






# iPREDICT: Characterization of Asthma Triggers and Selection of Digital Technology to Predict Changes in Disease Control

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**Purpose:** The iPREDICT program aimed to develop an integrated digital health solution capable of continuous data streaming, predicting changes in asthma control, and enabling early intervention.

**Patients and Methods:** As part of the iPREDICT program, asthma triggers were characterized by surveying 221 patients (aged  $\geq 18$  years) with self-reported asthma for a risk–benefit analysis of parameters predictive of changes in disease control. Seventeen healthy volunteers (age 25–65 years) tested 13 devices to measure these parameters and assessed their usability attributes.

**Results:** Patients identified irritants such as chemicals, allergens, weather changes, and physical activity as triggers that were the most relevant to deteriorating asthma control. Device testing in healthy volunteers revealed variable data formats/units and quality issues, such as missing data and low signal-to-noise ratio. Based on user preference and data capture validity, a spirometer, vital sign monitor, and sleep monitor formed the iPREDICT integrated system for continuous data streaming to develop a personalized/predictive algorithm for asthma control.

**Conclusion:** These findings emphasize the need to systematically compare devices based on several parameters, including usability and data quality, to develop integrated digital technology programs for asthma care.

**Keywords:** asthma, devices, digital, predictive algorithm, sensors

## Introduction

Asthma affects approximately 25 million Americans and imposes a considerable burden on patients and the United States (US) healthcare system.<sup>1</sup> Nearly half of all patients with asthma experience  $\geq 1$  asthma attack per year.<sup>2</sup> On an annual basis, this chronic respiratory disease costs the US more than \$80 billion dollars.<sup>3</sup> Furthermore, the intrusive symptoms of asthma limit physical and social activities and impair the mental and emotional wellbeing of patients.<sup>4,5</sup>

The burden of chronic inflammatory respiratory diseases, such as asthma, may be mitigated by providing patients with effective self-management options,<sup>6</sup> as outlined in current evidence-based strategies.<sup>7</sup> Self-management of asthma requires appreciation of symptom onset and deterioration of disease control.<sup>8</sup> However, patients may not always recognize personal asthma triggers and/or may lack sufficient knowledge to identify them.<sup>9,10</sup> For example, the agreement between triggers perceived by patients and their respective allergens confirmed by sensitization testing is only moderate.<sup>10</sup> Thus, patients would benefit from the ability to monitor their disease and to identify triggers to control symptoms and reduce the risk of future asthma attacks or exacerbation events.

Digital self-management solutions are increasingly providing new sources of data for patients to better self-manage their asthma.<sup>9,11–15</sup> Given the interplay of genetics and the environment in the progression of this heterogeneous disease,

to improve its clinical outcomes, the evolving era of precision medicine relies on novel real-time data sources in addition to historical evidence.<sup>16</sup> Many wearable sensors and digital devices capable of capturing biological and environmental data are currently under development and have been integrated into digital health solutions.<sup>13,15,17–20</sup> These devices promise to further the advancements in precision medicine and patient-centric care. However, challenges to the wider adoption of digital solutions include patient compliance, a lack of approved integrated systems, and unequal access to medical technology.<sup>9,21,22</sup> Thus, the selection of the right device(s) and data analysis strategies can improve the success of digital solutions in chronic disease management.

The individualized PREdiction of DIsease Control using digital sensor Technology (iPREDICT) program was conceptualized as a system of wearable biosensors and connected devices to characterize the individual experience of a patient with asthma and establish a prognostic model of disease control by measuring changes from baseline data. To accomplish this, the identification and selection of high-quality digital devices integrated with minimal burden on the daily lives of patients with asthma was required. Here, we describe the technology of the iPREDICT system, including the characterization of asthma triggers and measurable parameters, and the assessment and selection of optimal wearable devices and digital biosensors for inclusion in the iPREDICT system.

## Materials and Methods

### Measurable Parameter Analysis in Patients with Asthma

The development of the iPREDICT system required the initial establishment of a set of measurable parameters that correlated with changes in asthma control. This involved qualitative and quantitative assessments to characterize prodromal symptomatology and physiology in the period between initial appearance of symptoms and onset of disease worsening, such as heart rate, respiratory rate, and asthma triggers. To accomplish this, 221 patients aged  $\geq 18$  years with self-reported asthma ([Supplementary Figure 1](#)) completed an online survey to characterize their subjective perception of asthma control, impact of asthma on their daily lives, personal asthma triggers, and value of a predictive tool designed to detect changes in disease control. Asthma triggers were categorized into nine clusters. For each identified trigger cluster, characteristics such as digital detection potential, participant self-report, time to early detection (2–24 h), percentage of participants affected, and predictive power were analyzed. A risk–benefit analysis of measurable parameters, validated in the literature as potentially predictive of changes in asthma control, was conducted separately to identify those that were important to patients and could be recorded with minimal patient burden.

### Device Usability Testing in Healthy Volunteers

The conclusion of the risk–benefit analysis marked the beginning of the technology development phase, during which an optimal set of devices was selected, and user experience and system integration were tested.

Across a 4-week period, 13 devices were tested by 17 healthy volunteers aged 25–65 years who expressed an interest in health and technology. Three volunteers tested each device, and  $\geq 2$  devices were tested for each parameter. The devices included a wearable biometric patch (HealthPatch MD, VitalConnect, San Jose, California, USA), a vital sign monitor (Zephyr BioPatch, Zephyr, Maryland, USA), a chest-based wearable activity monitor (Zephyr BioHarness 3, Zephyr, Maryland, USA), four smart band activity trackers (Microsoft Band 2, Microsoft, Seattle, USA; Healbe GoBe, Healbe, Seattle, USA; Mio FUSE, Mio Global, Physical Enterprises, British Columbia, Canada; and Garmin Vivofit HR, Garmin Ltd, Canton of Schaffhausen, Switzerland), a heart rate monitor (BodyGuardian Heart, Preventice Solutions, Minnesota, USA), a sleep monitor (MySleep S+, ResMed, California, USA), an electronic peak expiratory flow meter (Smart Peak Flow, Smart Respiratory Products, London, UK), two smart spirometers (Spirobank II, Medical International Research, Italy; Smart Spirometry, NuvoAir Air, Pond Health Care Innovation, Sweden), and a fractional exhaled nitric oxide (FeNO) monitor (NiOx Vero, Circassia, North Carolina, USA).

The devices varied in their capacity to measure the types and numbers of parameters, multiple variables across parameters, and the frequency at which data were collected. At Weeks 2 and 4, volunteers responded to a set of survey questions derived from the System Usability Scale (SUS)<sup>23</sup> and an internally developed questionnaire to quantify the usability of the respective devices based on their first impressions, ease of start-up, ease of use, comfort, connectivity and

recording, data quality, and overall likelihood of recommendation, all of which could influence patient compliance in the study setting ([Supplementary Table 1](#)). In addition, the volunteers maintained a diary to record any thoughts and technical issues that they were experiencing with the device(s).

Based on an analysis of the measured parameters, user feedback, data type and quality, and device connectivity, a selected number of optimal biosensors and wearable devices for measuring parameters and delivering prospective data to a mobile application were identified.

## Results

### Measurable Parameter Analysis in Patients with Asthma

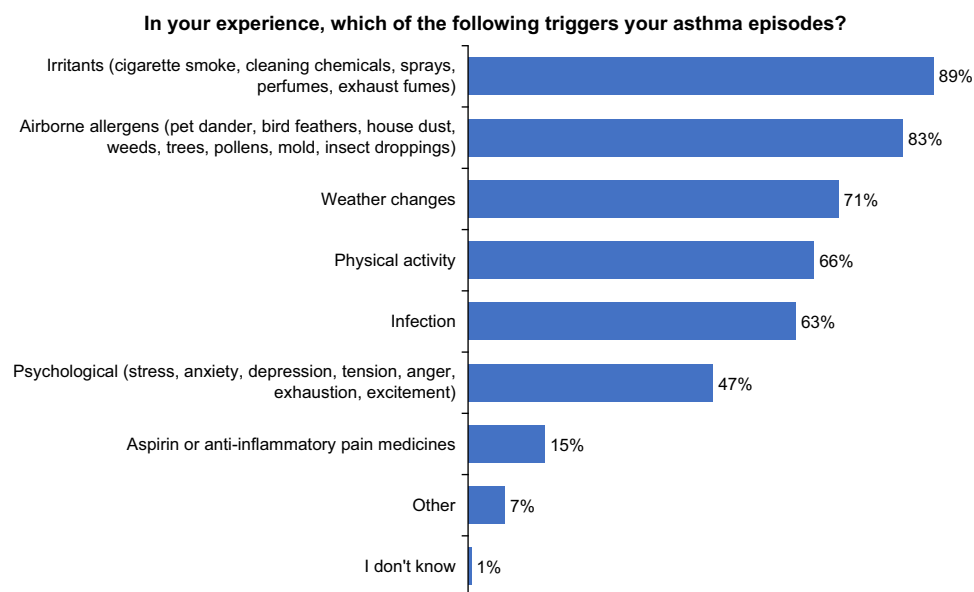
Of the patients who completed the survey, most were female (84%;  $n = 186$ ) and self-identified as having well-controlled asthma (89%;  $n = 197$ ). However, based on the 2016 Global Initiative for Asthma (GINA) criteria<sup>24</sup> ([Supplementary Figure 1](#)), 171 (77%) patients were classified as having poorly controlled disease, showing a lack of agreement between clinically defined and patients' view of disease control.

Survey responses from patients with poorly controlled asthma revealed that nearly all believed that they could identify their triggers, but the timing of the trigger identification varied according to the triggering factor. The most common self-reported triggers were irritants, such as smoke, chemicals, and perfumes (89%); aeroallergens, including animal dander, house dust, and molds (83%); weather changes (71%); and physical activity (66%) ([Figure 1](#)). Some triggers (infections, allergens, irritants, and weather changes) could be identified prior to the onset of an asthma episode, whereas others (psychological, drug, and physical activity) were identified during or after an event ([Figure 2](#)).

Participants reported that they would likely modify their behaviors after being notified of a change in asthma control, including ensuring access to asthma medication (98%); avoiding triggers (90%); and seeking assistance from family, friends (64%), or their physician (64%) ([Figure 3](#)).

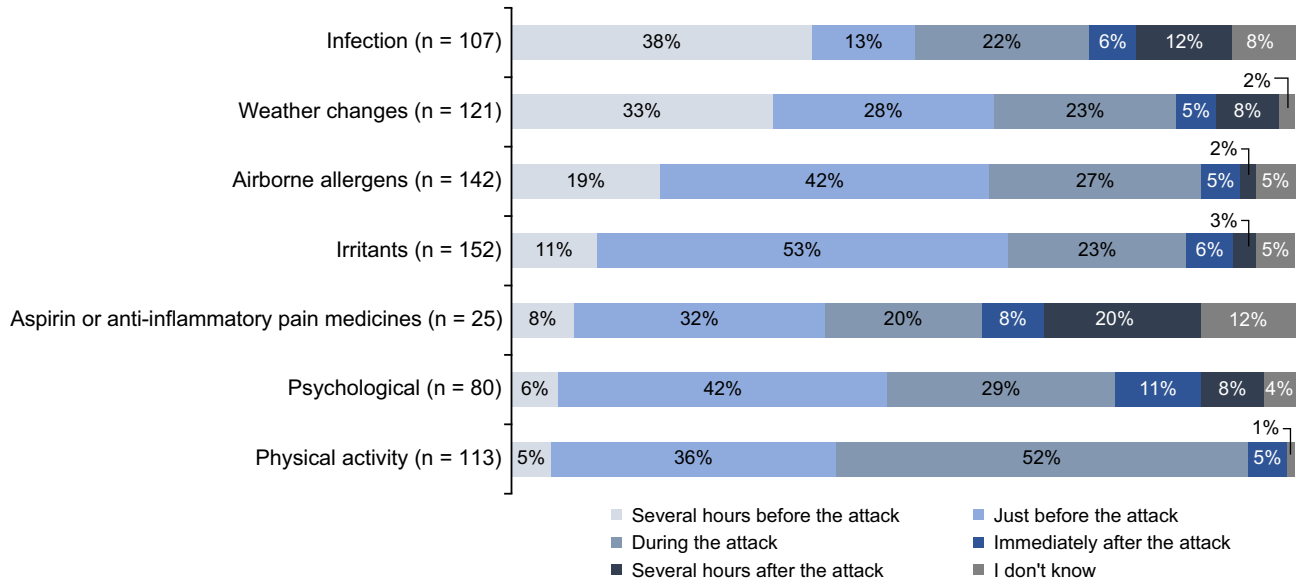
### Parameter Selection

Qualitative risk–benefit analysis of parameters deemed potentially predictive of changes in asthma control, as validated in the literature, identified those that could be recorded with minimal patient burden ([Figure 4](#)). These parameters varied based on whether they could be digitally detected or had to be patient-reported and the timing of trigger identification ([Table 1](#)). The final seven categories of parameters were chosen for the iPREDICT system based on those identified as important triggers by patients with poorly controlled asthma and the results of the risk–benefit analysis ([Figure 5](#)). These



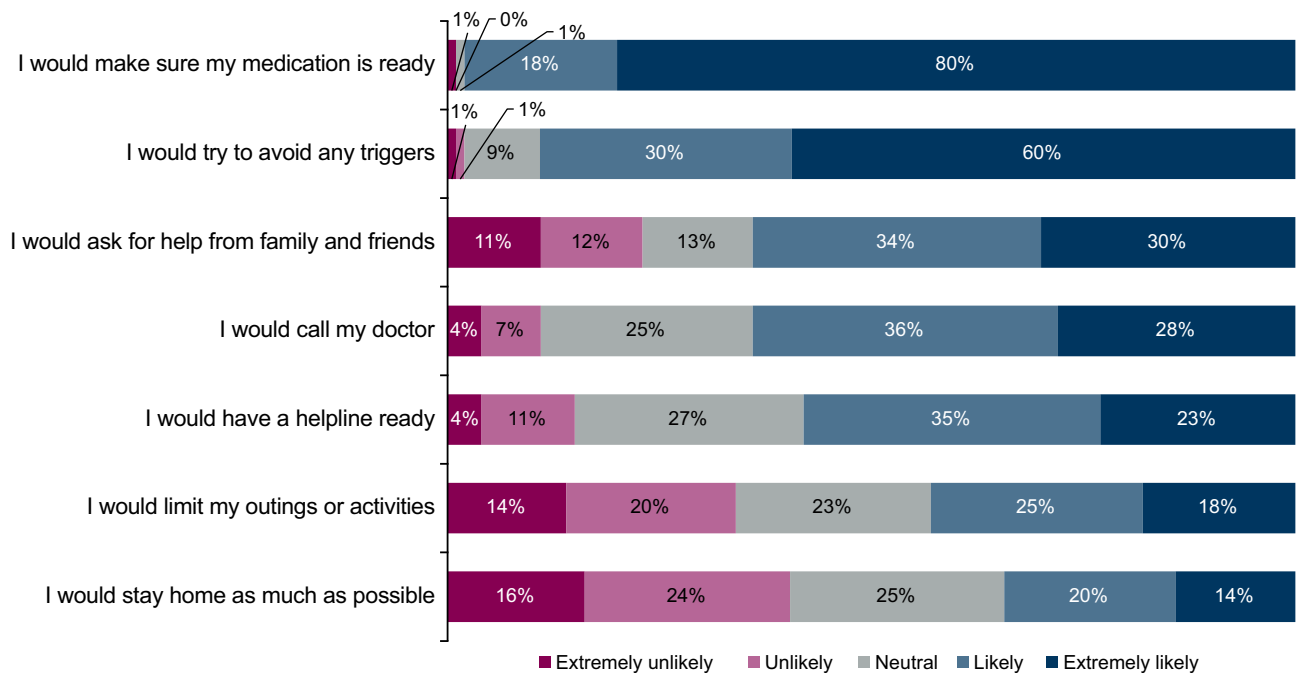
**Figure 1** Patient triggers survey: triggers of asthma episodes cited by patients.

**When can you usually identify the trigger?**



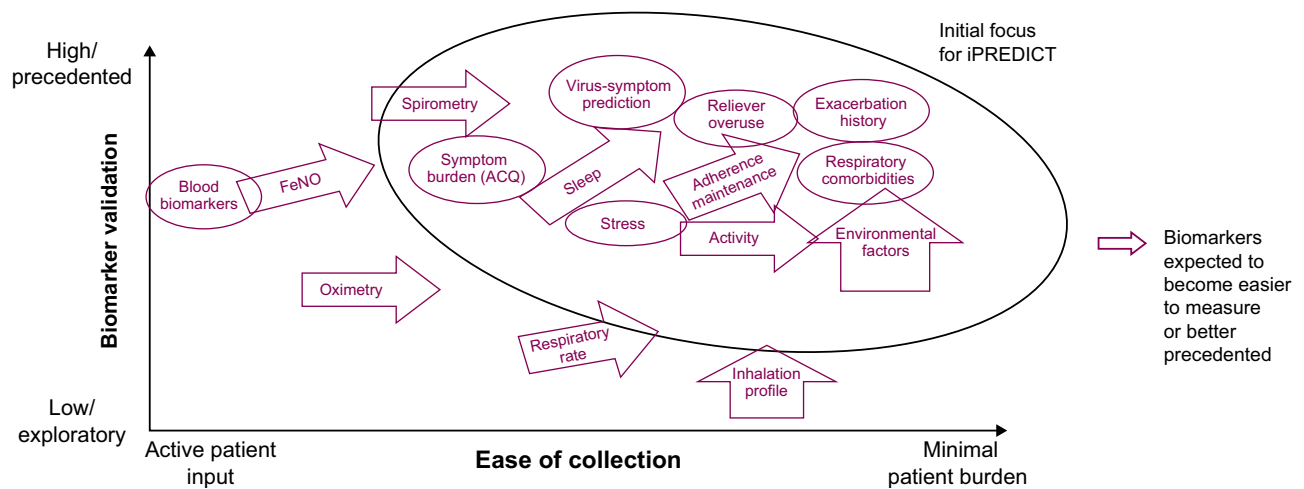
**Figure 2** Patient triggers survey: timing of trigger identification.

**If the tool was available to you, how likely are you to do the following to manage the risk of an impactful change in asthma control?**



**Figure 3** Patient triggers survey: patient behavior on receiving alerts from a predictive tool.

parameters included asthma symptoms, such as dyspnea, coughing, and wheezing; lung function parameters; physiological data, such as heart rate, respiratory rate, and activity; daily asthma medication use; sleep patterns and nocturnal awakenings; specific exposure to common triggers, such as animal dander, house dust, and smoke; and environmental data, including the air-quality index score and pollen count.



**Figure 4** A risk–benefit analysis of sensory and environmental triggers to identify measurable parameters predictive of changes in asthma control (predictive power versus ease of collection).

**Abbreviations:** ACQ, Asthma Control Questionnaire; FeNO, fractional exhaled nitric oxide.

### Device Usability Testing in Healthy Volunteers

All volunteers reported being very-to-extremely interested in their health and technology. Of the 17 healthy volunteers, only six were using a health- or wellness-related tool at the time of the study, and four others had previously used such tools. The devices tested varied by the type and number of parameters measured, with some, including the wearable biometric patch, vital sign monitor, and chest-based activity monitor, capable of measuring several variables across parameters, whereas others, such as sleep and FeNO monitors, focused on a single output ([Supplementary Table 2](#)).

The usability survey revealed a number of between-device differences that could influence user compliance in the study setting ([Table 2](#)). The FeNO monitor and one of the two spirometers evaluated achieved the highest usability scores at Week 2, whereas at Week 4, the sleep monitor attained the highest usability score.

**Table 1** Prioritization of Triggers Based on Qualitative and Quantitative Assessments

Trigger Cluster	Digital Detection	Patient Reported	Early Detection (2–24 h)	Parameter for Study
Irritants (smoke, chemicals, perfumes, fumes)	No	Yes	Some	PRO only
Airborne allergens (dander, dust, weeds, trees, pollen, mold, insect droppings, PM 2.5 and 10)	Some (PM, pollen, mold)	Some (pet dander, dust, insects, trees)	Some (PM, pollen, mold, trees)	PM, pollen, mold
Weather or air-quality changes (temperature, humidity, ozone, pressure, wind)	Yes	No	Yes	All
Physical activity	Yes (HR, steps)	Yes, limited	No	All
Infection (body temperature, RR, nasal symptoms, cough, sore throat)	Some (temperature, RR, cough)	Some (symptoms)	Some	Temperature, cough, RR
Psychological mediators (stress, anxiety, depression, tension, exhaustion, mood)	Some (stress via HR or GSR, sleep)	Some (mood, sleep, tension, stress)	Some	HR, sleep, mood via PRO
Medication (aspirin or anti-inflammatory)	No	Yes	No	No

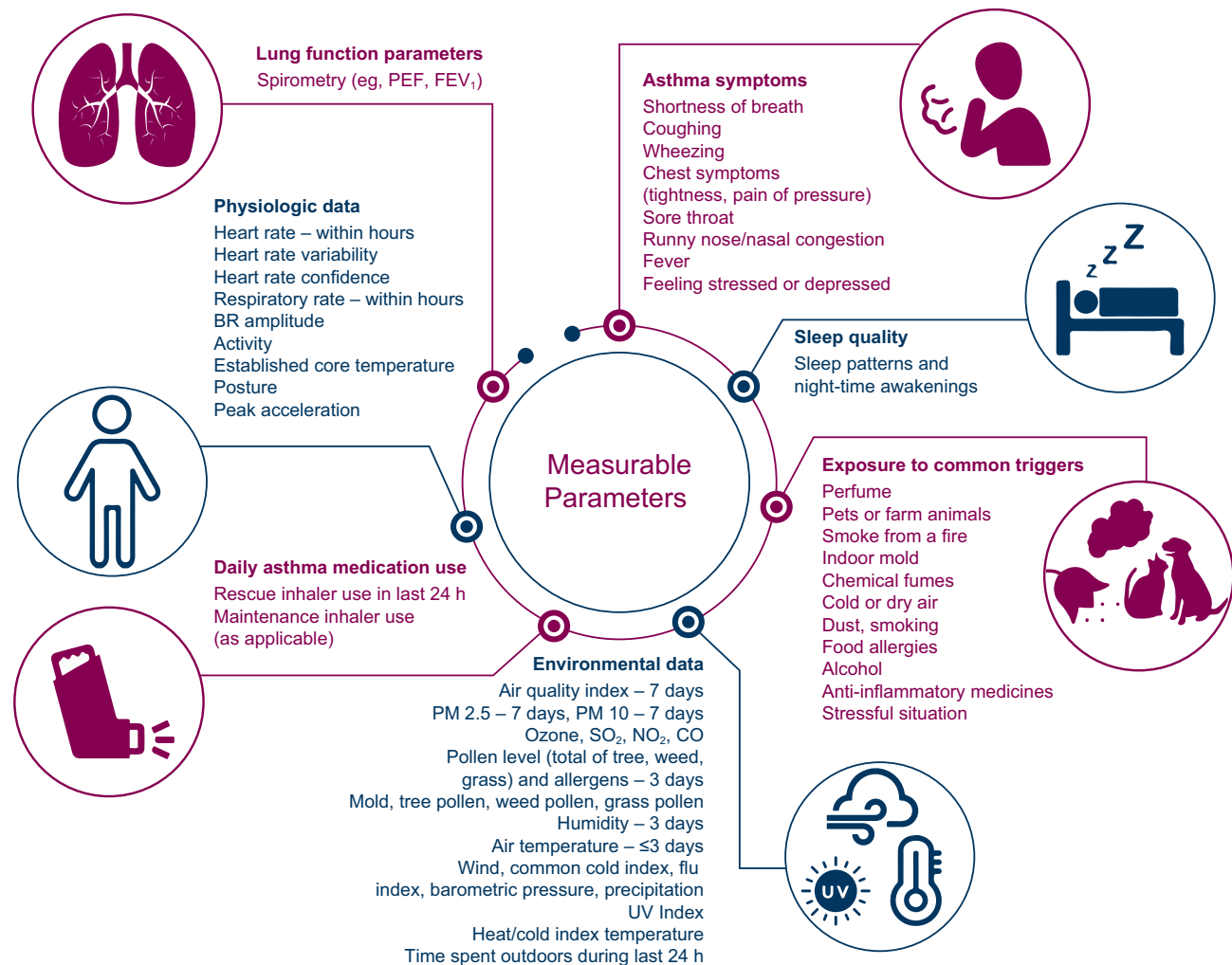
(Continued)

**Table 1** (Continued).

Trigger Cluster	Digital Detection	Patient Reported	Early Detection (2–24 h)	Parameter for Study
Food	No	Yes	No	Possible via PRO, but not early prediction
Hormonal	Some (clinical only)	Some (menstrual cycle, menopause)	Some	No

**Abbreviations:** GSR, galvanic skin response; HR, heart rate; PM, particulate matter; PRO, patient-reported outcome; RR, respiratory rate.

With respect to evaluation of the quality of the data captured, several disparities were discovered among the biosensors and connected devices (Figure 6). These included the presence of background noise, typically encountered with the spirometers, even when volunteers were not testing the devices, and data capture out of physiologic range such that unrealistic outputs were observed for data streams (Figure 7). In addition, missing data were common and appeared as no values or empty values, given as not available (NA) or NaN (not a number) by data export convention. Although



**Figure 5** Measurable parameters of the iPREDICT system.

**Abbreviations:** BR, breathing and relaxation; CO, carbon monoxide; FEV<sub>1</sub>, forced expiratory volume in 1 second; NO<sub>2</sub>, nitrogen dioxide; PEF, peak expiratory flow; PM, particulate matter; SO<sub>2</sub>, sulfur dioxide; UV, ultraviolet.

**Table 2** Usability Scores of Devices Tested

Device Type	Usability Survey (1–5) (2 Weeks)	Usability Survey (1–5) (4 Weeks)
Wireless biometric patch (HealthPatch MD)	3.33	3.50
Vital sign monitor (Zephyr BioPatch)	3.17	3.33
Chest-based activity monitor (Zephyr BioHarness 3)	NA	NA
Smart band activity tracker 1 (Microsoft Band 2)	3.33	3.33
Smart band activity tracker 2 (Healbe GoBe)	3.33	3.05
Smart band activity tracker 3 (Mio FUSE)	3.17	3.05
Smart band activity tracker 4 (Garmin Vivosmart HR)	2.33	3.39
Heart rate monitor (BodyGuardian Heart)	3.67	3.33
Sleep monitor (MySleep S+)	2.92	4.28
Peak flow meter (Smart Peak Flow)	2.89	2.82
Spirometer 1 (Spirobank II)	4.17	3.83
Spirometer 2 (Smart Spirometry)	3.39	4.11
FeNO monitor (NiOx Vero)	4.17	4.17

**Abbreviations:** FeNO, fractional exhaled nitric oxide; NA, not available.

the absence of values was the easiest to identify, a numeric entry of “0” could potentially be misinterpreted as an actual measurement.

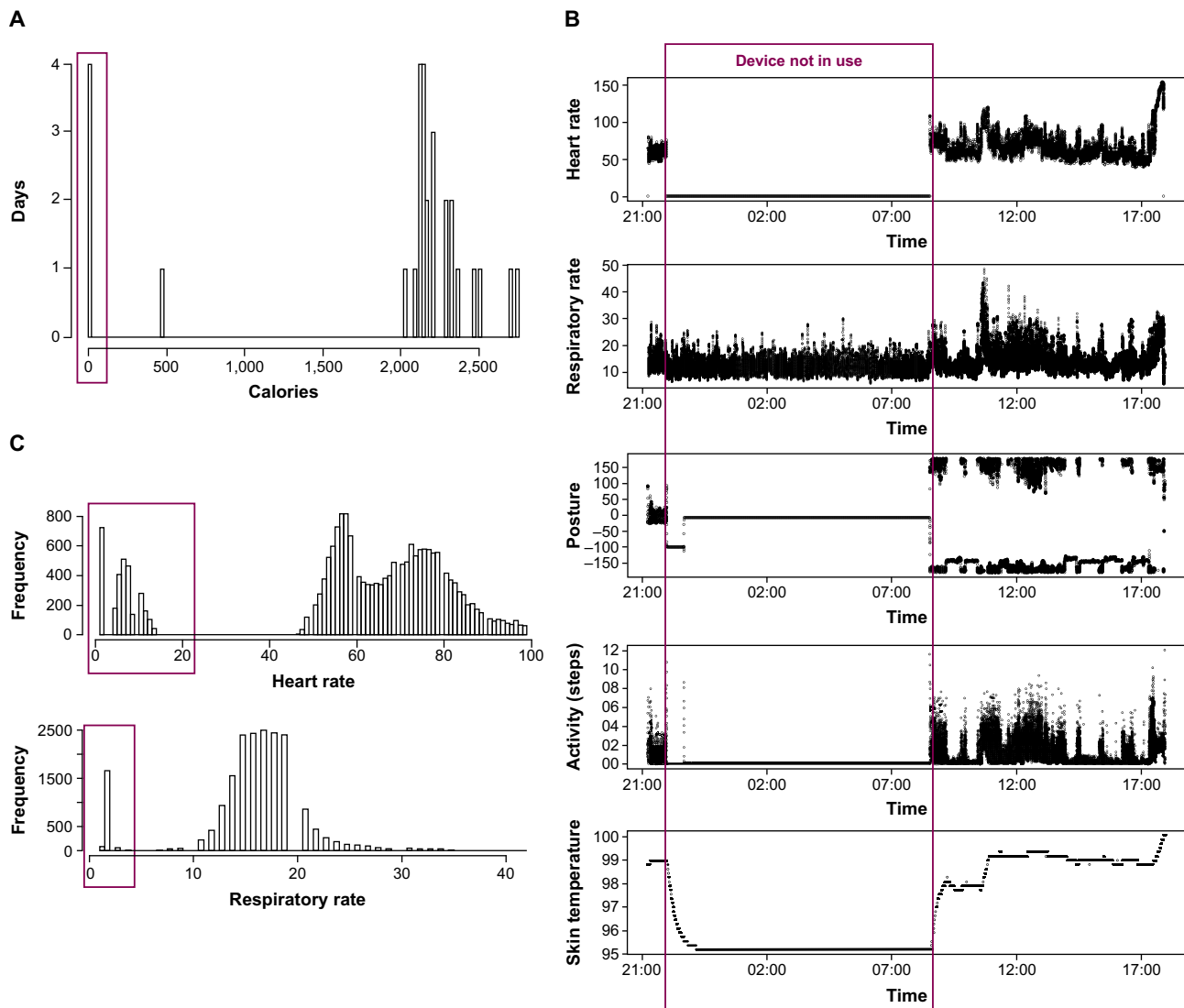
## Prioritized Devices

Based on the usability testing and validity of data capture, three devices, that is, a spirometer (Spirobank II, Medical International Research, Italy), a vital sign monitor (Zephyr BioPatch, Zephyr, Maryland, USA), and a sleep monitor (MySleep S+, ResMed, California, USA), were prioritized and selected for testing in the iPREDICT program. Together with an iPREDICT mobile application, which was developed to unobtrusively integrate data collected from most of the biosensors and connected devices, these components comprised the iPREDICT integrated system and were applied in the 24-week iPREDICT proof-of-concept study, which included patients with severe uncontrolled asthma to develop predictive models using identifiable, patient-specific disease parameters to anticipate changes in asthma control. The results of the pilot study are published separately.<sup>23</sup>

## Discussion

The iPREDICT program aims to transform disease management by applying digital health technologies to improve patient outcomes. To accomplish this overriding objective, we initially surveyed patients with asthma to understand their perceptions of asthma control, triggers, and management. We observed that most patients with asthma overestimated their degree of disease control. However, they reported an ability to identify environmental and physiological triggers and reacted positively to an accurate predictive tool that could signal the deterioration of asthma control. The most commonly cited asthma triggers were irritants, air pollution, airborne allergens, weather changes, and physical activity.

We then systematically characterized these sensory and environmental triggers to establish a set of measurable, validated, and non-invasive parameters that could be collected passively, imposing minimal patient burden and exhibiting the potential to predict changes in asthma control. These parameters included asthma symptoms, pulmonary function tests, physiological data, daily asthma medication use, sleep quality, environmental data, and exposure to common triggers. Subsequently, during the usability test portion of this study, healthy volunteers ranked devices and biosensors



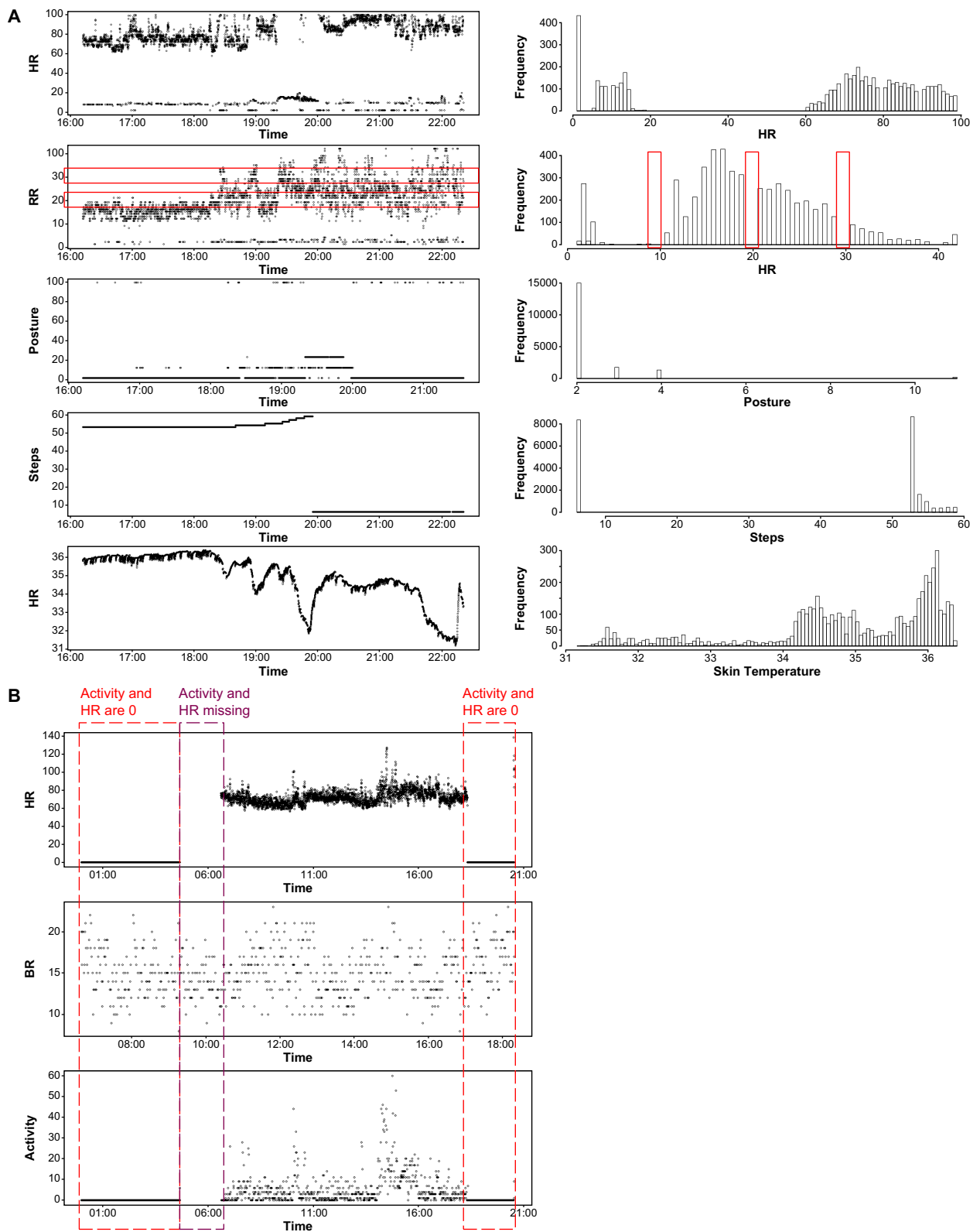
**Figure 6** Device usability testing: data properties for (A) missing data (smart band activity tracker), (B) background noise (wearable activity monitor), and (C) data out of physiologic range (wireless biometric patch).

that could passively capture related data based on the type and number of parameters, as well as any variables across the parameters that could measure usability, and data quality.

Based on comparative results from usability testing, an optimal set of three devices, that is, a spirometer, vital sign monitor, and sleep monitor, could be incorporated into the iPREDICT system while maintaining the necessary data quality. In the iPREDICT pilot study of patients with physician-diagnosed, severe, uncontrolled asthma, this integrated system of devices, together with up to two connected medication inhalers and two integrated mobile applications, were evaluated for their ability to generate multifaceted data, which could be leveraged to inform the development of an optimal prognostic algorithm for disease control from streaming data based on the detected changes from individual baseline variables. The results of this pilot study will be published separately.<sup>23</sup>

The findings from the patient perception and asthma trigger survey are consistent with published literature.<sup>14,15,24,25</sup> Patients commonly overestimate their asthma control, and reports indicate that as many as 80% of patients with uncontrolled disease perceive their asthma to be well controlled.<sup>24,25</sup> Additionally, the most common triggers for asthma episodes reside in the environment and may not be recognized or monitored accurately by the patient alone.<sup>15</sup> These





**Figure 7** Data properties of devices. **(A)** Missing measurement for respiratory rate observed at multiples of 10 for wireless biometric patch. **(B)** Missing activity and HR measurements observed for heart rate monitor.

**Abbreviations:** BR, breathing and relaxation; HR, heart rate; RR, respiratory rate.

observations suggest that an objective digital tool capable of tracking the disease status in real time may benefit patients with severe asthma and potentially those with other chronic diseases.

Technological advancements in wearable biosensors and connected devices capable of monitoring physiological and environmental parameters have enabled a vast amount of data capture. In parallel, machine learning has facilitated the analysis of large datasets and predictions of data variations in real time through statistical modeling.<sup>26,27</sup> However, to ensure high-quality data, the utility of rapidly evolving wearable sensor technology requires an iterative process of systematic, comparative assessments. The data quality evaluation in the device testing phase of the iPREDICT program unearthed several unexpected issues. Medical-grade devices, such as the wireless biometric patch, did not necessarily generate the most accurate data, and successfully integrating sensor data with other data streams will require consideration of both the frequency of data collection and the variability in their respective formats and units. Intrusive background noise would necessitate appropriate data smoothing to improve the signal-to-noise ratio. Thus, the development of a digitized intervention program for asthma management demands a proper framework for device selection, which accounts for the essential parameters of scaled usability, connectivity, and data quality.

Several other integrated digital health systems exist, distinguished by a variety of devices, sensors, and functionalities.<sup>11,13,15,28–32</sup> For instance, the Asthma Tuner, an electronic clinical decision support system, consists of a patient application (Android or iOS), healthcare interface, and spirometer connected via Bluetooth.<sup>19</sup> Patients register symptoms in the application and measure lung function using the spirometer. In turn, they receive automated feedback on asthma control and the recommended medication, including the required dose. In another digital health system, the kHealth asthma framework, the health status of the patient and environmental data are monitored continuously to convey information to physicians about personalized asthma triggers with the goal of fostering more individualized asthma management.<sup>15</sup> Similar to iPREDICT, the myAirCoach mobile health system features a portable spirometer, an inhaler adapter, an indoor air-quality monitor, a FeNO monitor, an exhaled breath temperature device, a FitBit HR Charge activity monitor, and smart inhalers that record medication adherence and the need for a rescue inhaler.<sup>13</sup> The mHealth system collects and analyzes data to determine parameters that may predict periods of uncontrolled asthma. Self-management, aided by the essential elements of myAirCoach, has proven effective in improving asthma control, quality of life, and acceptance of the technology among patients, in addition to reducing severe exacerbation rates.<sup>18</sup>

Patient compliance to asthma self-management plans is often low and declines over time,<sup>33</sup> potentially contributing to poor disease control. Additionally, dropout rates for patients with chronic diseases in mobile health self-management studies tend to be high,<sup>34</sup> highlighting the need for improving patient experience and engagement with digital health systems. While a wide range of devices have been developed for monitoring and improving compliance to a prescribed regimen,<sup>35</sup> most studies in asthma employing digital devices have focused on monitoring compliance to inhaled medications.<sup>20,36–39</sup> In the present study, assessment of device usability in healthy volunteers provided insights into factors that may influence compliance with the digital health system. Although device compliance was not assessed as part of the present study, findings from the iPREDICT proof-of-concept study conducted in patients with severe uncontrolled asthma showed that compliance to digital devices (75–90%)<sup>23</sup> was considerably higher than reported in previous studies (40–60%).<sup>40–42</sup> With the exception of a few studies that have employed the use of integrated digital health systems in asthma,<sup>15,19</sup> most research has explored the use of remote consultations and mobile phone text messaging to improve patient outcomes.<sup>43–45</sup> To our knowledge, findings from the present study represent the first step towards thorough identification of perceived asthma triggers and device usability assessment with the aim of developing the multimodal iPREDICT system, thereby paving the way for continuous data streaming, daily disease monitoring, and predicting changes in asthma control to enable early intervention.

Taken together, digital approaches to improve healthcare solutions that target medication adherence, real-time disease monitoring, trigger identification, and patient-physician communication offer opportunities for effective self-management in patients with asthma. The iPREDICT system, which aims to predict the deterioration of asthma control in real time via continuous monitoring of individual physiological and environmental data, represents a step forward in the field of digital healthcare. However, this model will require validation through long-term studies. For instance, the iPREDICT system did not include an FeNO monitor because a suitable device was not available during the earlier

study phases. Additional devices may be evaluated for non-invasive data acquisition as future iterations of iPREDICT technology evolve.

The limitations of digital health solutions should also be considered. Gaps in access to technology and an uneven technology infrastructure may restrict their dissemination to patients most in need.<sup>22,46</sup> The complexity of the connected devices, biosensors, data collection, systems integration, and access to broadband internet, compounded by privacy concerns, may also hinder broader uptake and application of digitized self-management programs.<sup>47</sup> The ingress of integrated digital solutions in routine medical practice will thus mandate privacy and data protection safeguards and greater digital inclusion. Nonetheless, digital solutions such as the iPREDICT system demonstrate the potential to benefit a variety of stakeholders. Patients may use this technology to better understand their personal experiences with asthma and its triggers, self-manage their disease, proactively modify risk factors toward an improved quality of life, and engage in a more informed and productive dialogue with their treating physicians. Physicians may also benefit from digital sensor technology as it provides objective information on individual disease status, thereby assisting in structuring tailored, optimized therapy. In the context of clinical trials, such a system can generate anonymized patient data that may not only expedite the identification of asthma treatment paths but also potential asthma phenotypes. For payers, the iPREDICT system can track medication adherence in real time and potentially generate quality-of-care metrics.

## Conclusion

In conclusion, a systematic approach that commenced with a survey of patients with asthma to better understand their perceptions of disease control and unmet self-management needs proceeded to identify measurable and validated parameters with the potential to predict changes in disease control. Finally, a structured, systematic comparison of devices and biosensors based on factors of usability, connectivity, data collection, and quality laid the foundation for the iPREDICT program. The findings reported herein delineate the framework for technology selection and testing that may inform future studies designed to evaluate the contribution of digital sensor technology to the management of chronic diseases such as asthma.

## Abbreviations

ACQ, Asthma Control Questionnaire; BR, breathing and relaxation; CO, carbon monoxide; FeNO, fractional exhaled nitric oxide; FEV1, forced expiratory volume in 1 second; GINA, Global Initiative for Asthma; GPP, Good Publication Practice; GSR, galvanic skin response; HR, heart rate; iPREDICT, individualized PRediction of DIsease Control using digital sensor Technology; NA not available; NaN, not a number; NO<sub>2</sub>, nitrogen dioxide; PEF, peak expiratory flow; PM, particulate matter; PRO, patient-reported outcome; RR, respiratory rate; SO<sub>2</sub>, sulfur dioxide; SUS, System Usability Scale; US, United States; UV, ultraviolet.

## Data Sharing Statement

Data underlying the findings described in this manuscript may be obtained in accordance with AstraZeneca's data-sharing policy described at <https://astrazenecagrouptrials.pharmacm.com/ST/Submission/Disclosure>. Data for studies directly listed on Vivli can be requested through Vivli at [www.vivli.org](http://www.vivli.org). Data for studies not listed on Vivli could be requested through Vivli at <https://vivli.org/members/enquiries-about-studies-not-listed-on-the-vivli-platform/>. AstraZeneca Vivli member page is also available outlining further details: <https://vivli.org/ourmember/astrazeneca/>.

## Ethics Approval and Informed Consent

The Regional Ethics Committee for Gothenburg (formerly known as Ethics Committee for Västra Götaland) exempted the part of the study involving healthy volunteers. IRB approval was not sought for part of the study involving patients with asthma as no intervention steps were involved and surveys were conducted by PatientsLikeMe, a web-based application where members are willing to share detailed computable data about symptoms, treatments, and health in order to learn from the experience of others and improve their outcomes.

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## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

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