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Digital Healthcare for Airway Diseases from Personal Environmental Exposure

Youngmok Park[1*], Chanho Lee[2*], and Ji Ye Jung[1]

[1]Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Severance Hospital, Yonsei University College of Medicine, Seoul;
[2]Severance Biomedical Science Institute, Yonsei Biomedical Research Institute, Yonsei University College of Medicine, Seoul, Korea.

Digital technologies have emerged in various dimensions of human life, ranging from education to professional services to well-being. In particular, health products and services have expanded by the use and development of artificial intelligence, mobile health applications, and wearable electronic devices. Such advancements have enabled accurate and updated tracking and modeling of health conditions. For instance, digital health technologies are capable of measuring environmental pollution and predicting its adverse health effects. Several health conditions, including chronic airway diseases such as asthma and chronic obstructive pulmonary disease, can be exacerbated by pollution. These diseases impose substantial health burdens with high morbidity and mortality. Recently, efforts have been made to develop digital technologies to alleviate such conditions. Moreover, the COVID-19 pandemic has facilitated the application of telemedicine and telemonitoring for patients with chronic airway diseases. This article reviews current trends and studies in digital technology utilization for investigating and managing environmental exposure and chronic airway diseases. First, we discussed the recent progression of digital technologies in general environmental healthcare. Then, we summarized the capacity of digital technologies in predicting exacerbation and self-management of airway diseases. Concluding these reviews, we provided suggestions to improve digital health technologies' abilities to reduce the adverse effects of environmental exposure in chronic airway diseases, based on personal exposure-response modeling.

Key Words: Asthma, digital technology, chronic obstructive pulmonary disease, environment, wearable electronic devices

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.[1] 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.[3] 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-

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Corresponding author: Ji Ye Jung, MD, PhD, Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Severance Hospital, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Korea.
Tel: 82-2-2228-1980, Fax: 82-2-393-6884, E-mail: stopyes@yuhs.ac

*Youngmok Park and Chanho Lee contributed equally to this work.
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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.[6] 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).

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.[7] 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.[6,8] Nowadays, efforts are being introduced to further enhance the accuracy and resolution of estimated

Table 1. Recent Advances in Estimating Air Pollution Exposure

Method	Example	Advances
Modelling ambient pollution		
Deterministic mixed-effect model	SHEDS AERMOD RLINE	- Incorporate new variables: pollution emissions data, topography, meteorological data, satellite data, personal behavior/time activity, and micro-environmental characteristics - Offer higher resolution
ML-based prediction	Di, et al., 2019[11] Huang, et al., 2021[9]	- Provide 100× higher resolution from satellite-based measurements by applying mixed-effect models with ML algorithms
Air pollution measurement		
Satellite-based sensors	Özkaynak, et al., 2013[8] van Donkelaar, et al., 2015[10]	- 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[13]	- Combine global air pollution station measurement and produce real-time data
Citizen science initiatives	iSPEX[14] xAire[15] CuriezeNeuzen[16,17]	- Produce air pollution measurement data from citizen volunteers with very high spatio-temporal resolution
Low cost sensors	Barkjohn, et al., 2021[27] Feinberg, et al., 2019[28]	- Increase resolution and accuracy of government measurement stations
Portable sensors	PAM[31-33] AirBeam[34]	- Gold standard for personal air pollution exposure assessment
Personal time-activity tracking		
mHealth based GPS records	Arku, et al., 2018[22]	- 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.

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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.[8-11] Measuring aerosol optical depth (AOD), the amount of light extinction in the given atmospheric column due to aerosols, gives estimates of particulate matter (PM)$_{2.5}$ at a 1×1 km resolution all over the Earth. These records can span timelines as long as a decade.[10] 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.[12] This approach enabled the collection of global-level data and comparison between capital cities of different countries.[13] Citizen science initiatives, such as iSPEX,[14] xAire,[15] CurieuzeNeuzen (Curious Noses) in Flanders[16] and many others have also contributed to new monitoring data from new sources. Citizens involved with CurieuzeNeuzen numbered 2000 in Antwerp[17] and 20000 in Flanders,[16] with each individual representing one nitrogen dioxide (NO_2) measurement location, compared to only 67 official reference stations in Flanders. De Craemer, et al.[16] normalized each short-term measurement of NO_2 into annual average concentrations at each location, resulting in very densely positioned NO_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.[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 innumerous 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 $PM_{2.5}$ concentration to 100×100 m in the US[11] and China.[9] 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.[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.[19] 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.[20] Based on spatiotemporal regularity in time-activity patterns,[21] it has been suggested that seasonal measurements of several days may be sufficient to capture individual variation in pollution exposure.[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,[22] 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.[23] In the Asthma Mobile Health Study (AMHS),[24] 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.[25] 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.[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_1), AirNut by Moji China ($PM_{2.5}$), Egg (2018) by Air Quality Egg (PM_1), PATS+ by Berkley Air ($PM_{2.5}$), S-500 by Aeroqual (NO_2, O_3) showed R^2 more than 0.85 with their prices lower than 500 EUR.[26] Researchers in the U.S. Environmental Protection Agency (EPA) recently reported that nationwide $PM_{2.5}$ 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^3.[27] In the CitySpace project[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 emission 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."[29] 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.[30] Therefore, further studies in calibration and validation, with appropriate reference measures, are required.

Personal measurement is the gold standard for air pollution exposure assessment.[6] 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, $PM_{2.5}$, PM_{10}) 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.[31-33] For instance, the Effects of AIR pollution on cardiopuLmonary disEaSe in urban and peri-urban reSidents in Beijing (AIRLESS) study[33] 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.[32] Preliminary study results emphasized the impacts of gaseous pollutants.[31] Ma, et al.[34] 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.[35,36] 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.[35] 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.[37] Acute exacerbation of these diseases often results in hospitalization, declined lung function, impaired quality of life, and high mortality.[38,39] Therefore, accurate detection of exacerbation would support early disease management and reduce morbidity and mortality.[40]

Several studies have developed prognostic tools to enable personalized prediction of exacerbation (Table 2). Guerra, et al.[41] 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.[42,43]

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.[44] 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.[45] 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.[46,47] 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

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Table 2. Modeling for Acute Exacerbation of Chronic Airway Disease

Studies	Statistical method	Measured outcomes	Findings
Guerra, et al., 2017[41] COPD (SR for 27 models)	Classic statistical methods (correlation analysis, logistic regression, Cox regression, Poisson regression, negative binomial regression, random forest)	- Outpatient-treated exacerbation - Hospitalization	- High risk of bias - Lack of validation - Heterogeneity of statistical methods
Loymans, et al., 2018[43] Asthma (SR for 24 models)	Classic statistical methods (classification and regression tree, Cox regression, Poisson regression)	- Systemic steroid use - ED visit - Hospitalization - Lung function decline	- Poor model calibration - Limited external validation
Zein, et al., 2021[44] Asthma	Classic statistical methods (logistic regression, random forests) vs. ML-based methods (light gradient boosting decision tree)	- Systemic steroid use - ED visit - Hospitalization	- Real-world data used -Better performance in ML-based models - Internal validation
Wu, et al., 2021[45] COPD	ML-based classification (random forest, decision trees, k-nearest neighbor clustering, linear discriminant analysis, adaptive boosting, deep neural network model)	- mMRC dyspnea scale - COPD assessment test	- High predictive power when lifestyle and environmental data are integrated - Internal validation
Sills, et al., 2021[46] Asthma	Classic statistical methods (random forest, logistic regression) vs. automated ML algorithm	- Hospitalization during ED visit	- Better performance in ML-based model - Internal validation
Peng, et al., 2020[47] COPD	ML-based classification (novel C5.0 decision tree classifier)	- Exacerbation during hospitalization	-Early detection of aggravation - Internal validation

COPD, chronic obstructive pulmonary disease; ED, emergency department; mMRC, modified medical research council; ML, machine learning; SR, systematic review.

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.[48] 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 3. Smartphone Apps for Chronic Airway Disease Management

Types	Subject characteristics	mHealth interventions	Findings
Smoking cessation			
Masaki, et al., 2019[52]	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., 2019[53]	n=1271	MobileQuit (for mobile devices) vs. Quit Online (for non-mobile desktop or tablets)	- MobileQuit more effective
Inhaler usage			
Nguyen, et al., 2021[57]	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., 2021[58]	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., 2016[59]	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., 2017[24]	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.

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.[61] 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]

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Table 4. Wearable Devices for Chronic Airway Disease

Types	Devices	Monitoring	Findings
Tele-monitoring[63]	- Pulse oximeter (smartphone, Bluetooth)	Oxygen saturation	- Devices are generally valid - Improvement during exercise required
	- Chest-mounted electrode array - Finger-mounted photoplethysmography - Camera-mounted distance photoplethysmography - Upper-abdomen-mounted triaxial accelerometer - Chest-worn pressure-sensor pad	RR	- Devices are generally valid - May underestimate the RR - Further test for reliability required
Digital stethoscope with AI[67]	- Clinicloud™ digital stethoscope - Littman™ 3200 electronic stethoscope - Neural network-based AI algorithm	Lung sounds	- Performance and generalizability of AI algorithm demonstrated - Device-dependent differences may exist - More digital stethoscopes are now available
Non-diaphragm stethoscope[68]	- Diaphragm-less acoustoelectric transducer	Lung sounds	- Clinical application study required
Home-based spirometry[69,70]	- Mobile spirometry system (AioCare®, MIR Spirobank Smart)	FVC, FEV_1	- Safety, feasibility and validity demonstrated
Integrated solution[72]	- Inhaler adapter - Indoor air quality monitor - Portable spirometer - Fitbit Charge HR - myAirCoach app	Inhaler technique Indoor air quality FEV_1 Physical activity Integrated data	- Self-management of asthma achieved - Limited number of participants

AI, artificial intelligence; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; HR, heart rate; PEF, peak expiratory flow; RR respiratory rate.

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.

Wearable monitoring devices could be expanded to target other respiratory diseases. Patients with non-severe COVID-19 may be allowed to stay home under close observation and receive timely management, minimizing the risk of viral transmission.[73] Therefore, future studies applying these technologies to various pulmonary diseases are expected.

SECTION 3: EFFECTS AND MANAGEMENT OF ENVIRONMENTAL EXPOSURE

Previous studies suggest that environment 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 NO_2.[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, NO_2, $PM_{2.5}$, and PM_{10} exposures, indicating that childhood exposure to TRAP contributes to the development of asthma.

Long-term exposure to PM_{10} and O_3 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 outside their homes. Higher asthma severity scores were significantly related to high 8-hour averages of ozone, and higher number of days with 8-hour ozone averages, above 110 ug/m^3 [odds ratio (OR) 2.22 for one class difference in score].

Air pollutants may aggravate airways inflammation in both allergic and non-allergic asthma. Air pollutants enhance aeroallergen sensitization by increasing the production of the specific Immunoglobulin E (IgE). The 2005–2006 National Health and Nutrition Survey reported that increased levels of NO_2 were associated with increased IgE in response to inhalant and outdoor allergens, while $PM_{2.5}$ levels were positively associated with indoor allergens.[77] Vimercati, et al.[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.[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.[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.[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).[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.[81] Hospital and pharmaceutical data indicated that the mortality associated with PM_{10} 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.[83]

Even indoor pollutants have been linked with AECOPD. A longitudinal study by Hansel, et al.[84] reported that indoor pollutant exposure, including $PM_{2.5}$ 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^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.[85]

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.[86] 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.[87] Individuals are simultaneously exposed to multiple environmental stressors during their daily lives.[88] 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.[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.[89]

Wearable camera technology has recently been used in health studies to assess physical activity, nutrition, and the environment.[90-92] Since previous studies have usually depended on participants' motivation and memory to acquire information, they are potentially biased. Salmon, et al.[90] reported on wearable cameras in combination with a personal $PM_{2.5}$ monitor. Microenvironmental 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 greenery both scientifically and efficiently. A wearable camera can automatically and passively record abundant imagery of an individual's exposure to greenery, which together with the technology of image detection helps clarify the role of greenery during individual lifelogging.[91]

Mallires, et al.[93] 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.[93]

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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.[95] 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

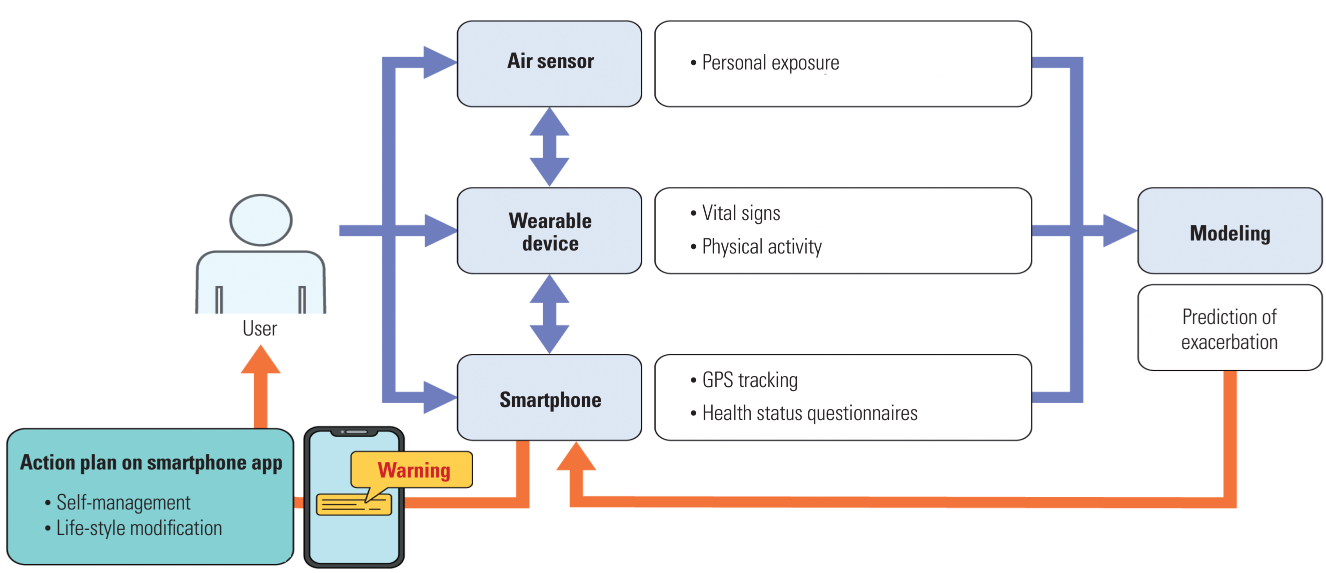

Fig. 1. Concept of exacerbation prediction in airway diseases using air sensors, wearable devices, and smartphone applications. GPS, global positioning system.

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.[22] An ultrasonic personal air sampler was used to measure personal exposure, and GPS data were collected through a smartphone app.[99] However, this study primarily built exposure models for cardiopulmonary disease events in a large general population. Das, et al.[100] 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.

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AUTHOR CONTRIBUTIONS

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ORCID iDs

Youngmok Park https://orcid.org/0000-0002-5669-1491
Chanho Lee https://orcid.org/0000-0003-2065-7379
Ji Ye Jung https://orcid.org/0000-0003-1589-4142

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