



2022



A scoping review of mHealth
monitoring of pediatric bronchial
asthma before and during the
COVID-19 pandemic

MTELEHEALTH

A scoping review of mHealth monitoring of pediatric bronchial asthma before and during COVID-19 pandemic

Nurlan Dauletbaev^{1 2 3 4}, S. Zoe Oftring⁵, Wided Akik⁶, Lukas Michaelis-Braun¹, Julia Korel¹,
Larry C. Lands^{2 3}, Susanne Waldmann⁷, Beate S. Müller⁸, Michael Dreher⁹, Gernot Rohde¹⁰,
Claus F. Vogelmeier¹, Sebastian Kuhn⁵

Authors' affiliations

¹ Department of Internal, Respiratory and Critical Care Medicine, Philipps University of Marburg, Marburg, Germany (Member of the German Center for Lung Research (DZL))

² Department of Pediatrics, Faculty of Medicine and Health Sciences, McGill University, Montreal, QC, Canada

³ The Research Institute of McGill University Health Centre, Montreal, QC, Canada

⁴ al-Farabi Kazakh National University, Almaty, Kazakhstan

⁵ Department of Digital Medicine, Medical Faculty OWL, Bielefeld University, Bielefeld, Germany

⁶ Division of Experimental Medicine, Faculty of Medicine and Health Sciences, McGill University, Montreal, QC, Canada

⁷ Central Medical Library, Philipps University of Marburg, Marburg, Germany

⁸ Institute of General Practice, Goethe-University Frankfurt, Frankfurt am Main, Germany

⁹ Department of Pneumology and Intensive Care Medicine, University Hospital Aachen, Aachen, Germany

¹⁰ Medical Clinic 1, Department of Respiratory Medicine, University Hospital Frankfurt, Frankfurt am Main, Germany

Corresponding author:

Dr. Nurlan Dauletbaev

Head, Translational Research Lab

Department of Internal, Respiratory and Critical Care Medicine

Philipps-University of Marburg

Biomedical Research Centre (BMFZ), Office +1/61300

Hans-Meerwein-Str. 2

35043 Marburg

Germany

Tel.: +49 (0) 6421-286-6041

Fax: +49 (0) 6421-286-5133

Email: nurlan.dauletbayev@uni-marburg.de

Abstract

Mobile (m) Health technology is well-suited for Remote Patient Monitoring (RPM) in a patient's habitual environment. In recent years there have been fast-paced developments in mHealth-enabled pediatric RPM, especially during the COVID-19 pandemic, necessitating evidence synthesis. To this end, we conducted a scoping review of clinical trials that had utilized mHealth-enabled RPM of pediatric asthma. MEDLINE, Embase and Web of Science were searched from September 1, 2016 through August 31, 2021. Our scoping review identified 25 publications that utilized synchronous and asynchronous mHealth-enabled RPM in pediatric asthma, either involving mobile applications or via individual devices. The last three years has seen the development of evidence-based, multidisciplinary, and participatory mHealth interventions. The quality of the studies has been improving, such that 40% of included studies reported were randomized controlled trials. In conclusion, there exists high-quality evidence on mHealth-enabled RPM in pediatric asthma, warranting future systematic reviews and/or meta-analyses of the benefits of such RPM.

Keywords: Remote Patient Monitoring; mHealth; Remote Sensing Technology; Pediatrics; Bronchial asthma; COVID-19; Respiratory Tract Diseases

Abbreviations

BPD	Bronchopulmonary dysplasia
CF	Cystic Fibrosis
COVID-19	Coronavirus Disease 2019
mHealth	Mobile Health
RDS	Respiratory Distress Syndrome
RPM	Remote Patient Monitoring

Educational Aims:**The reader will come to appreciate that:**

- mHealth and Internet-of-Things technologies enables remote monitoring of pediatric asthma in patients' habitual environments (home, daycare or school)
- This remote monitoring can be synchronous (i.e., real-time monitoring) or asynchronous (i.e., collection of health data and consultation by a healthcare professional occur at different time points)
- recent mHealth apps for pediatric asthma are being developed in an evidence-based, multidisciplinary, age-tailored, and participatory manner
- mHealth apps can simultaneously address multiple aspects of pediatric asthma (inhalation technique, therapy adherence control, symptom monitoring, educational content, family collaboration, etc)
- If needed (e.g., nighttime or school monitoring), monitoring of pediatric asthma is feasible without smartphones and mHealth apps, by using standalone wireless devices

Future research directions:

Future research should critically appraise quantitative and qualitative benefits for the patient and clinician of mHealth monitoring in pediatric asthma. These benefits may range from traditional benchmarks (such as, symptom score, number of asthma exacerbations, pulmonary function tests) to qualitative outcomes (better collaboration between patient + parent or caregiver and a healthcare professional, sense of better autonomy over health-related decisions, etc). Future research should also define the evidence-based and age-tailored guidelines for mHealth apps for pediatric asthma.

Introduction

Digital health interventions have increasingly been permeating into patient care, enabling the development of novel healthcare concepts, including in the field of remote patient monitoring (RPM). Mobile (m) Health is part of the aforementioned digital health interventions. Drawing from capacities of mobile and wireless digital technologies, mHealth supports the transfer of the concepts of patient care, public health, disease management, and health education to patients' homes, or places of study or work. When mHealth technology is combined with portable (wearable, implantable, etc) digital sensors, it enables RPM in the patients' habitual environment. Most frequently, RPM via mHealth technologies involves the use of smartphones and specialized mobile apps but can also be carried out through standalone wireless devices. This RPM can be asynchronous (that is, when a medical practitioner checks patient's health data at time points different from collection) or synchronous (i.e., a real-time remote observation of patient health data)¹⁻³.

Implementation of mHealth monitoring in a pediatric setting provides specific challenges, including reliance on support from a parent or caregiver, difficulty of RPM during schooltime, and requirements to the software and hardware to be tailored to the appropriate age groups. In addition, it has been a common recent trend that development of novel technological advancements outpaces the appropriate clinical testing⁴. Moreover, these fast-paced developments have been accelerated during the ongoing COVID-19 pandemic. All this justified conducting a comprehensive synthesis of the recently published evidence on mHealth monitoring in the pediatric respiratory disease. As the first step towards this objective, this scoping review aggregated and synthesized the recent available evidence of mHealth monitoring in pediatric asthma, including during the time of COVID-19 pandemic.

Materials and Methods

Objectives of the scoping review

Primary objectives:

We pursued the following primary objectives. The first primary objective was to obtain an overview of relative abundance of publications on mHealth monitoring in common respiratory diseases in the pediatric population. The second primary objective was to aggregate the published data on synchronous and asynchronous monitoring, be it RPM involving mHealth apps or via standalone (e.g., Internet-of-Things) devices. The third primary objective was to yield a structured synthesis of mHealth apps tailored to children and adolescents.

Secondary objective:

A secondary objective was to reach an informed decision as to whether a systematic review on the pediatric mHealth is warranted by the quantity and quality of the available evidence. We were interested to know which disease or medical condition a future systematic review should cover, and whether there are clinical trials of sufficient quality for critical appraisal of evidence of the benefits of mHealth-enabled RPM.

Pilot MEDLINE search

Towards the first primary objective, we wished to gauge the number of publications for common chronic pediatric respiratory diseases that would be identified by our search strategies (see below). Depending on the number of potential hits, a combined scoping review on several chronic respiratory diseases could be carried out, or the scoping review would focus on pediatric respiratory disease with the most hits. The latter was presumed to be pediatric asthma. The other common chronic pediatric respiratory diseases and conditions were bronchopulmonary dysplasia, cystic fibrosis and bronchiectasis, malformations (e.g.,

congenital cystic adenomatoid malformation, congenital diaphragmatic hernia, tracheomalacia, or tracheal stenosis), non-cystic fibrosis genetic diseases (e.g., alpha₁-antitrypsin deficiency, sickle cell anemia, ciliary dyskinesia, Duchenne muscular dystrophy), and home ventilation and neonatal respiratory distress syndrome. In addition, we also wished to conduct a search on mHealth monitoring in pediatric COVID-19.

To this end, we conducted a pilot search in MEDLINE. The MEDLINE search utilized Medical Subject Headings (MeSH) and Supplementary Concepts, as well as free-text keywords (Supplemental Table 1). Given the relative recent introduction of mHealth technology for RPM in pediatric chronic respiratory diseases, we limited the timeframe of the search for chronic diseases and conditions to the last 5 years (2016-09-01 to 2021-08-31; Supplemental Table 1). Since COVID-19 pandemic has been going on for about two years, the search was limited to the timeframe between 2020-01-01 and 2021-08-31 (Supplemental Table 1).

To ensure the relevance of search terminology, we consulted previous systematic reviews and/or scoping reviews and/or narrative reviews on this subject (e.g., ⁵⁻⁷), or bibliography recommendations on specialized websites (e.g., ⁸). Our COVID-19 search has been described previously⁹.

This search was tested in two different concepts. The first concept aimed for higher sensitivity¹⁰. The “high sensitivity” search concept was a modification from the popular PICO (*Population, Intervention, Comparator, Outcome*) criteria¹¹ and included only “*Population*” and “*Intervention*” (PI; Supplemental Table 1). The second concept aimed for higher precision¹⁰ and included “*Population*”, “*Intervention*”, and “*Outcome*” (PIO; Supplemental Table 1). In both search concepts, “*Population*” encompassed the common chronic respiratory diseases and conditions, plus COVID-19 (Supplemental Table 1). The “*Intervention*” comprehensively addressed various definitions of mHealth, in conjunction

with related terminology for individual devices and sensors (Supplemental Table 1). The “*Outcome*” encompassed different objectives of mHealth-enabled RPM, such as patient triage, timely recognition of disease exacerbation, etc (Supplemental Table 1).

Comprehensive search: MEDLINE, Embase, and Web of Science

Following the pilot MEDLINE search, we conducted a subsequent search in three major electronic literature databases: MEDLINE, Embase, and Web of Science (latest search: December 3, 2021). This comprehensive search is supposed to yield the sensitivity of more than 97%¹². The MEDLINE search terminology and concepts were translated into equivalent terminology in two other databases. This search addressed the second and third objectives of this scoping review.

Methodologically, the comprehensive search, and the following literature screening and synthesis followed the recommendations and guidelines for scoping reviews¹³⁻¹⁸, especially the PRISMA recommendation for scoping reviews (Supplemental Table 2 for PRISMA-ScR Checklist).

Reference selection

The most important criterion for inclusion in this scoping review was that the publication had had to present a quantitative, qualitative or mixed methods intervention study which would verify the usability of the proposed digital RPM in the clinical setting relevant to the disease of interest. Thereby, many potentially interesting publications that primarily focused on development of mHealth apps (or sensors, or online platforms), but featured no patient studies, or tested the proposed intervention only in healthy volunteers, would not be considered suitable.

The other inclusion criteria were the following. First, the included publication would have to be a publication in English, French or German, and show an obvious relationship to the disease of interest (e.g., bronchial asthma), and mHealth or mHealth monitoring (Supplemental Figure 1). Then, the publication would have to be an original publication (Supplemental Figure 1). For the purpose of this scoping review, we also decided to include case series with more than 5 patients (Supplemental Figure 1). In addition, mHealth technology presented in an included publication should be suitable for PRM, which could be synchronous or asynchronous. As RPM, we defined remote collection and transfer of digital health parameters (the so-called “digital biomarkers”) with the help of one or several mHealth sensor(s), or Internet-of-Things devices, and with or without the use of an mHealth app. Finally, the publication would need to clearly identify that mHealth intervention was intended, or was suitable, for pediatric population in the disease of interest.

The exclusion criteria fell into several categories: (1) language other than English, French or German (“foreign language”), (2) unsuitable patient population (e.g., only adult patients, or no separate data for children and adolescents), (3) publications focusing solely on description of mHealth app or sensor, without a supporting clinical study, (4) publications dedicated to development or a computational algorithm, website, sensor or device, (5) surveys or data mining publications. The publications in categories (2) - (5) were grouped together as “unsuitable study types”. Additional exclusion criteria were: (6) healthcare-related publications without a clinical intervention (e.g., publications on health economics or digital safety of mHealth apps; excluded as “unsuitable study types”) and (7) reviews of all kinds, meta-analyses, conference abstracts, retractions, commentaries or Editorials (these were grouped together as “unsuitable publication type”).

With several reviewers contributing to primary (title + abstract) screening, and with the anticipated heterogeneity in mHealth-related publications, the reviewers agreed on defining

any unclear cases as potentially relevant (i.e., apply a tag “maybe” during the title and abstract screening; see below). The “maybe” tag for potentially relevant publications, while increasing the workload at the step of full-text screening, aimed to avoid false-negative exclusion.

Screening for suitable publications and evidence synthesis

Following iterative deduplication¹⁹, the publications were subjected to manual screening. The first screening step was conducted in the online software Rayyan²⁰ and permitted publication inclusion based on their titles and abstracts. Given the volume of the publications for screening, the title and abstract screening was distributed among several co-authors of this manuscript (ND, SZO, WA, LMB, and JK). To ensure the uniformity of the screening, the lead author conducted one or several training sessions in Rayyan with every co-reviewer. Furthermore, a flow chart (Supplemental Figure 1) was prepared by the lead author to visually describe the screening process and selection of the reasons for publication exclusion. In addition, the lead author randomly double-checked some excluded publications to warrant the consistency of the screening by other co-reviewers.

Following the primary screening, full-text publications were screened by the lead author. Towards this, an Excel table was prepared to compile the following information: the last name of the first author, the year of publication, targeted study population, brief description of mHealth device or sensor or software or platform, study design, principal reasons for exclusion (if applicable). Publications’ outcomes and conclusions were also to be documented. Following exclusion of unsuitable references, the lead author descriptively compiled the information from the included full-text publications. The latter information comprised detailed description of mHealth intervention (using an app or a device / sensor), type of RPM (synchronous or asynchronous), as well as additional pertinent data. In addition

to descriptive (i.e., narrative) synthesis, we aimed for produce a structured and machine-searchable synthetic dataset which would compile the essential data of mHealth monitoring. Thereby, the evidence synthesis would be available in descriptive, semi-structured, and structured forms.

In some publications where the nature of mHealth intervention (e.g., app features) in the underlying clinical trials was not clear from the publication at hand, the preceding publications by the authors of these clinical trials were consulted in order to recover the missing details. In this case, some limited “snowballing” technique was applied to extract the necessary information.

Software and data visualization

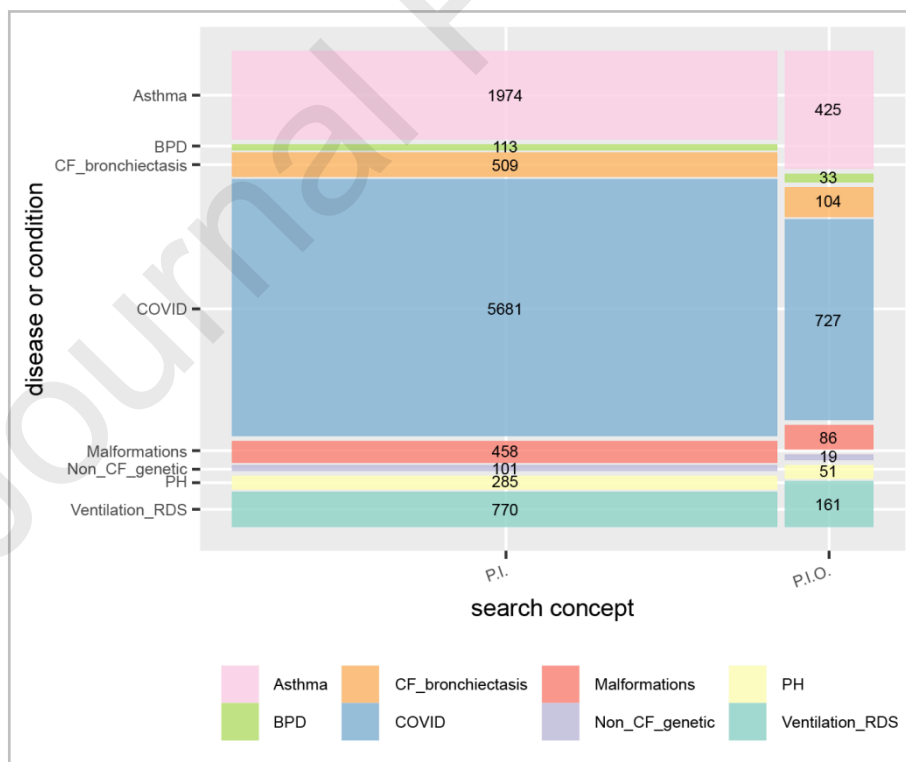
The principal activities related to this scoping review were conducted either in the online software Rayyan²⁰ or desktop version of the bibliography software Endnote (version 20.2.1.²¹, Clarivate, Philadelphia, PA, USA) The mosaic plot was generated using the package “ggmosaic”²² in conjunction with packages “ggplot2”²³, “svglite”²⁴, and “RColorBrewer”²⁵ for the statistical environment R²⁶ and graphics user interface RStudio²⁷. The PRISMA flow chart was prepared with the help of Adobe Illustrator 2021²⁸.

Results

Pilot MEDLINE searches

The first pilot MEDLINE search aimed at higher sensitivity and thus comprised only two search concepts, *Population* and *Intervention*. When the pertinent search criteria (Supplemental Table 1) were applied to the range of common chronic respiratory diseases and conditions in the pediatric population, as well as to COVID-19, we obtained the overwhelming majority of publications (5681 out of 9891 publications; 57%) being related to the latter condition (Figure 1, tiles in the left panel). Roughly 20% (1974 out of 9891) of the identified publications were related to pediatric asthma (Figure 1, tiles in the left panel), whereas the other diseases and conditions collectively made up the remaining 22.6% of the identified publications (Figure 1, tiles in the left panel).

Figure 1



Mosaic plot of pilot MEDLINE searches.

The y axis presents the searches in individual pediatric diseases and conditions. These searches were conducted, as indicated on the x axis, using the broader “*Population-Intervention*” (“P.I.”, tiles in the left panel) or more focused “*Population-Intervention-Outcome*” (P.I.O., tiles in the right panel) concepts. The areas are presented in different colors representing individual diseases and conditions, and proportional to the number of identified publications. The latter numbers are also shown in the middle of respective rectangles. “BPD”, bronchopulmonary dysplasia; “CF”, cystic fibrosis; “Non-CF genetic”, non-CF genetic pediatric diseases and conditions; “PH”, pulmonary hypertension; “Ventilation_RDS”, home ventilation and neonatal respiratory distress syndrome.

We then conducted the second pilot MEDLINE search using the more focused concept (i.e., aiming for higher precision). Specifically, this search utilized the “*Population-Intervention-Outcome*” concept (Figure 1). As expected, the number of recovered publications dropped several times (Figure 1). For example, while the broader search on mHealth monitoring in pediatric asthma yielded 1974 publications, the more focused search revealed only 425 potentially pertinent publications (Figure 1). Regardless of the utilized search strategy, the majority of identified publications were related to COVID-19. This was very astonishing, given the fact that non-COVID diseases and conditions were searched within the timeframe of 5 years, whereas the search for mHealth-related publications in COVID-19 was limited to the past 20 months only.

Potentially suitable publications on mHealth monitoring in asthma made up the second (after COVID-19) most numerous publication group, followed by publications related to home ventilation / neonatal respiratory distress syndrome (Figure 1). The publications related to cystic fibrosis and bronchiectasis made up the fourth most numerous group of identified publications (Figure 1), and this was also true regardless of the employed search strategy.

The pilot MEDLINE searches were, indeed, only an approximation to estimate the volume of publications that used mHealth technology for RPM in pediatric diseases or conditions, or in COVID-19. Obviously, a minority of these publications would be truly

representative of mHealth monitoring as per criteria of this scoping review. Our assumption, though, was that the relative yield of truly positive publications should be comparable across the searches in different diseases and conditions.

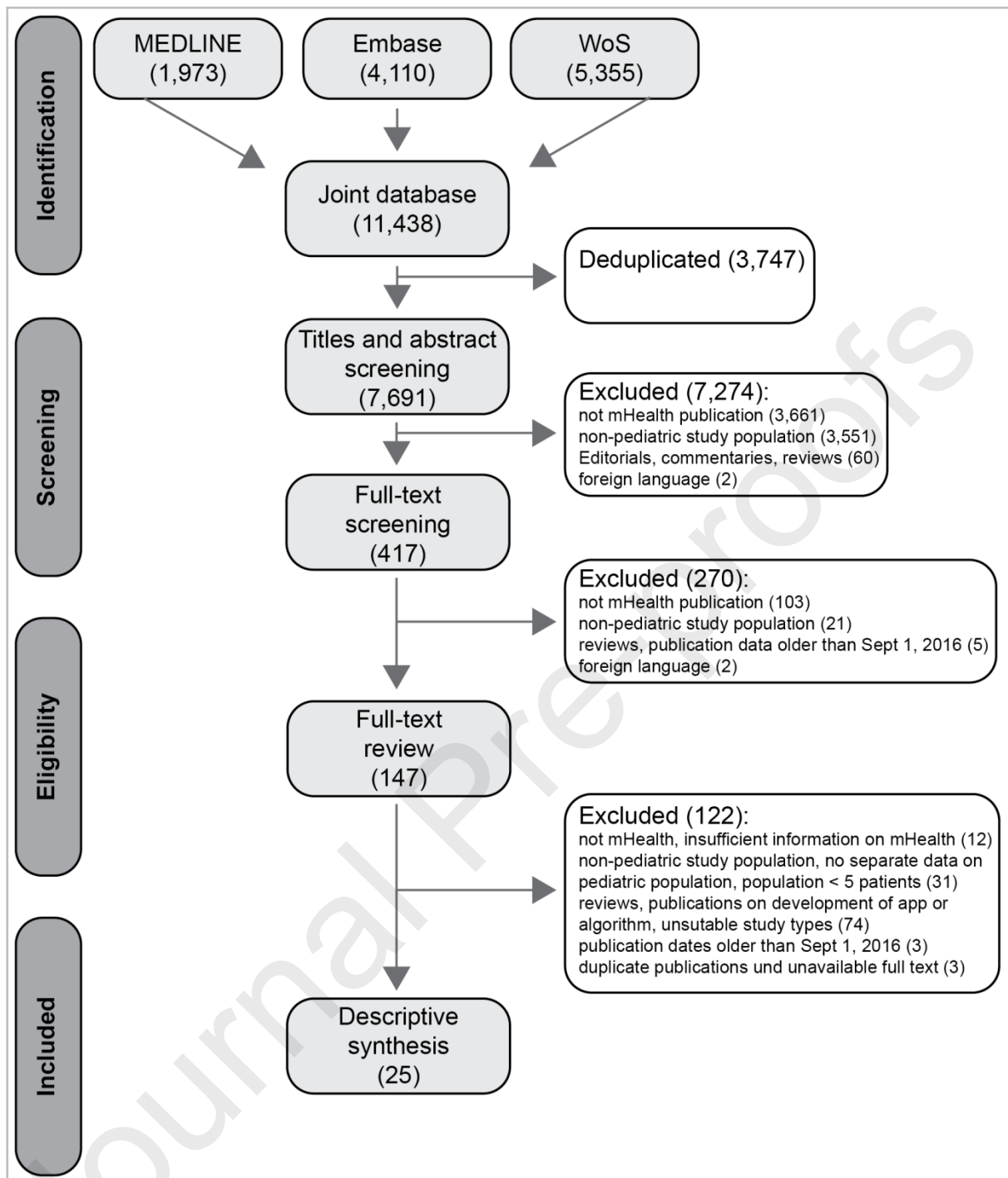
With this consideration, we next wanted to determine on which disease or condition to conduct this scoping review. We first turned our attention to COVID-19, the disease with the most numerous publications in both pilot MEDLINE searches (Figure 1). First, the lead author randomly screened some publications from the reference samples identified in the pilot MEDLINE searches. It turned out that the majority of these randomly selected COVID-19 publications were dedicated to telemedicine, such as the healthcare service administered via phone or video consultations, and not utilizing mHealth. Second, two co-authors (SZO and SK) undertook an independent unstructured PubMed search on mHealth in COVID-19 and identified very few potentially suitable publications. Third, both the lead author and the two co-authors observed that the greater majority of these publications described the use of telemedicine as a substitute to regular clinic visits. In contrast, there have been extremely few publications on RPM of pediatric COVID-19. It is possible that some more “fine-tuning” of the search strategy would be needed for better balancing out the specificity and precision on mHealth in COVID-19. This was left out for the subsequent scoping review.

Our subsequent decision was to conduct the scoping review on mHealth monitoring in pediatric asthma. The a pilot searches revealed the dominance of publication on mHealth in pediatric asthma, in comparison to other pediatric diseases and conditions (Figure 1). To ensure higher coverage, we decided to utilize concept enabling higher sensitivity and utilized the “*Population-Intervention*” search concept in the subsequent step of the scoping review.

Searches in MEDLINE, Embase, and Web of Science for mHealth publications in pediatric asthma

The combined search in these three databases identified 11,438 publications (Figure 2). The greater majority of retrieved publications were retrieved from Embase or Web of Science (respectively, 35.93% and 46.82%; combined: 82.75%; Figure 2, Supplemental Table 3). Iterative deduplication designed to maximize the exclusion of replicate publications¹⁹ removed only 3,747 (32.76%) publications. Thereby, the search in non-MEDLINE databases retrieved the bulk of non-duplicated publications that had potential suitability for this scoping review. This fact further indicated that the pilot searches conducted solely in MEDLINE may majorly underestimate the volume of mHealth-related publications.

Figure 2



PRISMA flow chart

The MEDLINE, Embase and Web of Science (WoS) databases were searched based on “*Population-Intervention*” concept. The identified publications were deduplicated and subjected to primary (title + abstract) and secondary (full-text) screening. This was followed by full text perusing and review, and descriptive semi-structured, and structured evidence synthesis. Each of these steps was associated with exclusion of publications

based on the reasons presented in this chart. Respective numbers of identified, deduplicated, and excluded publications are shown in parentheses in respective boxes.

There was the total of 287 publications tagged in primary screening in Rayyan as “maybe” (i.e. potentially relevant) and 130 publications tagged as “included” (i.e., deemed as highly relevant). Combined, there were 417 publications that transited further to full-text screening (Figure 2). Out of these, 147 publications (Figure 2) were selected for full-text review and assessment for suitability for evidence synthesis. The other 270 publications were excluded mostly because of being a publication not related to mHealth (“not mHealth publication”; Figure 2) or describing a non-pediatric population (Figure 2).

Out of the 147 publications, only 25 publications (17% of publications subjected to full-text review and assessment, or 0.325% of the original 7,691 non-duplicate publications; Figure 2) eventually made it to the evidence synthesis step of this scoping review. In our experience, this is not unusual for systematic searches for publications on telemedicine or mHealth to produce such a low relative yield of truly relevant publications (see for comparison e.g.,^{29,30}).

While not required *per se*, we still prepared a semi-structured compendium of excluded 122 publications (Supplemental Table 4). This information could be useful to subsequent studies (for instance, for those developing mHealth apps).

Descriptive, semi-structured and structured evidence syntheses

Most publications (19 out of 25, or 76% of publications) included in descriptive synthesis (Table 1), semi-structured synthesis (Supplemental Table 5), and structured, machine-searchable synthesis (Supplemental Table 6) utilized mHealth apps, or apps in conjunction with various online platforms or web portals. The remaining publications³¹⁻³⁶ utilized

combinations of different standalone digital sensors (that is, without integration by an app) or a single digital sensor.

A sizable minority of the included studies^{35,37-44} (10 out of 25, 40%) utilized a randomized controlled study design, while the remainder of the publications used different kinds of uncontrolled intervention studies or feasibility studies. Patient monitoring, at least in the studies that reported this parameter, ranged between 2 weeks³² and one year^{39,43}.

Out of 19 publications that utilized some mHealth app for patient monitoring, 13 (68.4%) publications^{39-41,44-53} tested the apps which had been developed by publication authors. An interesting app developing model has been presented in one publication⁵¹. In particular, this app has been developed using a “crowd-sourcing” collaboration method, such that designing, and programming of different app modules have been distributed among different volunteer programmers.

The majority of included publications (15 out 25, or 60%) targeted the objective of asthma self-management. These publications, not surprisingly, only represented the studies that utilized mHealth apps^{38-44,46,47,49-54}. Indeed, in the included publications, mHealth apps provided an opportunity to equip the patient with a versatile asthma control tool, whose applicability ranged from simpler tasks (e.g., quality assurance of inhalation technique, asthma treatment plan, asthma education) to more sophisticated options, such as instantaneous feedback to the patient about the level of his or her asthma control, and a timely advice from a healthcare professional (see Supplemental Table 5 for details). In addition, one publication³⁸ presented an mHealth platform that provided feedback to the patient and supported, via a decision-supporting software, the healthcare professional in fine-tuning the patient’s treatment plan.

Furthermore, upon the synthesis of publications on mHealth apps for pediatric asthma, we observed a clear trend towards increasing sophistication of recently developed apps. If in

earlier years, some mHealth platforms were used to enable a single health-related task, such as to provide treatment feedback through SMS text messages⁵⁵, the more recent mHealth apps comprised several interdependent asthma-related modules (e.g., for patient education, treatment plans, visualization of asthma control, instant messaging from automated RPM portals, etc.; see Supplemental Table 6 for details). Moreover, the apps incorporated specific contents (sports, etc.; Supplemental Tables 5 and 6) or features (e.g., “gamification”, rewards, etc.: Supplemental Tables 5 and 6) that were tailored to address children or adolescents with asthma. Some of these apps even address disease aspects beyond the conventional patient education or self-monitoring. For instance, three included publications^{41,45,47} targeted family management of pediatric asthma (that is, by actively involving parents or caregivers in the management process) or aimed to foster efficient communication between the family and a healthcare practitioner. Such complex mHealth apps for pediatric asthma were developed by the evidence-informed multidisciplinary teams and benefited from participatory patient contributions (Supplemental Tables 5 and 6).

Finally, at least 7 (28%) publications^{38,39,42,43,45,49,52} presented descriptions of online platforms which comprised mHealth apps and web portals. The former was utilized by the patients, while the latter by healthcare professionals. Such platforms typically enabled synchronous RPM by a healthcare professional, or even in an automated manner³⁸.

The more sophisticated options are surely not feasible with standalone devices that are not supported by mobile apps. Yet it appears that such devices are still capable of finding their own niche in the RPM of pediatric asthma. For instance, one publication³² described an interesting application of a standalone device to monitor nighttime symptoms to register the premonition of an asthma exacerbation (Supplemental Table 5). The incoming health data were integrated by the software at the site of the telemonitoring team³¹, rather than by a peripheral mHealth app on patient’s end. This setting enabled development of machine

learning approaches to health data, with building a subsequent computational model for timely recognition of nighttime indicators of a budding asthma exacerbation³¹. Another publication³³ utilized a standalone device that permitted monitoring adherence to therapy nebulization in pre-school children (Supplemental Table 5). A third publication³⁶ applied a standalone device to monitor the physical activity of asthmatic children and their whereabouts during the pandemic restrictions. These standalone devices connected with and transmitted the data to the telemonitoring team via WiFi access (i.e., in the Internet-of-Things manner), once the child returned home.

Interestingly, the latter publication³⁶ was the only one in the final pool of 25 included publications that specifically addressed asthma management during the COVID-19 pandemic. This publication³⁶ used standalone devices for monitoring of physical activity of asthmatic children, as well as for ensuring proper compliance with lockdown regulations. This publication could be viewed as another manifestation of how standalone devices could find their niche in the RPM of asthmatic children. Indeed, development of a multidisciplinary app for pediatric asthma cannot be as instantaneous as utilization of an available standalone device.

Table 1**Descriptive synthesis of included 25 publications**

First author, last name reference number	Publication year	Targeted patient group; targeted Childhood Asthma Control Test (C-ACT), if available	Brief description of mHealth app or device or software or platform, or Internet-of-Things device	Study design	Additional comments
Tony ³⁷	2021	Children and adolescents (8 - 18 years)	The Flo-tone device (Clement Clarke, Harlow, UK), generating a whistle upon the use of an MDI spacer, and Trainhaler app	Randomized controlled intervention study (RCT)	Technically, not a publication on RPM, since self-monitoring was the stated objective of this study. Nonetheless, it was included as one of the examples of potential RPM concerning therapy adherence
Kowatsch ⁴⁵	2021	Children and adolescents (10 - 15 years)	MAX, mHealth app (used by patient/parent or caregiver dyad) and web portal (used by a healthcare professional)	Uncontrolled intervention study	NA
Fedele ⁴⁶	2020	Children and adolescents (13 - 17 years)	Responsive Asthma Care for Teens (ReACT), with modules for passive monitoring of therapy adherence, feedback with fine-tuning of the treatment plan, and promote self-efficacy	Qualitative and/or mixed methods study	NA
Iio ⁴⁷	2020	Children (0 - 12 years), with individual groups for pre-school (0 - 6 years) and school (7 - 12 years) ages	Prototype app, with modules for improved asthma self-control, educational content (tailored to different age groups), and symptom monitoring	Qualitative and/or mixed methods study	NA

First author, last name reference number	Publication year	Targeted patient group; targeted Childhood Asthma Control Test (C-ACT), if available	Brief description of mHealth app or device or software or platform, or Internet-of-Things device	Study design	Additional comments
Hsia ⁴⁸	2020	Children and adolescents (4 - 17 years), C-ACT < 20	ASTHMAXcel Adventures, an mHealth app developed in view of the latest evidence (i.e., evidence-based) by a multidisciplinary team, with patient input, to tailor asthma education to a pediatric patient	App description, combined with an uncontrolled intervention study	NA
van der Kamp ³¹	2020	Children and adolescents (4 - 14 years)	Utilized different Internet-of-Things or mHealth devices: Actigraph WGT3X-BT wireless activity tracker (Actigraph inc. Pensacola, FL, USA), Spirobank advanced II portable spirometer (MIR Inc, Rome, Italy), Cohero Health smart inhalers (Cohero inc. New York, NY, USA), ECG by Emotion Faros 180° (Bittium, Oulu, Finland). No central integration via app or otherwise	Controlled intervention study	NA
Ljungberg ³⁸	2019	Children (≥ 6 years), adolescents, C-ACT score < 20	AsthmaTuner (MediTuner, Stockholm, Sweden), certified cloud computing-based platform with web portal and an mHealth app. This platform aims at promoting asthma self-management and education. The platform is enhanced by computational decision-making support system	Cross-over randomized controlled intervention study (RCT)	NA
Lv ³⁹	2019	Children (6 – 11.9 years), C-ACT score < 20	Prototype app that enables asthma monitoring by a study nurse. The app further features the modules for medication reminders, facilitation of therapy adherence, various alerts, and educational component	Randomized controlled intervention study (RCT)	NA

First author, last name reference number	Publication year	Targeted patient group; targeted Childhood Asthma Control Test (C-ACT), if available	Brief description of mHealth app or device or software or platform, or Internet-of-Things device	Study design	Additional comments
Real ⁴⁰	2019	Children (4 - 11 years), C-ACT score < 20	CHANGE Asthma ("Clinic, Home, And on the Go Education for Asthma") mHealth app, whose primary purposes were asthma knowledge and self-management, with educational components tailored to pediatric audience	Randomized controlled intervention study (RCT)	NA
Kosse ⁴⁹	2019	Adolescents (mean [SD] age: 15.0 [2.0] years)	ADolescent Adherence Patient Tool (ADAPT), based on a validated questionnaires, (Control of Allergic Rhinitis and Asthma Test, CARAT). This mHealth app permits asthma self-monitoring and synchronous monitoring by a healthcare professional, as well as direct communication with the latter (via chat)	Qualitative and/or mixed methods study	NA
Huffaker ³²	2018	Children and adolescents (5 - 18 years)	BCG accelerometer-based passive bed sensor (SCA11H; Murata Technologies, Kyoto, Japan) for nighttime collection of important functional health parameters (e.g., heart rate, heart rate variability, stroke volume, respiration rate, respiration rate variability, and derivatives of these parameters; activity indication)	Uncontrolled intervention study	NA
Grossman ⁵⁰	2017	Children (11 - 16 years)	The mHealth system comprises a Bluetooth-enabled inhaler and a Social Pervasive Visualization (SPV) Asthma app, in conjunction with the cloud server	Development of an mHealth platform, combined with an uncontrolled intervention study	NA
Gahleitner ⁵⁵	2016	Children (5 - 11 years)	SMS text messages	Uncontrolled intervention study	NA

First author, last name reference number	Publication year	Targeted patient group; targeted Childhood Asthma Control Test (C-ACT), if available	Brief description of mHealth app or device or software or platform, or Internet-of-Things device	Study design	Additional comments
Fedele ⁴¹	2021	Adolescents (12 - 15 years), with ACT < 19, and their caregivers	AIM2ACT	Randomized controlled intervention study (RCT)	NA
Makhecha ³⁵	2020	Children and adolescents (6 - 16 years)	Used the following mHealth devices and an app: (1) Hailee sensor (Adherium, New Zealand) for therapy adherence monitoring, (2) Flo-Tone (Clement Clarke, UK) for monitoring of inhalation technique, in conjunction with the Rafi-tone acoustic enabled app (clin-e-cal, UK), (3) INCA sensor (INCA, Ireland) for monitoring of therapy adherence, and (4) R-DOT (Continga, UK) for filming inhaler use via a smartphone	Randomized controlled intervention study (RCT); Qualitative and/or mixed methods study	Some study arms comprised less than 5 patients, therefore, only the devices tested in study arms of > 5 patients were included in the descriptive synthesis
Hollenbach ⁴²	2021	Children and adolescents (8 - 17 years)	Bluetooth-enabled tracker of inhaler actuation (both inhaled corticosteroids and rescue inhaler); BreatheSmart as mHealth app; the CoheroConnect provider portal for synchronous transmitting the collected data to a healthcare practitioner	Randomized controlled intervention study (RCT)	NA
Davis ⁵¹	2021	Adolescents (> 15 years) and young adults (18 - 25 years)	Kiss myAsthma, a crowd-developed asthma self-management mHealth app	Randomized controlled intervention study (RCT); Qualitative and/or mixed methods study	NA

First author, last name reference number	Publication year	Targeted patient group; targeted Childhood Asthma Control Test (C-ACT), if available	Brief description of mHealth app or device or software or platform, or Internet-of-Things device	Study design	Additional comments
Mayoral ⁵²	2021	Children, adolescents (different ages for different stages of the app development), parents, pediatricians	Prototype app and web portal for asthma self-monitoring and synchronous monitoring by a healthcare professional	Development of an mHealth app	This publication describes all steps necessary for development of evidence-based, multidisciplinary, and participatory mHealth app
Chen ³³	2020	Children (6 months - 3 years)	Monitoring of therapy adherence through SmartTrack Device (Shanghai Sonmol Internet Technology Co. Ltd, China). The device is attached to the nebulizer and monitors nebulizer use	Randomized controlled intervention study (RCT)	NA
Cushing ⁵³	2016	Adolescents (11 - 18 years)	Bluetooth-enabled tracker of inhaler actuation; an iPhone app; a server	Uncontrolled intervention study	NA
Kruizinga ⁵⁴	2021	Children (mean [SD] age: 9.3 [2.2] years) with acute exacerbations of asthma	Withings Steel HR Smartwatch (Withings, Issyles-Moulineux, France), Air Next spirometer. Both devices connected via Bluetooth with HealthMate, Thermo, and CHDR MORE apps	Uncontrolled intervention study	NA
Bian ³⁴	2017	Adolescents (14 - 17 years)	Fitbit Charge HR (Fitbit, San Francisco, CA, USA) wristband in combination with various asthma questionnaires	Uncontrolled intervention study	NA

First author, last name reference number	Publication year	Targeted patient group; targeted Childhood Asthma Control Test (C-ACT), if available	Brief description of mHealth app or device or software or platform, or Internet-of-Things device	Study design	Additional comments
Gupta ⁴³	2021	Children and adolescents (4 - 17 years), in dyads with their parents or caregivers	Platform, comprising Propeller Health's (Madison, WI, USA) FDA-approved Bluetooth-enabled inhaler sensors, for both inhaled corticosteroids and short-acting beta-agonists, mHealth app, and a Web portal	Randomized controlled intervention study (RCT)	NA
Kouis ³⁶	2020	Children (6 - 11 years)	The EMBRACE smartwatch (Embrace Tech LTD, Nicosia, Cyprus)	Uncontrolled intervention study	NA
Stukus ⁴⁴	2018	Children (mean [SD] age: 7.84 [5.0] and 6.24 [4.2] years in respectively, intervention and control groups)	AsthmaCare app, for asthma self-management, with rewarding point system for adherence	Randomized controlled intervention study (RCT)	NA

Footnote: ACT, Asthma Control Test; BCG, Ballistocardiographic; ECG, Electrocardiography; HR, Heart Rate; MDI, Metered Dose Inhaler; NA, Not Available; R-DOT, Remote Directly Observed Therapy; RCT, randomized controlled trial; RPM, remote patient monitoring; SD, Standard Deviation; SMS, Short Message Service.

Discussion

The present scoping review aggregated and synthesized the recently published knowledge on mHealth interventions in pediatric asthma. Our searches revealed publications that had addressed several major aspects of mHealth interventions in infants, children and adolescents with asthma. Our overall impression of the included publications was that the quality of mHealth interventions has been improving. This was in contrast to conclusions by the 2017 Editorial⁵⁶ that observed only a moderate quality in most studies on mHealth in asthma. In contrast, among the publications included in this scoping review, 40% of the studies^{35,37-44} (i.e., 10 out of 25) utilized different types of randomized controlled study designs. Furthermore, some randomized trials had similar primary outcomes (e.g., Asthma Control Test score or exacerbation frequency; Supplemental Table 7), potentially enabling a systematic review on this subject. Obviously, some of these studies could reach their primary outcomes, while others could not (Supplemental Table 7), necessitating quantitative synthesis. A further argument supporting systematic review and quantitative synthesis comes from the fact that the great majority of the publications included in our synthesis (23 out of 25 publications, 92%) were published recently, that is, between 2018 and 2021. There have been systematic reviews⁵⁷⁻⁵⁹ on a related subject, which, however, addressed telemedicine in general but not specifically mHealth.

Further supporting the need for synthetic quantitative analyses on mHealth in pediatric asthma is the fact that true savings for the healthcare may be seen only after a certain number of patients utilize a digital health intervention. For example, one publication⁶⁰ estimated such a minimal number at nearly a thousand. None of the studies included in this scoping review recruited a comparable number of patients to achieve such economy of scale.

In addition, the beneficial effects of mHealth interventions can go beyond just an improved control over the disease. These benefits can comprise increased health autonomy of

the patient and enhanced participatory nature of the healthcare⁶¹⁻⁶³. Such qualitative beneficial aspects would require dedicated analysis and synthesis.

Whether focusing on quantitative or qualitative beneficial aspects of mHealth interventions in pediatric asthma, we anticipate that the future systematic review would be dealing with heterogeneity⁶⁴ of the analyzed studies. In this regard, one important source of heterogeneity is patient's age. Illustrating this, the publications included in this scoping review, even those that utilized the randomized controlled study design, demonstrated a high heterogeneity of this important variable. In particular, the patients' age ranged from 8 months to 18 years (^{35,37,38,43,44}; Supplemental Table 7). Another inherently heterogenous variable is the nature of digital health intervention (e.g., an app-enabled intervention vs. an intervention utilizing individual wireless sensors; apps focusing on educational content vs. apps enabling synchronous remote patient monitoring, etc). Most studies presented in this scoping review utilized their own mHealth apps and/or their own set of mHealth sensors. This fact will certainly make the quantitative synthesis more challenging in comparison to the typically well-defined pharmacological interventions. A third important variable, which could inherently be different between the studies, is the specifics of pediatric asthma. Some studies^{38-41,48} in this scoping review addressed labile pediatric asthma or asthma exacerbation, whereas other studies addressed the asthma in general (such as, by providing an age-tailored educational content).

It is worth mentioning that the association between therapy adherence and prevention of asthma exacerbations seems not to be fully established yet. Some publications have not observed such an association^{44,65}. Other publications advocate the opinion that while asthma can exacerbate despite supreme therapy adherence⁶⁶ (potentially, due to the complex biological nature of this disease⁶⁷), poor adherence almost inevitably leads to poor asthma control⁶⁸. In this regard, mHealth technology can enable an instantaneous alert about

dangerous levels of extrinsic factors (e.g., pollen counts⁶⁹, air pollution⁷⁰, or viral factors⁷¹⁻⁷³) that commonly trigger an asthma exacerbation.

While attractive, mHealth monitoring, especially if it is smartphone- and app-based, encounters certain barriers in the pediatric setting. These barriers include access to a smartphone, inability to use the phone at school, and time restraints during the school days⁷⁴. While there are workarounds to compensate for a lack of access to a smartphone (e.g., via the use of webtools⁷⁵), the restrictions of school rules and schedules may be harder to overcome. Nonetheless, the interest of the patients in mHealth as a disease control tool is high⁷⁶. Even adolescent patients, with increased self-awareness, appreciate mHealth interventions, provided that these won't draw unnecessary attention to their asthma⁷⁷. Future studies of mHealth interventions should be able to capitalize on patients' interest and general appreciation of technology by developing evidence-based, participatory and age-tailored app contents for pediatric asthma.

It is also important to consider that some sensors or devices (e.g., a spirometer) require an extensive training to obtain informative and reliable (i.e., high veracity) monitoring data. Examples of programs with such extensive trainings can be found in the literature (e.g., ⁷⁸). An alternative is to develop mHealth devices that will require little or no training of the patient, or those that could be utilized during normal activities (e.g., during the sleep^{32,79}).

Our scoping review has certain limitations. For example, we limited the literature search to published sources in the three major electronic databases. Neither grey literature nor mobile app repositories were consulted as part of this scoping review. Furthermore, we utilized only a limited "snowballing" search (such as to find out details about a particular mHealth app). In addition, our pilot search on mHealth monitoring in pediatric diseases did not include rare pediatric conditions (e.g., pediatric pulmonary fibrosis⁸⁰). Similarly, some systemic conditions with implications on the respiratory system (e.g., pediatric obesity-

related asthma⁸¹) were not explored. Nonetheless, we believe that the evidence synthesis in this scoping review convincingly demonstrated the recent trends towards development of evidence-based, interdisciplinary and participatory mHealth interventions for the pediatric patient.

In conclusion, among pediatric respiratory diseases, and with the sole exception of COVID-19, asthma is the disease with the most publications on mHealth interventions accumulated to date. This scoping review presented descriptive, semi-structured, and structured synthesis of recent published evidence on mHealth monitoring in pediatric asthma. The quality of published studies on this subject has been improving in the recent years, and the employed mHealth apps increasingly become evidence-based, interdisciplinary, and participatory. Future synthetic studies, including systematic reviews and/or meta-analyses, should critically appraise the evidence of the benefits of mHealth technology in the pediatric setting, both for RPM and qualitative aspects of disease management.

Contributions

ND, SZO, LCL, and SK contributed to the development of the concept of this scoping review; ND and SW developed the search strategy; ND conducted the pilot and main literature searches; ND, SZO, WA, LMB, and JK carried out the title and abstract screening; ND carried out the full-text screening and evidence synthesis, and wrote the manuscript; BSM, MD, GR, and CFV provided critical inputs to the concept of this scoping review and the manuscript. All authors approved the final version of the manuscript.

Funding

This study was supported by internal funds of Department of Internal, Respiratory and Critical Care Medicine (Philipps-University of Marburg, Marburg, Germany), German Centre for Lung Research (DZL), The Federal Ministry of Education and Research (BMBF; egePAN Unimed Project, award number 01KX2021), Kriebler Family Foundation, Marcel and Rolande Gosselin Foundation, and Le Réseau de recherche en Santé Respiratoire du Québec (RSRQ). The funders were not involved in the design of this scoping review, and did not participate or influence the execution, analyses, interpretation of the data, the descriptive synthesis, or decisions about manuscript submission.

Conflict of Interest

The authors declare no conflicts of interest.

Journal Pre-proofs

References

1. MacGeorge CA, Andrews AL, King KL. Telehealth for Pediatric Asthma. In: Ford DW, Valenta SR, eds. *Telemedicine: Overview and Application in Pulmonary, Critical Care, and Sleep Medicine (Respiratory Medicine)*. 1st ed: Humana Press; 2021:129-141.
2. Mechanic OJ, Persaud Y, Kimball AB. *Telehealth Systems*. StatPearls. Treasure Island (FL): StatPearls Publishing LLC; 2021.
3. Portnoy JM, Wu AC. Is telemedicine as effective as usual care? *J Allergy Clin Immunol Pract* 2019;7:217-218.
4. Bender BG. Technology interventions for nonadherence: new approaches to an old problem. *J Allergy Clin Immunol Pract* 2018;6:794-800.
5. Ferrante G, Licari A, Marseglia GL, et al. Digital health interventions in children with asthma. *Clin Exp Allergy* 2021;51:212-220.
6. Lechtzin N, Mayer-Hamblett N, West NE, et al. Home monitoring of patients with cystic fibrosis to identify and treat acute pulmonary exacerbations. eICE study results. *Am J Respir Crit Care Med* 2017;196:1144-1151.
7. Ramaswamy VV, Bandyopadhyay T, Nanda D, et al. Assessment of postnatal corticosteroids for the prevention of bronchopulmonary dysplasia in preterm neonates: a systematic review and network meta-analysis. *JAMA Pediatr* 2021;175:e206826.
8. Special Ovid filters for MEDLINE: children - focussed. (<https://ospguides.ovid.com/OSPguides/medline.htm>).
9. Dauletbaev N, Kuhn S, Holtz S, et al. Implementation and use of mHealth home telemonitoring in adults with acute COVID-19 infection: a scoping review protocol. *BMJ Open* 2021;11:e053819.
10. *Cochrane handbook for systematic reviews of interventions version 6.2 (updated February 2021)*: Cochrane, 2021, 2021.
11. Richardson WS, Wilson MC, Nishikawa J, et al. The well-built clinical question: a key to evidence-based decisions. *ACP J Club* 1995;123:A12-3.

12. Bramer WM, Rethlefsen ML, Kleijnen J, et al. Optimal database combinations for literature searches in systematic reviews: a prospective exploratory study. *Syst Rev* 2017;6:245.
13. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. *Int J Soc Res Methodol* 2005;8:19–32.
14. Colquhoun HL, Levac D, O'Brien KK, et al. Scoping reviews: time for clarity in definition, methods, and reporting. *J Clin Epidemiol* 2014;67:1291-4.
15. Levac D, Colquhoun H, O'Brien KK. Scoping studies: advancing the methodology. *Implement Sci* 2010;5:69.
16. Lockwood C, Tricco AC. Preparing scoping reviews for publication using methodological guides and reporting standards. *Nurs Health Sci* 2020;22:1-4.
17. Tricco AC, Lillie E, Zarin W, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. *Ann Intern Med* 2018;169:467-473.
18. Peters MD, Godfrey CM, Khalil H, et al. Guidance for conducting systematic scoping reviews. *Int J Evid Based Healthc* 2015;13:141-6.
19. Bramer WM, Giustini D, de Jonge GB, et al. De-duplication of database search results for systematic reviews in EndNote. *J Med Libr Assoc* 2016;104:240-3.
20. Ouzzani M, Hammady H, Fedorowicz Z, et al. Rayyan-a web and mobile app for systematic reviews. *Syst Rev* 2016;5:210.
21. Team TE. EndNote. EndNote X20 ed. Philadelphia, PA, USA: Clarivate; 2021.
22. Jeppson H, Hofmann H, Cook D. ggmosaic: mosaic plots in the 'ggplot2' framework. R package version 0.3.3. 2021.
23. Wickham H. ggplot2. Elegant graphics for data analysis. New York, NY: Springer-Verlag, 2016.
24. Wickham H, Henry L, Pedersen TL, et al. svglite: an 'SVG' graphics device. R package version 2.0.0. <https://CRAN.R-project.org/package=svglite2021>.

25. Neuwirth E. RColorBrewer: colorBrewer palettes. R package version 1.1-2. <https://CRAN.R-project.org/package=RColorBrewer2014>.
26. R Core Team (2020). R: a language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. <https://www.R-project.org/>.
27. Team R. RStudio: integrated development environment for R. <http://www.rstudio.com/2021>.
28. Adobe Inc. Adobe Illustrator. 2021.
29. De Vera K, Challa P, Liu RH, et al. Virtual primary care implementation during COVID-19 in high-income countries: a scoping review. *Telemed J E Health* 2021.
30. Hoque MR, Rahman MS, Nipa NJ, et al. Mobile health interventions in developing countries: A systematic review. *Health Informatics J* 2020;26:2792-2810.
31. van der Kamp MR, Klaver EC, Thio BJ, et al. WEARCON: wearable home monitoring in children with asthma reveals a strong association with hospital based assessment of asthma control. *BMC Medical Inform Decis Mak* 2020;20:192.
32. Huffaker MF, Carchia M, Harris BU, et al. Passive nocturnal physiologic monitoring enables early detection of exacerbations in children with asthma. A proof-of-concept study. *Am J Respir Crit Care Med* 2018;198:320-328.
33. Chen J, Xu J, Zhao L, et al. The effect of electronic monitoring combined with weekly feedback and reminders on adherence to inhaled corticosteroids in infants and younger children with asthma: a randomized controlled trial. *Allergy Asthma Clin Immunol* 2020;16:68.
34. Bian J, Guo Y, Xie MJ, et al. Exploring the association between self-reported asthma impact and Fitbit-derived sleep quality and physical activity measures in adolescents. *JMIR mHealth uHealth* 2017;5:e105.
35. Makhecha S, Jamalzadeh A, Chan A, et al. Novel electronic adherence monitoring devices in children with asthma: a mixed-methods study. *BMJ Open Respir Res* 2020;7:e000589.
36. Kouis P, Michanikou A, Anagnostopoulou P, et al. Use of wearable sensors to assess compliance of asthmatic children in response to lockdown measures for the COVID-19 epidemic. *Sci Rep* 2021;11:5895.

37. Tony SM, Abdelrahman MA, Osama H, et al. Advanced counselling using training device and smartphone application on inhalation technique from metered-dose inhaler with spacer equipped with different interfaces in asthmatic children. *Int J Clin Pract* 2021;75:e14413.
38. Ljungberg H, Carleborg A, Gerber H, et al. Clinical effect on uncontrolled asthma using a novel digital automated self-management solution: a physician-blinded randomised controlled crossover trial. *Eur Respir J* 2019;54.
39. Lv S, Ye X, Wang Z, et al. A randomized controlled trial of a mobile application-assisted nurse-led model used to improve treatment outcomes in children with asthma. *J Adv Nurs* 2019;75:3058-3067.
40. Real FJ, Beck AF, DeBlasio D, et al. Dose matters: a smartphone application to improve asthma control among patients at an urban pediatric primary care clinic. *Games Health J* 2019;8:357-365.
41. Fedele DA, Voorhees S, Janicke DM, et al. Using mobile Health to improve asthma self-Management in early Adolescence: a pilot randomized controlled trial. *J Adolesc Health* 2021;69:1032-1040.
42. Hollenbach J, Simoneau T, Sun Y, et al. Design, methods, and baseline characteristics of a pilot, randomized, controlled trial of the effects of an electronic monitoring device on medication adherence in children with asthma. *Contemp Clin Trials Commun* 2021;21:100706.
43. Gupta RS, Fierstein JL, Boon KL, et al. Sensor-based electronic monitoring for asthma: a randomized controlled trial. *Pediatrics* 2021;147:e20201330.
44. Stukus DR, Farooqui N, Strothman K, et al. Real-world evaluation of a mobile health application in children with asthma. *Ann Allergy Asthma Immunol* 2018;120:395-400.e391.
45. Kowatsch T, Schachner T, Harperink S, et al. Conversational agents as mediating social actors in chronic disease management involving health care professionals, patients, and family members: multisite single-arm feasibility study. *JMIR* 2021;23:e25060.
46. Fedele DA, Cushing CC, Koskela-Staples N, et al. Adaptive mobile Health intervention for adolescents with asthma: iterative user-centered development. *JMIR mHealth uHealth* 2020;8:e18400.

47. Iio M, Miyaji Y, Yamamoto-Hanada K, et al. Beneficial features of a mHealth asthma app for children and caregivers: qualitative study. *JMIR mHealth uHealth* 2020;8:e18506.
48. Hsia BC, Singh AK, Njeze O, et al. Developing and evaluating ASTHMAXcel adventures: a novel gamified mobile application for pediatric patients with asthma. *Ann Allergy Asthma Immunol* 2020;125:581-588.
49. Kosse RC, Bouvy ML, Belitser SV, et al. Effective engagement of adolescent asthma patients with mobile health-supporting medication adherence. *JMIR mHealth uHealth* 2019;7:e12411.
50. Grossman B, Conner S, Mosnaim G, et al. Application of Human Augmentics: a persuasive asthma inhaler. *J Biomed Inform* 2017;67:51-58.
51. Davis SR, Smith LD, Peters D, et al. A consumer designed smartphone app for young people with asthma: pilot of engagement and acceptability. *J Asthma* 2021;58:253-261.
52. Mayoral K, Ferrer M, Garin O, et al. Smartphone app for monitoring asthma in children and adolescents. *Qual Life Res* 2021;30:3127-3144.
53. Cushing A, Manice MP, Ting A, et al. Feasibility of a novel mHealth management system to capture and improve medication adherence among adolescents with asthma. *Patient Prefer Adherence* 2016;10:2271-2275.
54. Kruizinga MD, Moll A, Zhuparris A, et al. Postdischarge recovery after acute pediatric lung disease can be quantified with digital biomarkers. *Respiration* 2021.
55. Gahleitner F, Legg J, Holland E, et al. The validity and acceptability of a text-based monitoring system for pediatric asthma studies. *Pediatr Pulmonol* 2016;51:5-12.
56. Bousquet J, Chavannes NH, Guldemond N, et al. Realising the potential of mHealth to improve asthma and allergy care: how to shape the future. *Eur Respir J* 2017;49:1700447.
57. Kim CH, Lieng MK, Rylee TL, et al. School-based telemedicine interventions for asthma: a systematic review. *Acad Pediatr* 2020;20:893-901.
58. Culmer N, Smith T, Stager C, et al. Telemedical asthma education and health care outcomes for school-age children: a systematic review. *J Allergy Clin Immunol Pract* 2020;8:1908-1918.

59. Jeminiwa R, Hohmann L, Qian J, et al. Impact of eHealth on medication adherence among patients with asthma: a systematic review and meta-analysis. *Respir Med* 2019;149:59-68.
60. Wagner NM, Ritzwoller DP, Raebel MA, et al. Can digital communication technology reduce health system personnel time? An evaluation of personnel requirements and costs in a randomized controlled trial. *Transl Behav Med* 2021;11:863-869.
61. Rowland SP, Fitzgerald JE, Holme T, et al. What is the clinical value of mHealth for patients? *NPJ Digit Med* 2020;3:4.
62. National Institute for Health and Care Excellence. Evidence standards framework for digital health technologies. <https://www.nice.org.uk/about/what-we-do/our-programmes/evidence-standards-framework-for-digital-health-technologies>. Last updated 23 April 2021.
63. Schmietow B, Marckmann G. Mobile health ethics and the expanding role of autonomy. *Med Health Care Philos* 2019;22:623-630.
64. Meta-analyses: what is heterogeneity? *BMJ* 2015;350:h1435.
65. Papi A, Ryan D, Soriano JB, et al. Relationship of inhaled corticosteroid adherence to asthma exacerbations in patients with moderate-to-severe asthma. *J Allergy Clin Immunol Pract* 2018;6:1989-1998.e3.
66. De Keyser HH, Szeffler S. Asthma attacks in children are always preceded by poor asthma control: myth or maxim? *Breathe (Sheff)* 2020;16:200169.
67. Stempel H, Federico MJ, Szeffler SJ. Applying a biopsychosocial model to inner city asthma: Recent approaches to address pediatric asthma health disparities. *Paediatr Respir Rev* 2019;32:10-15.
68. Liptzin DR, Szeffler SJ. Evolution of asthma self-management programs in adolescents: from the crisis plan to Facebook. *J Pediatr* 2016;179:19-23.
69. Jones PJ, Koolhof IS, Wheeler AJ, et al. Characterising non-linear associations between airborne pollen counts and respiratory symptoms from the AirRater smartphone app in Tasmania, Australia: A case time series approach. *Environ Res* 2021;200:111484.

70. Chan YY, Wang P, Rogers L, et al. The Asthma Mobile Health Study, a large-scale clinical observational study using ResearchKit. *Nat Biotechnol* 2017;35:354-362.
71. Saglani S, McKenzie SA. Environmental factors relevant to difficult asthma. *Paediatr Respir Rev* 2002;3:248-54.
72. Graham LM. All I need is the air that I breath: outdoor air quality and asthma. *Paediatr Respir Rev* 2004;5 Suppl A:S59-64.
73. Pike KC, Akhbari M, Kneale D, et al. Interventions for autumn exacerbations of asthma in children. *Paediatr Respir Rev* 2018;27:37-39.
74. Schneider T, Baum L, Amy A, et al. I have most of my asthma under control and I know how my asthma acts: Users' perceptions of asthma self-management mobile app tailored for adolescents. *Health Informatics J* 2020;26:342-353.
75. Nkoy FL, Fassel BA, Wilkins VL, et al. Ambulatory management of childhood asthma using a novel self-management application. *Pediatrics* 2019;143.
76. Jácome C, Almeida R, Pereira AM, et al. Asthma app use and interest among patients with asthma: a multicenter study. *J Investig Allergol Clin Immunol* 2020;30:137-140.
77. Howard S, Lang A, Sharples S, et al. See I told you I was taking it! - Attitudes of adolescents with asthma towards a device monitoring their inhaler use: implications for future design. *Appl Ergon* 2017;58:224-237.
78. Richardson CH, Orr NJ, Ollosson SL, et al. Initiating home spirometry for children during the COVID-19 pandemic - a practical guide. *Paediatr Respir Rev* 2021;Feb 19;S1526-0542(21)00004-X:Online ahead of print.
79. Gracia-Tabuenca J, Seppa VP, Jauhiainen M, et al. Tidal breathing flow profiles during sleep in wheezing children measured by impedance pneumography. *Respir Physiol Neurobiol* 2020;271:103312.
80. Deterding RR, DeBoer EM, Cidon MJ, et al. Approaching clinical trials in childhood interstitial lung disease and pediatric pulmonary fibrosis. *Am J Respir Crit Care Med* 2019;200:1219-1227.
81. Dooley AA, Pillai DK. Paediatric obesity-related asthma: disease burden and effects on pulmonary physiology. *Paediatr Respir Rev* 2021;37:15-17.