying air monitoring data at the ground level to calibrate remote-sensed air pollution data. Real-time air quality index data is now available for more than 30000 stations in 2000 major cities from 133 countries, provided by a non-profit project known as the World Air Quality Index project.\textsuperscript{12} This approach enabled the collection of global-level data and comparison between capital cities of different countries.\textsuperscript{15} Citizen science initiatives, such as iSPEX,\textsuperscript{14} xAire,\textsuperscript{15} CurieuzeNeuzen (Curious Noses) in Flanders\textsuperscript{16} and many others have also contributed to new monitoring data from new sources. Citizens involved with CurieuzeNeuzen numbered 2000 in Antwerp\textsuperscript{17} and 20000 in Flanders,\textsuperscript{16} with each individual representing one nitrogen dioxide (NO\textsubscript{2}) measurement location, compared to only 67 official reference stations in Flanders. De Craemer, et al.\textsuperscript{16} normalized each short-term measurement of NO\textsubscript{2} into annual average concentrations at each location, resulting in very densely positioned NO\textsubscript{2} measure data. On the other hand, ISPEX is a newer citizen-based approach using mass-producible air sensors. Using a smartphone add-on for iPhones, Snik, et al.\textsuperscript{14} produced AOD data with a 2-km spatial resolution, and improved temporal resolution as compared to satellite data. These new approaches are creating a paradigm shift and tremendously improving spatiotemporal resolution of pollution models.

Personalized mobile sensors and wearables have emerged as new data sources with innumerable variables and immeasurable measurements, and their advances are discussed later in this review. With these new-generation data, models combining machine learning (ML) algorithms have increased the spatial resolution of daily ambient PM\textsubscript{2.5} concentration to 100×100 m in the US\textsuperscript{14} and China.\textsuperscript{3} The more “big data” is generated, the more model resolutions can be increased and improved.

**Mobile health (mHealth) technologies**

The global spread of smartphone usage has allowed mHealth to expand worldwide. As of 2021, more than 6 billion smartphone subscriptions are operating across the planet.\textsuperscript{18} With the maturity of information and communication technology, the use of digital technologies for healthcare offers unique opportunities for product and service accessibility and affordability.\textsuperscript{18} Furthermore, mHealth products—mostly smartphones and wearable devices—also have the capacity to collect time-activity patterns, easily recruit participants based on mobile applications (apps), and record external and internal biomarkers of air pollution exposure.

Time-activity patterns, which link stationary air pollution concentration data to dynamic real-world personal exposure, are recorded in high spatiotemporal resolution using the smartphones’ global positioning system (GPS). Smartphone GPS can distinguish distances less than 10 meters and record every 5 to 10 minutes.\textsuperscript{19} Based on spatiotemporal regularity in time-activity patterns,\textsuperscript{19} it has been suggested that seasonal measurements of several days may be sufficient to capture individual variation in pollution exposure.\textsuperscript{6} Studies are now utilizing such GPS data in estimating individual air pollution exposure. For example, in the Prospective Urban and Rural Epidemiological (PURE) Air study,\textsuperscript{20} researchers were able to differentiate personal exposures with high spatiotemporal resolution by combining their time-matched travel records, even within the same city.

The mHealth apps are a novel primary platform to conduct air pollution epidemiologic studies and design interventions to encourage health-positive behaviors. One of the most popular mHealth platforms for research is ResearchKit, provided by Apple. It is an open source framework that provides codes from established apps to recruit and survey participants, obtain digital consent, collect biometric data, provide notifications (“push interventions”), and secure data transmission and storage.\textsuperscript{21} In the Asthma Mobile Health Study (AMHS),\textsuperscript{22} this app was downloaded 49963 times during the first 6 months after its launch, recruiting 7593 participants across the United States. The researchers were able to link asthma exacerbation to increased heat, pollen, and air pollution, caused by wildfires in the U.S. state of Washington. This study publicly made available data from 6346 consenting participants as well.\textsuperscript{23} The very nature of mHealth app allows rapid enrollment, poses minimal risks, and facilitates frequent data collection with high temporal resolution in real-world settings. These qualities are best suited for pollution exposure epidemiology studies.\textsuperscript{24,25} However, selection bias, reporting bias, and privacy issues are major concerns that need to be addressed.

**Air sensors—outdoor, indoor, portable, and wearable**

Recent inventions of air sensors have made air pollution monitoring more affordable, accessible, and accurate. According to the Joint Research Centre (JRC) of the European Union, PA-II by PurpleAir (PM\textsubscript{1}), AirNut by Moji China (PM\textsubscript{2.5}), Egg (2018) by Air Quality Egg (PM\textsubscript{1}), PATS+ by Berkley Air (PM\textsubscript{2.5}), S-500 by Aeraloaq (NO\textsubscript{2}, O\textsubscript{3}) showed R\textsuperscript{2} more than 0.85 with their prices lower than 500 EUR.\textsuperscript{26} Researchers in the U.S. Environmental Protection Agency (EPA) recently reported that nationwide PM\textsubscript{2.5} measurements can be corrected using PurpleAir data all over the U.S. by reducing the root mean square error of the raw data from 8 to 3 μg/m\textsuperscript{3}.\textsuperscript{27} In the CitySpace project\textsuperscript{28} conducted by the EPA, 17 Alphasense OPC-N2 PM sensors were deployed as a network. Although only six sensors passed the quality control tests, 1-minute data from them were able to locate an emis-
tion source responsible of 20% of local PM$_{2.5}$ emissions. Advances in indoor low-cost sensor technologies have also emerged in research, due to the expansion of digital products, termed the “Internet of Things.” However, out of 35 research studies which developed unique devices from 2012 to now, only 16 studies focused on calibration and validation, and even fewer conducted tests with references. Therefore, further studies in calibration and validation, with appropriate reference measures, are required.

Personal measurement is the gold standard for air pollution exposure assessment. To derive long-term exposure effects, data should be collected over sufficiently long periods of time, with highly validated accuracy. “Personal air monitor” (PAM) is one of the most recent and useful portable air sensors, developed at the University of Cambridge. This sensor can measure concentrations of particulate matters (PM$_{1}$, PM$_{1.5}$, PM$_{2.5}$) and gaseous pollutants (CO, NO, NO$_2$, O$_3$) every 20 seconds while recording personal activity and meteorological variables simultaneously. This cube-shaped small device is sized 13×9×10 cm, and weighs only around 400 grams. It is now being used in many studies. For instance, the Effects of AIR pollution on cardiopulmonary disEaSe in urban and peri-urban residents in Beijing (AIRLESS) study was conducted as a part of a joint UK-China program named Air Pollution and Human Health in a Developing Megacity (APHH-Beijing). In consecutive groups, 251 participants carried 60 PAMs for several times a week to expose to strong emission sources at home. The PAM device was simultaneously. This cube-shaped small device is sized 13×9×10 cm, and weighs only around 400 grams. It is now being used in many studies. For instance, the Effects of AIR pollution on cardiopulmonary disEaSe in urban and peri-urban residents in Beijing (AIRLESS) study was conducted as a part of a joint UK-China program named Air Pollution and Human Health in a Developing Megacity (APHH-Beijing). In consecutive groups, 251 participants carried 60 PAMs for several times a week to measure personal exposure to ambient and indoor air pollution. Preliminary data of this study showed considerable difference between personal exposure and ambient air pollution measures, especially in winter when participants were often exposed to strong emission sources at home. The PAM device was also used in the “characterisation of COPD exacerbations using environmental exposure modelling (COPE)” study in UK. Preliminary study results emphasized the impacts of gaseous pollutants. Ma, et al. used the AirBeam (HabitatMap) portable sensor with Android-based GPS trajectory data, which are recorded every second and uploaded to the AirCasting website. This study was also able to detect considerable differences between real-time personal exposure data and measurement station data, even when the participants were outside.

Wearable sensors are expected to accelerate new methodologies that can provide not only human biomarkers, such as pulse rate, respiratory rate, oxygen saturation, physical activity, sleep patterns, and stress levels, but also personal pollution exposure data with the highest spatiotemporal resolution. However, currently affordable, minimally-sized sensors still lack accuracy, and their data are confounded by various factors including the weather, location of sensor on the body, or urban structures. Until now, portable sensors with reliable functioning are at least as large as palm-sized (AirBeam, Atmotube PRO, etc.). Nevertheless, future science will make truly “wearable” sensors possible.

SECTION 2: CURRENT STATUS OF DIGITAL HEALTHCARE TECHNOLOGIES FOR AIRWAY DISEASES

Digital healthcare technologies, characterized by high computing power and mobile connectivity, are changing the mode and quality of patient care and clinical research. The current research on digital healthcare in airway diseases differs across various fields, but is an active line of enquiry.

**Modeling for exacerbation prediction**

Chronic airway diseases, such as asthma and COPD, are major causes of chronic morbidity and mortality in global health. Acute exacerbation of these diseases often results in hospitalization, declined lung function, impaired quality of life, and high mortality. Therefore, accurate detection of exacerbation would support early disease management and reduce morbidity and mortality.

Several studies have developed prognostic tools to enable personalized prediction of exacerbation (Table 2). Guerra, et al. evaluated 27 models for acute exacerbation of COPD (AECOPD), which used traditional statistical methods such as logistic regression analysis and Cox regression analysis. The authors stated that most models were at high risk of bias due to improper statistical methodology. Systematic reviews of prediction models for asthma exacerbation also found that the models were primarily grounded in epidemiological studies and population-based risks; consequently, their predictive powers were suboptimal.

The evolution of computer science offered the capacity to integrate multiple data sources, increasing the accuracy of predictive models. Approaches with ML showed promise in improving prediction ability; therefore, many studies have used ML algorithms for the acute exacerbation of airway diseases. Zein, et al. developed a ML-based model to predict asthma exacerbation using real-world data from ambulatory patients. Its prediction performance in utilization of healthcare resources, such as asthma-related emergency department (ED) visits and hospitalization, was superior as compared to those using classic logistic regression. Moreover, the authors gathered data directly from electronic health records from healthcare systems instead of clinical trials, reflecting the variety of real-world situations. Wu, et al. also developed a ML-based model to predict AECOPD. Lifestyle and environment data of patients with COPD were integrated into the model, which improved its prediction power as compared to previous models using clinical questionnaires.

The ML-based approach was extended to severity assessment tools for acute exacerbation of airway diseases after ED visits and hospital admission. ML markedly improved the ability to predict clinical courses, in comparison to conventional approaches. Through the real-world implementation of ML, ED management and healthcare resources utilization could
be optimized, and early intervention could be applied.
Although ML-based models have the strength of accuracy, they cannot define causality. Therefore, well-designed randomized clinical trials are still required. In addition, most of the current models use internal validation. Therefore, external validation in different populations would be necessary to establish these models.

### Smartphone apps

Digital healthcare for patients with airway diseases has been extended from acute management in hospitals to daily self-management within communities. Telemedicine and telemonitoring have been widely studied in chronic airway diseases, but mHealth technologies, particularly smartphone apps, have emerged to improve patient health in an easily accessible and patient engaging manner. In 2020, approximately 47140 mHealth apps were available for download; their global market value was estimated at $40 billion, and this is expected to grow annually by 17.7% between 2021 and 2028.49

Smoking cessation is mandatory for chronic airway disease. Most smoking cessation apps are not only aimed at cognitive behavioral therapy as well as acceptance and commitment therapy, but they also provide access to community resources and connections to social network. A systematic review in 2019 found that automated text messaging interventions were effective at motivating people to quit smoking, and improved quitting rates by 50%–60%.50 However, the reviewers also stated that there was insufficient evidence for mobile app-based interventions. Nowadays, studies on app-based smoking cessation are ongoing.51 A Japanese group validated the feasibility and usefulness of smartphone apps to help long-term, continuous abstinence from smoking (Table 3).52 Danaher, et al.53 also found that mobile apps and text messaging were more effective in encouraging smoking cessation, as compared to the conventional internet approach designed for use on non-mobile devices.

**Optimized disease assessment and regular inhalation of therapeutic drugs contribute to controlling asthma and COPD.54 Although geographical barriers or global pandemic circumstances hinder the face-to-face relationship between doctors and patients, mHealth technologies empower patients to maintain self-management at home.55,56** A systematic review in 2021 found that mHealth apps paired with inhaler-based sensors improved inhaler adherence and reduced rescue inhaler use, but did not affect Asthma Control Test scores.57 The reviewers found that the quality of current evidence is moderate, and the availability of relevant products is limited. Mosnaim, et al.58 recently reported a randomized controlled trial of a digital platform-based asthma self-monitoring system. The intervention group, who received audiovisual reminders for inhaler medications and had access to their usage data on the app, maintained high inhaler adherence and decreased rescue medication use. Future studies in mHealth-based self-management systems would help patients make healthy decisions at home.

**Smartphone apps to support pulmonary rehabilitation and long-term care for patients with chronic airway diseases have been designed, but evidence of their effectiveness remains inconclusive.** Vorrink, et al.59 conducted a randomized clinical trial of 157 patients with COPD after they had completed a pulmonary rehabilitation program in the Netherlands. The intervention group using the smartphone app did not improve or main-

### Table 2. Modeling for Acute Exacerbation of Chronic Airway Disease

| Studies                  | Statistical method                                                                 | Measured outcomes                                      | Findings                              |
|--------------------------|----------------------------------------------------------------------------------|--------------------------------------------------------|---------------------------------------|
| Guerra, et al., 2017     | Classic statistical methods (correlation analysis, logistic regression, Cox regression, Poisson regression, negative binomial regression, random forest) | - Outpatient-treated exacerbation                        | - High risk of bias                   |
| COPD (SR for 27 models)  |                                                                                   | - Hospitalization                                       | - Lack of validation                   |
| Zein, et al., 2021       | Classic statistical methods (logistic regression, random forests) vs. ML-based methods (light gradient boosting decision tree) | - Systemic steroid use                                   | - Heterogeneity of statistical methods |
| Asthma (SR for 24 models)|                                                                                   | - ED visit                                              |                                       |
| Wu, et al., 2021         | ML-based classification (random forest, decision trees, k-nearest neighbor clustering, linear discriminant analysis, adaptive boosting, deep neural network model) | - mMRC dyspnea scale                                     | - Poor model calibration               |
| COPD                     |                                                                                   | - COPD assessment test                                   | - Limited external validation         |
| Sills, et al., 2021      | Classic statistical methods (random forest, logistic regression) vs. automated ML algorithm | - Hospitalization during ED visit                       | - Better performance in ML-based model|
| Asthma                   |                                                                                   |                                                         | - Internal validation                  |
| Peng, et al., 2020       | ML-based classification (novel CS.0 decision tree classifier)                      | - Exacerbation during hospitalization                    | - Early detection of aggravation       |
| COPD                     |                                                                                   |                                                         | - Internal validation                  |

COPD, chronic obstructive pulmonary disease; ED, emergency department; mMRC, modified medical research council; ML, machine learning; SR, systematic review.
tain physical activity levels compared to the standard care group. The authors stated that actual physical activity levels should be measured more accurately, and that the smartphone interface to provide immediate feedback should be optimized to motivate participants to adhere to their physical activity goals. 

Another systematic review of systematic reviews by Marcolino, et al.60 also stated that evidence for the efficacy of mHealth in chronic airway diseases is limited.

Recently, a novel mHealth research platform, ResearchKit, demonstrated its value and validity in an asthma study.24 The platform enabled a prospective multidimensional study across the U.S., in which the authors found that self-reported asthma symptoms increased in regions affected by known environmental triggers of asthma, such as heat, pollen, and wildfires. Further large-scale studies are also expected to be conducted using ResearchKit.

However, mHealth studies need to address significant concerns, including selection bias, low retention rates, reporting bias, as well as data security and privacy. To date, most studies have been conducted on younger, wealthier, and more educated Caucasians in high-income countries. Therefore, future studies in low-income countries with different demographics are required. Financial support may facilitate access to mHealth and produce more evidence from the most vulnerable populations.64

In addition, proper regulation of mHealth apps by the Food and Drug Administration should be called for.19,62

### Wearable devices

The COVID-19 pandemic has increased the need for remote health monitoring systems. Technology-enabled biomedical sensors and wearable devices, combined with artificial intelligence, telemedicine, and telemonitoring, have been widely applied in the management of chronic diseases.36,63 Recording individual long and short-term events, and segregation of physiological data from multiple sources, have allowed physicians and patients to monitor patient parameters in any environment.

Oxygen saturation and respiratory rates are proxies of AECOPD. Mehdipour, et al.64 conducted a systematic review of the reliability, validity, and responsiveness of wearable devices that monitor oxygen saturation and respiratory rates in patients with COPD (Table 4). After reviewing seven studies representing 11 devices, the authors stated that remote monitoring devices demonstrate validity in detecting hypoxemia and tachypnea, although their accuracy needs improvement. Effective remote monitoring could facilitate early management and prevention of AECOPD, which would stabilize patients and reduce their medical expenditures.65

Digital stethoscopes and home-based spirometry tests have enabled physicians to monitor more diverse parameters, leading to precise evaluation of the patients’ health status. Digital stethoscopes transform acoustic sounds, refine digital signals, and convey information at optimal sound levels; however, interrater disagreements still exist.66 With artificial intelligence, pathologic breathing sounds can be detected more accurately.67

---

| Table 3. Smartphone Apps for Chronic Airway Disease Management |
|---------------------------------------------------------------|
| **Types** | **Subject characteristics** | **mHealth interventions** | **Findings** |
| Smoking cessation | | | |
| Masaki, et al., 201952 | n=55 | Usual smoking cessation therapies plus CureApp Smoking Cessation app (single arm) | - High continuous abstinence rate  
- High patient retention rates  
- Improvement of cessation-related symptoms |
| Danaher, et al., 201953 | n=1271 | MobileQuit (for mobile devices) vs. Quit Online (for non-mobile desktop or tablets) | - MobileQuit more effective |

Inhaler usage

Nguyen, et al., 202157 | n=7 (SR) Asthma | mHealth apps integrating an inhaler-based sensor | - Small number of available products  
- Positive effects on rescue inhaler use, inhaler adherence, and patient satisfaction  
- ACT scores not affected |

Mosnaim, et al., 202164 | n=100 Asthma | Intervention: real-time tracking and audiovisual feedback of inhaler usage via mHealth app; Control: real-time tracking without feedback | - Intervention group improved baseline ICS adherence and decreased SABA usage |

Pulmonary rehabilitation

Vorrink, et al., 201664 | n=157 COPD | Intervention: mHealth app for physical activity; Control: usual care | - mHealth intervention did not improve or maintain physical activity in patients with COPD after pulmonary rehabilitation |

Self-reported symptom acquisition

Chan, et al., 201724 | n=6470 Asthma | Acquisition of asthma symptoms via mHealth app | - Demonstrated feasibility of the mHealth app in a broad-scale asthma study |

ACT, asthma control test; COPD, chronic obstructive pulmonary disease; ICS, inhaled corticosteroid; SABA, short-acting beta-agonist; SR, systematic review.
Recently, a non-diaphragm wearable stethoscope has been designed as well.68 Altogether, AI-based remote auscultation have the potential to be widely implicated. Furthermore, mobile spirometry tests have demonstrated both feasibility and validity.69,70 They are expected to be widely utilized during the COVID-19 pandemic and other resource-limited circumstances.71 When combined with mHealth apps, telemonitoring with wearable devices can support the patients’ self-management. For instance, Khusial, et al.72 remotely monitored the physiological parameters, inhaler usage, and environmental data in patients with asthma. They found that their mHealth system, myAirCoach, reduced severe asthma exacerbation.

**SECTION 3: EFFECTS AND MANAGEMENT OF ENVIRONMENTAL EXPOSURE**

Previous studies suggest that environmental exposures, especially air pollution, play an important role in increasing newly developed chronic airway diseases or triggering exacerbation of previously diagnosed airway diseases. Therefore, it is an urgent need to develop interventions to minimize environmental harm using integrated digital health technologies through smartphones, air-sensors, wearable devices, and prediction models.

**Effects of environmental exposure on asthma**

Poorly controlled asthma is related to fatal exacerbation, causing high disease burden. Evidence suggests that environmental exposure not only triggers the aggravation of respiratory symptoms, but also leads to the development of asthma. In six European cohorts, moderately significant positive associations were observed between asthma incidence and exposure to NO and NO2.74 Khreis, et al.75 systematically reviewed and meta-analyzed the association between traffic-related air pollution (TRAP) and childhood asthma development in 41 studies. Asthma development was significantly associated with black carbon, NO2, PM2.5, and PM10 exposures, indicating that childhood exposure to TRAP contributes to the development of asthma.

Long-term exposure to PM10 and O3 is associated with uncontrolled asthma in adults, defined by severe symptoms, exacerbation, and decreased lung function.76 Rage, et al.3 assessed the relationship between the participants’ asthma severity during the past 12 months and concentrations of air pollution (TRAP) and childhood asthma development in 41 studies. Asthma development was significantly associated with black carbon, NO2, PM2.5, and PM10 exposures, indicating that childhood exposure to TRAP contributes to the development of asthma.

Air pollutants may aggravate airways inflammation in both allergic and non-allergic asthma. Air pollutants enhance allergen sensitization by increasing the production of the specific Immunoglobulin E (IgE). The 2005–2006 National Health and Nutrition Survey reported that increased levels of NO2 were associated with increased IgE in response to inhalant and out-
door allergens, while PM_{2.5} levels were positively associated with indoor allergens.\textsuperscript{77} Vimercati, et al.\textsuperscript{78} investigated allergic diseases among traffic wardens as compared to a control group of administrative employees. The study found that 60% of traffic wardens were positive to clinical allergological tests, and half of them were diagnosed with allergic diseases.

In nonallergic asthma, Th2 inflammation is often observed in lungs with eosinophilia and nasal polyps, while neutrophilic inflammation is also observed in severe asthma or steroid-resistant asthma with increased IL-17 in airway epithelial cells.\textsuperscript{79} Mice exposed to diesel exhaust particles (DEP) and house dust mites showed markedly enhanced airway hyper-responsiveness, with mixed Th2 and Th17 responses. Children with asthma exposed to high DEP had higher serum IL-17 levels compared to those exposed to low DEP.\textsuperscript{80}

Effects of environmental exposure on COPD

Outdoor air pollution may increase airway inflammation and deteriorate lung functioning for the long term, leading to the development of COPD in the general population. The hazardous effects are more prominent in COPD patients who already experience chronic airway inflammation and air flow limitation. A meta-analysis reported an 11% increased pooled prevalence risk of COPD due to exposure to high levels of PM.\textsuperscript{81} Long-term exposure to air pollution, from industrial sources and traffic, has been demonstrated to worsen lung function and respiratory health in middle-aged women. The OR for the association of COPD and living close to busy roads has been reported to be significantly high (OR=1.79).\textsuperscript{82}

Higher outdoor pollution increases the mortality of COPD patients. Another meta-analysis reported a 3% higher risk for COPD deaths due to outdoor air pollution.\textsuperscript{83} Hospital and pharmaceutical data indicated that the mortality associated with PM_{2.5} was five times higher in COPD patients compared to non-COPD patients. Moreover, elevated PM_{2.5} and NO_{2} also increased mortality among COPD patients.\textsuperscript{84}

Even indoor pollutants have been linked with AECOPD. A longitudinal study by Hansel, et al.\textsuperscript{85} reported that indoor pollutant exposure, including PM_{1.5} and NO_{2}, was associated with increased respiratory symptoms and risk of exacerbation among moderate to severe COPD patients in the Baltimore area. A further meta-analysis reported that a 10 mcg/m\textsuperscript{3} increase in PM_{10} could be associated with a 2.7% increase in COPD hospitalizations, with an OR of 1.03, and a 1.1% increase in COPD mortality, with an OR of 1.01.\textsuperscript{86}

In 16 cities across Canada, high hourly ozone concentrations were found to be positively associated with hospital admissions for respiratory issues, including COPD, in the following days. As ozone increases by 30 ppb, the relative risk for hospitalization varied from 1.024 to 1.043.\textsuperscript{87} This consistent relationship between environmental exposure and COPD suggests that the prediction of AECOPD and management of environment exposures may play an important role in respiratory healthcare for COPD patients.

Personal environmental exposure and digital technology

The concept of the exposome was developed to draw attention to the critical need for more complete assessment of environmental exposure in epidemiological studies.\textsuperscript{88} Individuals are simultaneously exposed to multiple environmental stressors during their daily lives.\textsuperscript{89} Personalized risk stratification of environmental exposure is important to predict the adverse effects of pollutants on health, according to the exposome concept. However, most studies have depended on small numbers of fixed air-quality monitoring sites, while people spend most of their time indoors. Therefore, developing a wearable device that tracks personal microenvironments is important. Although various types of sensors have been introduced, few combined technologies or systems using exposure-measurement sensors and other detectors have been developed.

For long-term, continuous monitoring of wellness status and relevant environmental factors of those with respiratory problems, Dieffenderfer, et al.\textsuperscript{89} presented a system that consists of a wristband, a chest patch, and a handheld spirometer. The ambient ozone concentration, temperature, and relative humidity were measured. The heart rate was assessed via photoplethysmography and electrocardiography; the respiratory rate via photoplethysmography, skin impedance, three-axis acceleration, and expiratory airflow; and wheezing via a microphone. The data from each sensor were continually streamed to a peripheral data-aggregation device and were subsequently transferred to a dedicated server for cloud storage.\textsuperscript{89}

Wearable camera technology has recently been used in health studies to assess physical activity, nutrition, and the environment.\textsuperscript{90,91} Since previous studies have usually depended on participants’ motivation and memory to acquire information, they are potentially biased. Salmon, et al.\textsuperscript{90} reported on wearable cameras in combination with a personal PM_{2.5} monitor. Micro-environmental data derived from wearable cameras provided locations and activities that influenced personal PM_{2.5} exposure. This technology is also valuable to track and measure personal exposure to urban greeneries both scientifically and efficiently. A wearable camera can automatically and passively record abundant imagery of an individual’s exposure to greeneries, which altogether with the technology of image detection helps clarify the role of greeneries during individual lifelogging.\textsuperscript{91}

Mallires, et al.\textsuperscript{90} developed a commercial wrist-worn device that monitors ozone, total volatile organic compounds (VOC), temperature, humidity, and the activity level of users at 1-minute intervals. The data can be either stored locally or transferred via its Bluetooth module to a centralized database. The device provides a research tool for epidemiologists to study how asthma triggers and their combinations exacerbate respiratory symptoms. An eventual goal is to provide real-time feedback and warnings to the user.\textsuperscript{91}
To collect personal exposure data, wearable sensors to gather local and personal concentrations of environmental stressors are essential. Despite the advantages of wearable devices compared to static devices, data accuracy is a major issue to be assessed before their utilization in applied research projects.94,95 However, easily usable devices can improve wearing compliance, operator satisfaction with the participants, and the overall success of an exposure study.96 Smartphone software can fully integrate sensor data processing, storage, and visualization.

Current status for environmental exposure and digital health management in airway disease
Acute exacerbation is directly linked with higher disease burden, increased medical expenses, and mortality in chronic airway diseases. Therefore, lowering the severity and cases of exacerbation are the main goals of relevant treatments. In order to prevent exacerbation and detect it early, predicting it is necessary.

As previously described, several studies have developed prognostic and predicting models for exacerbation of chronic airway diseases, but they can only predict upcoming exacerbation within short and long-term follow-up periods.44,45 These prediction models do not reflect patients’ real-time health status, and they can only guide physicians toward future treatment and healthcare. Moreover, physicians can only assist patients after the patients utilize healthcare and medical services. Therefore, self-management at home is required to assure real-time and consistent symptom monitoring and management, and it is important to educate patients on the same and provide them with action plans.96,97 However, self-management may result in inconsistent quality of management, and limit medication changes and modifications. Therefore, objective and systematic guidance, including lifestyle and behavioral modifications, should be provided by evaluating and collecting real-time health and environmental exposure data. These medical approaches can be established by combining recent technologies from mHealth, personal measurements of environmental exposure, wearable devices, and ML prediction models.

Hurst, et al.98 reported that composite heart rates and oxygen saturation scores distinguished exacerbation onset from symptom variations, potentially facilitating prompt therapy for ambulatory patients with stable, moderate, and severe COPD. However, day-to-day variations of heart rate and oxygen saturation were recorded by patients only at certain daily times. Wu, et al.45 recently developed an early AECOPD prediction system using wearable devices and smartphone apps, in order to study the patients’ lifestyle factors, environmental factors, and medical questionnaires. For 7-day AECOPD prediction, the developed predictive model achieved an accuracy of 92.1%. They also found that physiological and environmental data were more powerful predictors than questionnaire data. However, in this prediction model, environmental data collection was spatially restricted to the participants’ bedrooms. To overcome this limitation, tracing the patients by GPS functions and linking with environmental open public data, or measuring personal exposure using personal air-sensors, would be the next steps.

Future directions for personal air pollution exposure-response assessment and airway disease management
To facilitate early detection and prompt treatment of acute exacerbation of chronic airway diseases in response to environmental exposures, real-time data collection of environmental exposure, personal position tracking, and physiological and symptomatic changes in patients is required. Fig. 1 illustrates the conceptual architecture of how combining air sensors for measuring personal exposure, wearable devices for detection

Fig. 1. Concept of exacerbation prediction in airway diseases using air sensors, wearable devices, and smartphone applications. GPS, global positioning system.

https://doi.org/10.3349/ymj.2022.63.S1
of change in vital signs, smartphone apps for GPS tracing and medical questionnaires, and prediction algorithms can improve real-time prediction simultaneously with personal air pollution exposure.

Although the data collected in each domain is distinct from other domains, interactions between the different domains are expected in the development of prediction models. For example, personal air pollution exposure is not just measured by air sensors, but it also depends on changes in vital signs such as heart rates or respiratory rates collected by wearable devices. As patients inhale more frequently, the effects of air pollution may increase. Current health status data collected by questionnaires on smartphone apps may also influence the effects of personal exposure. The effects of air pollution exposure may differ in patients with different severities of airflow limitation, or different experiences of previous exacerbations.

The PURE-AIR is a representative study for integrating smartphones, air sensors, and air models to investigate associations between air pollution and cardiopulmonary diseases. An ultrasonic personal air sampler was used to measure personal exposure, and data were collected through a smartphone app. However, this study primarily built exposure models for cardiopulmonary disease events in a large general population. Das, et al. developed a smartphone-based real-time VOC sensor using fluorescence spectroscopy. However, only a range can be reported in the case of unknown VOC mixtures, and only VOC concentrations above 50 ppm can be detected.

Once the exacerbation of chronic airway diseases can be predicted by prediction models using health status questionnaires and real-time personal exposure and health data, self-management and lifestyle modification action plans can be suggested for patients through a variety of resources, including smartphone apps.

As we reviewed in this study, the impact of air pollution on health is closely related with the integration of pollution-people-place-time. The Center for Digital Biomarkers Research in Korea is developing a personalized service model for managing the exposure to environmental risk factors among vulnerable individuals, in which patients with chronic airway diseases are also included. This research center is supported by the Korea Environment Industry and Technology Institute (KEITI) and funded by the Korean Ministry of Environment. They plan to develop a real-time prediction model for airway disease exacerbations, integrating the previously introduced four domains, in order to suggest the aforementioned personalized self-management plans.

CONCLUSIONS

Extensive research has demonstrated that air pollution exposure is associated with adverse health outcomes. In particular, symptoms of chronic airway diseases are heavily affected by environmental exposure; hence, patients experiencing these diseases are categorized as populations vulnerable to environmental exposure. Therefore, their health management should not be limited to the utilization of medical services, but should be extended to encourage self-management at any time and at any place. Currently, highly developed technologies that are available provide the possibility of approaching individualized management of chronic airway diseases in real time by combining the capacities of air sensors, wearable devices, smartphone apps, and prediction models. However, as environmental research continues to advance technologically, there is also a growing need for establishing policies for personal information protection.

ACKNOWLEDGEMENTS

This work was supported by the Korea Environment Industry & Technology Institute (KEITI) through the Digital Infrastructure Building Project for Monitoring, Surveying and Evaluating the Environmental Health, funded by Korean Ministry of Environment (MOE) (2021003340002). The authors also thank Medical Illustration & Design, part of the Medical Research Support Services of Yonsei University College of Medicine, for all of the artistic support related to this work.

AUTHOR CONTRIBUTIONS

Conceptualization: Ji Ye Jung. Data curation: all authors. Formal analysis: all authors. Funding acquisition: Ji Ye Jung. Investigation: all authors. Project administration: Ji Ye Jung. Resources: all authors. Supervision: Ji Ye Jung. Validation: all authors. Visualization: all authors. Writing—original draft: all authors. Writing—review & editing: all authors. Approval of final manuscript: all authors.

ORCID iDs

Youngmok Park https://orcid.org/0000-0002-3669-1491
Chanho Lee https://orcid.org/0000-0003-2063-7379
Ji Ye Jung https://orcid.org/0000-0003-1589-4142

REFERENCES

1. GBD 2015 Risk Factors Collaborators. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet 2016;388:1659-724.
2. Bae S, Kwon HJ. Current state of research on the risk of morbidity and mortality associated with air pollution in Korea. Yonsei Med J 2019;60:243-56.
3. Rage E, Siroux V, Künzli N, Pin I, Kauffmann F; Epidemiological Study on the Genetics and Environment of Asthma. Air pollution and asthma severity in adults. Occup Environ Med 2009;66:182-8.
4. Pfeffer PE, Mudway IS, Grigg J. Air pollution and asthma: mechanisms of harm and considerations for clinical interventions. Chest 2021;159:1346-55.
5. Song DJ, Choi SH, Song WJ, Park KH, Jee YK, Cho SH, et al. The effects of short-term and very short-term particulate matter exposure on asthma-related hospital visits: National Health Insurance data. Yonsei Med J 2019;60:952-9.

6. Larkin A, Hystad P. Towards personal exposures: how technology is changing air pollution and health research. Curr Environ Health Rep 2017;4:463-71.

7. Yatkina S, Gerboles M, Belis CA, Karagialian F, Lagler F, Barbier M, et al. Representativeness of an air quality monitoring station for PM2.5 and source apportionment over a small urban domain. Atmos Pollut Res 2020;11:225-33.

8. Özkaynak H, Baxter LK, Dionsisio KL, Burke J. Air pollution exposure prediction approaches used in air pollution epidemiology studies. J Expo Sci Environ Epidemiol 2013;23:566-72.

9. Huang C, Hu J, Xue T, Xu H, Wang M. High-resolution spatiotemporal modeling for ambient PM2.5 exposure assessment in China from 2013 to 2019. Environ Sci Technol 2021;55:2152-62.

10. van Donkelaar A, Martin RV, Brauer M, Boys BL. Use of satellite observations for long-term exposure assessment of global concentrations of fine particulate matter. Environ Health Perspect 2015;123:135-43.

11. Di Q, Amini H, Shi L, Kloog I, Silvern R, Kelly J, et al. An ensemble-based model of PM2.5 concentration across the contiguous United States with high spatiotemporal resolution. Environ Int 2019;130:104909.

12. World Air Quality Index Project. Air pollution in world: real-time observations for long-term exposure assessment of global concentrations of fine particulate matter. Environ Int Perspectives 2015;123:135-43.

13. Rodríguez-Urrego D, Rodríguez-Urrego L. Air quality during the COVID-19: PM2.5 analysis in the 50 most polluted capital cities in the world. Environ Pollut 2020;266:115402.

14. Snik F, Rietjens JH, Apituley A, Volten H, Mijling B, Di Noia A, et al. Mapping atmospheric aerosols with a citizen science network of smartphone spectropolarimeters. Geophys Res Lett 2014;41:7351-8.

15. Perelló J, Cigarini A, Lagler F, Barbier M, Ketsev A, Lagler F, Borowiak A. Review of sensors for air quality monitoring. Luxembourg: Publications Office of the European Union; 2019.

16. De Craemer S, Vercauteren J, Fierens F, Lefebvre W, Meysman FJR. Using large-scale NO2 data from citizen science for air-quality compliance and policy support. Environ Sci Technol 2020;54:11070-8.

17. Van Brussel S, Huysse H. Citizen science on speed? Realising the triple objective of scientific rigour, policy influence and deep citizen engagement in a large-scale citizen science project on ambient air quality in Antwerp. J Environ Plan Manag 2018;62:534-51.

18. Jonsson P, Carson S, Davis S, Linder P, Lindberg P, Ramiro J, et al. Ericsson mobility report. Mobile subscriptions shifting towards 5G [accessed on 2021 August 25]. Available at: https://www.ericsson.com/en/mobility-report/reports/june-2021.

19. World Health Organization. WHO guideline: recommendations on digital interventions for health system strengthening. Geneva: World Health Organization; 2019.

20. Merry K, Bettinger P. Smartphone GPS accuracy study in an urban environment. PLoS One 2019;14:e0219980.

21. González MC, Hidalgo CA, Barabási AL. Understanding individual human mobility patterns. Nature 2008;453:77-82.

22. Arku RE, Birch A, Shupler M, Yusuf S, Hystad P, Brauer M. Characterizing exposure to household air pollution within the prospective urban rural epidemiology (PURE) study. Environ Int 2018;114:307-17.

23. Ritter S. Apple’s research kit development framework for iPhone apps enables innovative approaches to medical research data collection. J Clin Trials 2015;5:e1120.

24. Chan YY, Wang P, Rogers L, Tignor N, Zweig M, Hershman SG, et al. The asthma mobile health study, a large-scale clinical observational study using ResearchKit. Nat Biotechnol 2017;35:354-62.

25. Chan YY, Bot BM, Zweig M, Tignor N, Ma W, Suver C, et al. The asthma mobile health study, smartphone data collected using ResearchKit. Sci Data 2018;5:180096.

26. González MC, Hidalgo CA, Barabási AL. Understanding individual human mobility patterns. Nature 2008;453:77-82.

27. Barkjohn KK, Gaht B, Clements AL. Development and application of a United States wide correction for PM2.5 data collected with the PurpleAir sensor. Atmos Meas Tech 2021;14:4617-37.

28. Feinberg SN, Williams R, Hagler G, Low J, Smith L, Brown R, et al. Examining spatiotemporal variability of urban particulate matter and application of high-time resolution data from a network of low-cost air pollution sensors. Atmos Environ (1994) 2019;213:579-84.

29. Saini J, Dutta M, Marques G. Sensors for indoor air quality monitoring and assessment through internet of things: a systematic review. Environ Monit Assess 2021;193:66.

30. Chojer H, Branco PTBS, Martins FG, Alvim-Ferraz MCM, Sousa SIV. Development of low-cost indoor air quality monitoring devices: recent advancements. Sci Total Environ 2020;727:138385.

31. Evangelopoulos D, Chatzidiakou L, Walton H, Katsouyann K, Kelly FJ, Quint JK, et al. Personal exposure to air pollution and respiratory health of COPD patients in London. Eur Respir J 2021;58:20003432.

32. Moore E, Chatzidiakou L, Jones RL, Smeeth L, Beever S, Kelly FJ, et al. Linking e-health records, patient-reported symptoms and environmental exposure data to characterise and model COPD exacerbations: protocol for the COPE study. BMJ Open 2016;6:e011330.

33. Han YQ, Chen W, Chatzidiakou L, Krause A, Yan L, Zhang HB, et al. Effects of AIR pollution on cardiopulmonary disease in urban and peri-urban residents in Beijing: protocol for the AIRLESS study. Atmospheric Chem Phys 2020;20:15775-92.

34. Ma J, Tao YH, Kwan MP, Chai Y. Assessing mobility-based real-time air pollution exposure in space and time using smart sensors and GPS trajectories in Beijing. Ann Am Assoc Geogr 2020;110:434-48.

35. Helbig C, Ueberham M, Becker AM, Marquart H, Schlink U. Wearable sensors for human environmental exposure in urban settings. Curr Pollution Rep 2021;7:417-33.

36. Mackinnon GE, Brittain EL. Mobile health technologies in cardiopulmonary disease. Chest 2020;157:654-64.

37. GBD 2015 Chronic Respiratory Disease Collaborators. Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet Respir Med 2017;5:691-706.

38. Wedzicha JA, Seemungal TA. COPD exacerbations: defining their cause and prevention. Lancet 2007;370:786-96.

39. O’Byrne PM, Pedersen S, Lamm CJ, Tan WC, Busse WW; START Investigators Group. Severe exacerbations and decline in lung function in asthma. Am J Respir Crit Care Med 2009;179:19-24.

40. Bhogal SK, Mcgillivray D, Bourbeau J, Benedetti A, Bartlett S, Ducharme FM. Early administration of systemic corticosteroids reduces hospital admission rates for children with moderate and severe asthma exacerbation. Ann Emerg Med 2012;60:84-91.e3.
41. Guerra B, Gavekaitė V, Bianchi C, Puhan MA. Prediction models for exacerbations in patients with COPD. Eur Respir Rev 2017; 26:160061.

42. Fleming L. Asthma exacerbation prediction: recent insights. Curr Opin Allergy Clin Immunol 2018;18:117-23.

43. Loymans RJB, Debray TPA, Honkoop PJ, Termeer EH, Snoek-Stroband JB, Schermer TRJ, et al. Exacerbations in adults with asthma: a systematic review and external validation of prediction models. J Allergy Clin Immunol Pract 2018;6:1942-52.e15.

44. Zein JG, Wu CP, Attaawy AH, Zhang P, Nazha A. Novel machine learning can predict acute asthma exacerbation. Chest 2021;159: 1747-57.

45. Wu CT, Li GH, Huang CT, Chen CH, Chien JY, et al. Acute exacerbation of a chronic obstructive pulmonary disease prediction system using wearable device data, machine learning, and deep learning development and cohort study. JMIR Mhealth Uhealth 2019;5:e22591.

46. Sills MR, Ozkaynak M, Jang H. Predicting hospitalization of pediatric asthma patients in emergency departments using machine learning. Int J Med Inform 2021;151:104468.

47. Peng J, Chen C, Zhou M, Xie X, Zhou Y, Luo CH. A machine-learning approach to forecast aggravation risk in patients with acute exacerbation of chronic obstructive pulmonary disease with clinical indicators. Sci Rep 2020;10:3118.

48. Barbosa MT, Sousa CS, Moraes-Almeida M, Simões MI, Mendes P. Telemedicine in COPD: an overview by topics. COPD 2020;17:601-17.

49. Grand View Research, Inc. mHealth apps market size, share & trends analysis report by type (fitness, medical), by region (North America, APAC, Europe, MEA, Latin America), and segment forecasts, 2021-2028 [accessed on 2021 August 25]. Available at: https://www.grandviewresearch.com/industy-analysis/mhealth-app-market.

50. Whittaker R, McRobbie H, Bullen C, Rodgers A, Gu Y, Dobson R. Mobile phone text messaging and app-based interventions for smoking cessation. Cochrane Database Syst Rev 2019;10:CD006611.

51. Lüscher J, Berli C, Schwanninger P, Scholz U. Smoking cessation with smartphone applications (SWAPP): study protocol for a randomized controlled trial. BMC Public Health 2019;19:1400.

52. Masaki K, Tateno H, Kameyama N, Morino E, Watanabe R, Sekine K, et al. Impact of a novel smartphone app (CareApp smoking cessation) on nicotine dependence: prospective single-arm interventional pilot study. JMIR Mhealth Uhealth 2019;7:e12694.

53. Danaher BG, Tyler MS, Crowley RC, Brendryen H, Seeley JR. Outcomes and device usage for fully automated internet interventions designed for a smartphone or personal computer: the MobileQuit smoking cessation randomized controlled trial. J Med Internet Res 2019;21:e13290.

54. George M. Adherence in asthma and COPD: new strategies for an old problem. Respir Care 2018;63:818-31.

55. Berlinski A, Chervinskiy SK, Simmons AL, Leisenring P, Harwell SA, Lawrence DJ, et al. Delivery of high-quality pediatric spirometry in rural communities: a novel use for telemedicine. J Allergy Clin Immunol Pract 2018;6:1042-4.

56. Persaud YK, Portnoy JM. Ten rules for implementation of a telemedicine program to care for patients with asthma. J Allergy Clin Immunol Pract 2021;9:13-21.

57. Nguyen E, Miao B, Pugliese N, Huang D, Sobieraj DM. Systematic review of mHealth applications that interface with inhaler sensors in asthma. J Allergy Clin Immunol Pract 2021;9:844-52.e3.

58. Msonaim GS, Stempel DA, Gonzalez C, Adams B, BenIsrael-Olive N, Gondalia R, et al. The impact of patient self-monitoring via electronic medication monitor and mobile app plus remote clinician feedback on adherence to inhaled corticosteroids: a randomized controlled trial. J Allergy Clin Immunol Pract 2021;9:1586-94.

59. Vorrink SN, Kort HS, Troosters T, Zanen P, Lammers J. Efficacy of an mHealth intervention to stimulate physical activity in COPD patients after pulmonary rehabilitation. Eur Respir J 2016;48:1019-29.

60. Marcolino MS, Oliveira JAQ, D’Agostino M, Ribeiro AL, Alkmim MBM, Novillo-Ortiz D. The impact of mHealth interventions: systematic review of systematic reviews. JMIR Mhealth Uhealth 2018; 6:e23.

61. Taylor K, Silver L. Smartphone ownership is growing rapidly around the world, but not always equally [accessed on 2021 August 25]. Available at: https://www.pewresearch.org/global/2019/02/05/smartphone-ownership-is-growing-rapidly-around-the-world-but-not-always-equally/.

62. Steinbuhl SR, Muse ED, Topol EJ. The emerging field of mobile health. Sci Transl Med 2015;7:283rv3.

63. Kamei T, Kamonari T, Yamamoto Y, Edirippulige S. The use of wearable devices in chronic disease management to enhance adherence and improve telehealth outcomes: a systematic review and meta-analysis. J Telemed Telecare 2020 Aug 20. [Epub]. Available at: https://doi.org/10.1177/1357663X20937573.

64. Mehdipour A, Wiley E, Richardson J, Beauchamp M, Kuspinar A. The performance of digital monitoring devices for oxygen saturation and respiratory rate in COPD: a systematic review. COPD 2021;18:469-75.

65. Kim C, Kim Y, Yang DW, Rhee CK, Kim SK, Hwang YI, et al. Direct and indirect costs of chronic obstructive pulmonary disease in Korea. Tuberc Respir Dis (Seoul) 2019;82:27-34.

66. Brooks D, Thomas J. Interrater reliability of auscultation of breath sounds among physical therapists. Phys Ther 1995;75:1082-8.

67. Kevat A, Kalirajah A, Roseby R. Artificial intelligence accuracy in detecting pathological breath sounds in children using digital stethoscopes. Respir Res 2020;21:253.

68. Yilmaz G, Rapin M, Pessoa D, Rocha BM, de Sousa AM, Rusconi R, et al. A wearable stethoscope for long-term ambulatory respiratory health monitoring. Sensors (Basel) 2020;20:5124.

69. Kupczyk M, Hofman A, Kołowski L, Kuna P, Łukaszek M, Buczyłko K, et al. Home self-monitoring in patients with asthma using a mobile spirometry system. J Asthma 2021;58:505-11.

70. Ramsey RR, Plevinsky JM, Milgrim L, Hommel KA, McDowell KM, Shepard J, et al. Feasibility and preliminary validity of mobile spirometry in pediatric asthma. J Allergy Clin Immunol Pract 2021;9:3821-3.

71. Du Plessis E, Swart E, Maree D, Heydenreich J, Van Heerden J, Estherhuizen TM, et al. The utility of hand-held mobile spirometer technology in a resource-constrained setting. S Afr Med J 2019;109:219-22.

72. Khusial RJ, Honkoop PJ, Usmani O, Soares M, Simpson A, Biddiscombe M, et al. Effectiveness of myAirCoach: a mHealth self-management system in asthma. J Allergy Clin Immunol Pract 2020;8:1972-9.e8.

73. Silven AV, Petrus AHJ, Villalobos-Quesada M, Dirikgil E, Oerlemans CR, Landstra CP, et al. Telemonitoring for patients with COVID-19: recommendations for design and implementation. J Med Internet Res 2020;22:e20853.

74. Jacquemin B, Stroux V, Sanchez M, Carsin AE, Schikowski T, Adam M, et al. Ambient air pollution and adult asthma incidence in six European cohorts (ESCAPE). Environ Health Perspect 2021;129:613-21.

75. Khreis H, Kelly C, Tate J, Parslow R, Lucas K, Nieuwenhuijse M. Exposure to traffic-related air pollution and risk of development...
of childhood asthma: a systematic review and meta-analysis. Environ Int 2017;100:1–31.
76. Jacquemin B, Kauffmann F, Pin J, Le Moual N, Bousquet J, Gormand F, et al. Air pollution and asthma control in the epidemiological study on the genetics and environment of asthma. J Epidemiol Community Health 2012;66:796–802.
77. Weir CH, Yeatts KB, Sarnat JA, Vizuete W, Salo PM, Jaramillo R, et al. Nitrogen dioxide and allergic sensitization in the 2005–2006 National Health and Nutrition Examination Survey. Respir Med 2013;107:1763–72.
78. Vimercati L, Gatti ME, Baldassarre A, Nettis E, Favia N, Palma M, et al. Occupational exposure to urban air pollution and allergic diseases. Int J Environ Res Public Health 2015;12:12977–87.
79. Barnes PJ. Corticosteroid resistance in patients with asthma and chronic obstructive pulmonary disease. J Allergy Clin Immunol 2013;131:636–45.
80. Brandt EB, Kovacic MB, Lee GB, Gibson AM, Acciani TH, Le Cras TD, et al. Diesel exhaust particle induction of IL-17A contributes to severe asthma. J Allergy Clin Immunol 2013;132:1194–204.e2.
81. Song Q, Christiani DC, XiaorongWang, Ren J. The global contribution of outdoor air pollution to the incidence, prevalence, mortality and hospital admission for chronic obstructive pulmonary disease: a systematic review and meta-analysis. Int J Environ Res Public Health 2014;11:11822–32.
82. Schikowski T, Sugiri D, Ranft U, Gehring U, Heinrich J, Wichmann HE, et al. Long-term air pollution exposure and living close to busy roads are associated with COPD in women. Respir Res 2005;6:152.
83. Faustini A, Staiafoglia M, Cappai G, Forastiere F. Short-term effects of air pollution in a cohort of patients with chronic obstructive pulmonary disease. Epidemiology 2012;23:861–79.
84. Hansel NN, McCormack MC, Belli AJ, Matsui EC, Peng RD, Aloe C, et al. In-home air pollution is linked to respiratory morbidity in former smokers with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2013;187:1085–90.
85. Zhu R, Chen Y, Wu S, Deng F, Liu Y, Yao W. The relationship between particulate matter (PM10) and hospitalizations and mortality of chronic obstructive pulmonary disease: a meta-analysis. COPD 2013;10:307–15.
86. Burnett RT, Brook JR, Yung WT, Dales RE, Krewski D. Association between ozone and hospitalization for respiratory diseases in 16 Canadian cities. Environ Res 1997;72:24–31.
87. Wild CP. The exposome: from concept to utility. Int J Epidemiol 2012;41:24–32.
88. Ueberham M, Schlink U. Wearable sensors for multifactorial personal exposure measurements-A ranking study. Environ Int 2018;121:130–8.
89. Dieffenderfer J, Goodell H, Mills S, McKnight M, Yao S, Lin F, et al. Low-power wearable systems for continuous monitoring of environment and health for chronic respiratory disease. IEEE J Biomed Health Inform 2016;20:1251–64.
90. Salmon M, Milà C, Bhogadi S, Addanki S, Madhira P, Muddepaka N, et al. Wearable camera-derived microenvironments in relation to personal exposure to PM2.5. Environ Int 2018;117:300–7.
91. Zhang Z, Zhong Y, Chen L, Chen C. Assessing personal exposure to urban greenery using wearable cameras and machine learning. Cities 2021;109:103006.
92. Milà C, Salmon M, Sanchez M, Ambrós A, Bhogadi S, Sreekanth V et al. When, where, and what? Characterizing personal PM2.5 exposure in periurban India by integrating GPS, wearable camera, and ambient and personal monitoring data. Environ Sci Technol 2018;52:13481–90.
93. Mallires KR, Wang D, Tipparaju VV, Tao N. Developing a low-cost wearable personal exposure monitor for studying respiratory diseases using metal–oxide sensors. IEEE Sens J 2019;19:8252–61.
94. Jerrett M, Donaire-Gonzalez D, Popoola O, Jones R, Cohen RC, Almanza E, et al. Validating novel air pollution sensors to improve exposure estimates for epidemiological analyses and citizen science. Environ Res 2017;158:286–94.
95. Lewis A, Edwards P. Validate personal air-pollution sensors. Nature 2016;535:29–31.
96. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease. 2021 gold reports [accessed on 2021 August 25]. Available at: https://goldcopd.org/2021-gold-reports/.
97. Global Initiative for Asthma. Global strategy for asthma management and prevention. 2021 GINA main report [accessed on 2021 August 25]. Available at: https://ginasthma.org/gina-reports/.
98. Hurst JR, Donaldson GC, Quint JK, Goldring JJ, Patel AR, Wedzicha JA. Domiciliary pulse-oximetry at exacerbation of chronic obstructive pulmonary disease: prospective pilot study. BMC Pulm Med 2010;10:52.
99. Volckens J, Quinn C, Leith D, Mehaffy J, Henry CS, Miller-Lionberg D. Development and evaluation of an ultrasonic personal aerosol sampler. Indoor Air 2017;27:409–16.
100. Das T, Mohar M. Development of a smartphone-based real time cost-effective VOC sensor. Heliyon 2020;6:e05167.