

The Design, Development, and Utilization of breathe: Patient-Centered Mobile Health System That Supports Asthma Self-Management

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Table of Contents

Original Manuscript	



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Plinio Pelegrini Morita^{2,3,4}, BSc, MSc, PhD; Melanie S Yeung⁴, MHSc; Madonna Ferrone⁵, RRT, CRE; Ann K Taite^{6,7}; Carole Madeley⁸, RRT, CRE, MAppSC; Andrea Stevens Lavigne⁸, MBA; Teresa To^{9,10}, PhD; M Diane Lougheed^{6,7}, MD, MSc; Samir Gupta^{11,12}, MD, MSc; Andrew G Day^{6,13}, MSc; Joseph A Cafazzo^{4,14,15}, PEng, PhD; Christopher Licskai^{16,17}, MD

² School of Public Health and Health Systems, Faculty of Applied Health Sciences, University of Waterloo, Waterloo, Canada.

- ⁴ Centre for Global eHealth Innovation, Techna Institute, University Health Network, Toronto, Canada.
- ⁵ Hotel Dieu Grace Healthcare, , , Windsor, Canada.

- ⁷ Kingston General Hospital Research Institute, Kingston Health Sciences Center, , Kingston, Canada.
- ⁸ Ontario Lung Association, , , Toronto, Canada.
- ⁹ The Hospital for Sick Children, , , Toronto, Canada.
- ¹⁰ Dalla Lana School of Public Health, , University of Toronto, Toronto, Canada.
- ¹¹ Division of Respirology, Department of Medicine, University of Toronto, Toronto, Canada.
- ¹² Li Ka Shing Knowledge Institute, St. Michael's Hospital, , Toronto, Canada.
- ¹³ Kingston General Hospital, , , Kingston, Canada.
- ¹⁴ Institute of Health Policy, Management, and Evaluation, , University of Toronto, Toronto, Canada
- ¹⁵ Institute of Biomaterials and Biomedical Engineering, , University of Toronto, Toronto, Canada.
- ¹⁶ Western University, , , London, Canada.
- ¹⁷ London Health Sciences, Victoria Hospital, , London, Canada.

Corresponding Author:

Plinio Pelegrini Morita, BSc, MSc, PhD School of Public Health and Health Systems Faculty of Applied Health Sciences University of Waterloo 200 University Avenue West Waterloo Canada Phone: 1 8884567 ext 31567 Fax: 1 519-746-6776 Email: plinio.morita@uwaterloo.ca

Abstract

Background: Uncontrolled asthma poses substantial negative personal and health system impacts. Web-based technologies, including smartphones, are novel means to enable evidence-based care and improve patient outcomes.

Objective: The aim of this study was to design, develop, and assess the utilization of an asthma collaborative self-management (CSM) platform (breathe) using content based on international evidence-based clinical guidelines.

Methods: We designed and developed breathe as a Web-based mobile health (mHealth) platform accessible on smartphones, tablets, or desktop with user-centered design methods and International Organization for Standardization–certified quality development processes. Moreover, breathe was envisioned as a multifunctional, CSM mHealth platform, with content based on international clinical practice guidelines and compliant with national privacy and security specifications. The system enabled CSM (patient, provider, and breathe) and self-monitoring of asthma patients through (1) assessment of asthma control, (2) real-time access to a dynamic asthma action plan, (3) access to real-time environmental conditions, and (4) risk-reduction messaging.

¹ School of Public Health and Health Systems, Faculty of Applied Health Sciences, University of Waterloo, Waterloo, Canada.

³ Institute of Health Policy, Management, and Evaluation, University of Toronto, , Toronto, Canada.

⁶ Queens University, , , Kingston, Canada.

The data collection protocol collected user data for 12 months, with clinic visits at baseline and 6 and 12 months. Utilization outcomes included user interactions with the platform, user impressions, self-reported medication use, asthma symptom profile, reported peak flow measurement, and the delivery and impact of email reminders.

Results: We enrolled 138 patients with a mean age of 45.3 years to receive the breathe intervention. Majority were female (100/138, 72.5%), had a smartphone (92/138, 66.7%), and had a mean Asthma Control Test score of 18.3 (SD 4.9). A majority reported that breathe helped in the management of their asthma. Moreover, breathe scored 71.1 (SD 18.9) on the System Usability Scale. Overall, 123 patients had complete usage analytics datasets. The platform sent 7.96 reminder emails per patient per week (pppw), patients accessed breathe 3.08 times, journaled symptoms 2.56 times, reported medication usage 0.30 times, and reported peak flow measurements 0.92 times pppw. Furthermore, breathe calculated patients' action plan zone of control 2.72 times pppw, with patients being in the green (well-controlled) zone in 47.71% (8300/17,396) of the total calculations. Usage analysis showed that 67.5% (83/123) of the participants used the app at week 4 and only 57.7% (71/123) by week 45. Physician visits, email reminders, and aged 50 years and above were associated with higher utilization.

Conclusions: Individuals with asthma reported good usability and high satisfaction levels, reacted to breathe notifications, and had confidence in the platform's assessment of asthma control. Strong utilization was seen at the intervention's initiation, followed by a rapid reduction in use. Patient reminders, physician visits, and being aged 50 years and above were associated with higher utilization.

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Original Manuscript

Original Paper

The design, development, and utilization of *breathe*: A patientcentered mHealth system that supports asthma self-management

Plinio P. Morita PhD, PEng^{1,2,3}, Melanie Yeung MHSc², Madonna Ferrone⁴, Ann Taite⁵, Carole Madeley RRT, CRE, MAppSC ⁶, Andrea Stevens Lavigne MBA ⁶, Teresa To PhD^{7,8}, M. Diane Lougheed MD, MSc, FRCP(c)^{5,9}, Samir Gupta MD, MSc^{10,11}, Andrew G. Day MSc^{5,9}, Joseph A. Cafazzo PhD, PEng^{2,3,12}, and

Christopher Licskai MD, FRCP(c)^{13,14}

¹School of Public Health and Health Systems, University of Waterloo, Waterloo, ON, Canada.

²Centre for Global eHealth Innovation, Techna Institute, University Health Network, Toronto, ON, Canada.

³Institute of Health Policy, Management, and Evaluation, University of Toronto, Toronto, ON, Canada ⁴Hotel Dieu Grace Healthcare, Windsor, ON, Canada.

⁵Queens University, Kingston, ON, Canada.

⁶Ontario Lung Association, Toronto, ON, Canada.

⁷The Hospital for Sick Children, Toronto, ON, Canada.

⁸Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada.

plinio.morita@uwaterloo.ca

⁹Kingston General Hospital, Kingston, ON, Canada.

¹⁰University of Toronto, Toronto, ON, Canada.

¹¹St. Michael's Hospital, Toronto, ON, Canada.

¹²Institute of Biomaterials and Biomedical Engineering, University of Toronto, Toronto, ON, Canada.¹³Western University, London, Canada. ¹⁴London Health Sciences, Victoria Hospital, London, Canada.

CONTACT INFORMATION

Plinio Pelegrini Morita

(corresponding author)

MAILING ADDRESS

200 University Avenue West

Waterloo, Ontario, Canada

N2L 3G1

Original Paper

The design, development, and utilization of breathe: A patientcentered mHealth system that supports asthma self-management

Abstract

Background

Uncontrolled asthma poses substantial negative personal and health system impacts. Web-based technologies, including smartphones, are novel means to enable evidence-based care and improve patient outcomes.

Objective

To design, develop, and assess the utilization of an asthma collaborative self-management platform (breathe) using content based on international evidence-based clinical guidelines.

Methods

We designed and developed breathe as a web-based mHealth platform accessible on smartphones, tablets, or desktop with user-centered design methods, and ISO-certified quality development processes. breathe was envisioned as a multifunctional, collaborative self-management mHealth platform, with content based on international clinical practice guidelines, and compliant with national privacy and security specifications. The system enabled collaborative self-management (patient, provider and breathe) and self-monitoring of asthma patients through: (1) assessment of asthma control, (2) real-time access to a dynamic asthma action plan, (3) access to real-time environmental conditions, and (4) risk-reduction messaging. The data collection protocol collected user data for 12 months, with clinic visits at baseline, six, and 12 months. Utilization outcomes included user interactions with the platform, user impressions, self-reported medication use, asthma symptom profile, reported peak flow measurement, the delivery and impact of e-mail reminders.

Results

We enrolled 138 patients to receive the breathe intervention with a mean age of 45.3 years. A majority were female (72.5%), had a smartphone (66.7%), and had a mean Asthma Control Test score of 18.3 (Standard deviation (SD) ±4.9). A majority reported that breathe helped in the management of their asthma. *breathe* scored 71.1 ± 18.9 on the System Usability Scale. 123 patients had complete usage analytics datasets. The platform sent 7.96 reminder e-mails per patient per week (pppw), patients accessed *breathe* 3.08, journaled symptoms 2.56, reported medication usage 0.30, and reported peak flow measurements 0.92 times pppw. *breathe* calculated patients' action plan zone of control 2.72 times pppw, with patients being in the green (well-controlled) zone in 48% of the total calculations. Usage analysis showed that 60% of the participants used the app at week 4 and only 30% by week 45. Physician visits, e-mail reminders, and age \geq 50 were associated with higher utilization.

Conclusions

Individuals with asthma reported good usability and high satisfaction levels, reacted to breather notifications, and had confidence in the platform's assessment of asthma control. Strong utilization was seen at the intervention's initiation, followed by a rapid reduction in use. Patient reminders, physician visits, and age >50 years were associated with higher utilization.

Keywords: asthma; self-management; data-driven design; user centered design; collaborative care; mhealth; mobile health; user evaluation; usability.

Introduction

Asthma is a common chronic disease that poses a serious global health problem. In Canada alone, asthma affects 10.8% of Canadians [1]. Globally, the Global Burden of Diseases, Injuries, and Risk Factors Study estimated that 339 million people suffer from asthma, where asthma is the most common chronic disease among children [2,3]. Fifty percent of patients with asthma are uncontrolled, leading to substantial personal and health system impacts [4–8]. In Canada, there are 150,000 emergency room visits and 60,000 hospitalizations triggered annually by asthma [9].

Collaborative self-management (CSM) is defined as "a system of coordinated healthcare interventions and communications for populations with conditions in which self-care efforts are significant" [10]. National and international guidelines, and systematic review evidence, recommend CSM, including a written asthma action plan, patient education, and regular clinical review [11–14]. CSM has been shown to substantially improve important patient and health system challenges, by reducing hospitalizations, emergency room visits, unscheduled visits to a doctor, absenteeism, nocturnal asthma symptoms, and significantly improving quality of life [14]. Moreover, a majority of patients prefer an active or collaborative role in their asthma management, particularly in the context of an asthma exacerbation [15,16]. Despite this strong evidence, these patient preferences, and consistent recommendations in international guidelines [11–13], CSM continues to be available to only a minority of patients (2-11%) [5,17]. For these reasons, asthma is a chronic disease well suited for an examination of the transformative promise of smartphone mobile health apps (mHealth apps) in support of collaborative self-management.

Smartphones have become ubiquitous and mHealth apps have the potential to transform elements of chronic disease management [18,19]. mHealth apps offer new opportunities for access to care, disease specific education, monitoring and disease management, personalized goal setting, adherence reminders, and communication. Requisite to the success of smartphone apps as new tools in the management of chronic diseases are a commitment to, and evidence of, user-centered design, development, and evaluation to ensure privacy, efficacy and safety. Beyond the requirements of good design and development, the central question of whether patient facing asthma app that support CSM are efficacious, remains unanswered.

We sought to design and develop a multifunctional, collaborative self-management mobile health (mHealth) platform, based on clinical content from international evidence-based guidelines, following a user-centered design process, and to then evaluate its utilization to inform iterative product improvement.

Methods

The *breathe* development program was structured in two main phases: (1) the design and development process for building the *breathe* mHealth platform including architecture, design, platform content, functional elements, user experience and ultilization (University Health Network REB 12-0102-AE and 12-0102-AE_Amendment); and (2) an evaluation of the patient outcomes by randomized controlled trial (RCT) (Western University HSREB 102842, Queens University HSREB 6007261, clinicaltrials.gov NCT01964469) and by a population-based cohort study. The utilization data reported in this manuscript is derived from the intervention (*breathe*) arm of the RCT. The RCT comparing conventional best practice plus the breathe platform to conventional best practice has been completed and the main results are published in abstract form [20]. The focus of this manuscript is to share the design and development of the breathe platform, breathe utilization, and the user experience. The results of the RCT will be published in an upcoming manuscript.

Design and Development of *breathe*

breathe Development Specifications

Specifications were developed collaboratively with Canada Health Infoway and included: (1) a usercentered web-based asthma self-management platform available on any web-enabled device including mobile phone browsers and standard web browsers on laptop, desktop, tablet to ensure equitable access of the application; (2) patient access to their personal health information and electronic health records through connectivity with TELUS health space®, which was a localized version of Microsoft Health Vault® (web-based personal health record developed by Microsoft); (3) alignment with national and provincial clinical and electronic health (eHealth) priorities, as per the Canadian Thoracic Society (CTS), Ontario Lung Association (OLA), eHealth Ontario (a provincial agency tasked with the implementation of the Ontario's public Electronic Health Record System), and the Ontario Ministry of Health and Long-Term Care; and (4) scalability to the provincial level and ability to be leveraged by other jurisdictions within Canada. Evidence-based best practices from the CTS Asthma Guidelines [11] and the Global Initiative for Asthma Guidelines [12] guided clinical content development.

The Development Team

breathe was developed by the Centre for Global eHealth Innovation at the University Health Network in collaboration with clinicians, researchers, and scientists from Western University, Queen's University, Hospital for Sick Children, and the University of Toronto. The Centre is certified under ISO 13485, an international quality management system, to ensure the safety and quality of innovations. The mHealth platform development was guided by a 16-member interdisciplinary steering committee including asthma expert respirologists, certified asthma educators, population health scientists, knowledge translation experts, and eHealth experts. These experts were informed by four working groups: benefits evaluation, technical, consumer engagement (patients with asthma), and clinical. Working groups were comprised of a few members of the steering committee, along with additional individuals who contributed specific expertise such as consumers (patients with asthma), IT professionals, and clinicians.

The Design Process

breathe (Figure 1) was designed using user-centered design (UCD) methods [18,21,22], ensuring that the input and requirements of final users of the technology (patients, caregivers, physicians) were included in the design process. The iterative UCD process included 11 interviews, and five usability testing and cognitive walkthrough cycles [21,22]. The semi-structured interviews were conducted with representative end-users (adults who have asthma) to test assumptions related to the use of a

monitoring system as an intervention to enhance healthy self-management behaviours and diseaserelated decision-making. These interviews employed a qualitative, ethnographic approach. Information was gathered and organized by extracting common themes identified by the participants. This initial user research provided the necessary evidence for the conceptualization and initial prototypes of the intervention which was subsequently used in usability testing and walkthroughs. This UCD process explored the intuitiveness of the application, identified user preferences and expectations. Multiple cycles of cognitive walkthroughs and usability testing allowed the breathe team to improve the design based on user feedback and observed issues, focusing on the needs of the platform's final users and avoiding the paradoxes of expertise [21]. The final design of the platform ensured that functionality was aligned with clinical needs and patient preferences and limitations.

Evaluation of the Patient Experience, Platform Usability, and Utilization

Patient Recruitment

The utilization data reported in this manuscript is derived from the intervention (*breathe*) arm of the RCT designed to evaluate patient outcomes [20]. Participants were recruited from six primary care and two specialty asthma clinics in Ontario, Canada. A convenience sample of patients self-identified after viewing posters in the clinic or were invited to participate by clinic staff. The participating clinics were geographically distributed – e.g. north, east, southwest and central Ontario – with a range of urban and rural communities. All participants randomized to *breathe* had a baseline onboarding clinic visit where they were provided with *breathe* accounts, received a brief orientation, and completed a six and 12-month follow-up visit.



Figure 1: Examples of the various features designed for breathe. Thre first row provides examples of the main home screen, the current zone of control that the patient is in, and environment information. The second row provides examples of the jornaling feature where users can report simptoms, medication intake, and review entries. The last row has examples of the desktop version of breathe, where the zone of control review and action plans are displayed. These are not actual plans, medications, or patient data, but instead, prototypes of the breathe interface.

Platform Usability, Consumer Satisfaction and Confidence

Two customized consumer satisfaction questionnaires and the standardized System Usability Scale (SUS) [23] were administered at six and 12 months post-enrollment.

Measuring Platform Utilization

breathe was designed to collect usage data (in-app analytics) to enable data-driven design and evaluation. Information flowing through the *breathe* data server was logged and used as part of this evaluation. The *breathe* server tracked: medications prescribed to patients, self-reported medication use, peak flow actual compared to personal best or normal, action plan zone of control, general access, and e-mail notifications sent by the system. Each entry to the database was identified with a unique user ID and time stamped to enable further analysis.

Statisical Methods

The statistics reported in this manuscript are primarily descriptive. We reported counts and percentages for categorical variables as well as means and standard deviations for continuous variables or pseudo-continuous variables derived as means of multiple ordinal questionnaire items. We used the Wilcoxon Rank-Sum test to compare the number of weeks with at least one login during the 52 weeks between groups defined by: age, college education, smartphone use and baseline ACT score. Age groups were defined as <50 versus \geq 50 because it approximately divided the population in half.

Results

breathe: mHealth Platform Architecture

breathe is a web-based mHealth platform that utilizes HTML5 and responsive design allowing a single version of the platform to be accessible on any device (smartphone, tablet or personal computer) (Figure 2). *breathe* interfaces with TELUS health space, ® where it receives up-to-date medication and peak flow ranges from the integration of clinical data repositories (electronic medical records). As well, *breathe* retrieves real-time environmental conditions directly from Environment Canada, which include current and forecasted weather conditions, in addition to the Air Quality Health Index (AQHI) with relevant risk-reduction health messaging from Health Canada. The AQHI is a simple 1-10 scale designed to help individuals understand air quality, the impact of poor air quality on their health, and what actions to take to minimize health risks [24].

breathe: Functionality

The healthcare provider developed an 'asthma app prescription' in a collaborative triad of patient, provider, and app. The healthcare provider determined the patient's asthma medications, their individualized action plan by zone, and peak flow ranges for control zone calculations (if applicable). The *breathe* platform did not advise on the selection of medications and did not create the action plan. This remained a physician responsibility. Integrating with TELUS Health Space® offered patients the option to share *breathe* data with family members and/or other healthcare providers, which could be accomplished through the Health Space® online profile. The *breathe* features can be seen in Figure 1. Each of these features was designed to engage users and to collect relevant data to support self-management, as described below:



Figure 2: Architecture of the *breathe* platform (OLA – Ontario Lung Association, AQHI – Air Quality Health Index, CDR – Clinical Data Repository). In cases where peak flow was part of the action plan, peak flow ranges were entered by the provider. Patients were responsible for entering peak flow measurements.

Journal – The Journal feature allows patients to track daily symptoms, record reliever and controller medication usage, and to log peak flow measurements. The historical review feature allows users to look back at previous journal entries and peak flow values entered.

Your Zone – The journal entries feed an integrated asthma control algorithm at the breathe server, based on the CTS Asthma Guidelines [11,12], that analyses patient inputs and immediately advises the patient of their current zone of control: (1) green zone – in control, (2) yellow zone – uncontrolled, or (3) red zone – dangerously uncontrolled. The zone of control assessment is paired with the actionable recommendations from patients' personalized asthma action plan. The zone of control is dynamic, immediately updated with any new journal entries and re-sets after the action plan has been executed, ensuring a tailored and customized intervention to the patient [25]. Patients were notified of changes on their zone of control thorugh the app dashboard and in the Your Zone section.

Trends – Data visualization and analysis of several trends, including identified triggers, control zone, and peak flow values was available to users. An example of the usefulness of this feature is that trigger frequency reported back to patients may enable patient insights into which triggers to avoid in the future.

Environment – This feature provides real-time current and forecast of location-specific (based on users' input about their location) environmental conditions including temperature, humidex, weather forecast and the Air Quality Health Index with specific poor air quality risk-reduction health messaging.

Account – This feature includes a variety of options including changing default (7pm EST) time and email address to receive emailed medication adherence reminders, and setting a location for location-specific environmental information. E-mail adherence reminders were automatically generated based on predefined rule-based logic including a welcome e-mail, "check-in" e-mails for users not accessing the platform within seven days, and daily adherence reminders for controller medications. There was no limit to the daily reminder emails, however we designed the system to try to mitigate fatigue by creating approximately 30 different body messages that were randomly emailed to the user.

A demonstration of how the *breathe* platform works can be found in the Canada Health Infoway website, with a detailed description of functionalities and platform capabilities

(https://www.infoway-inforoute.ca/en/component/edocman/resources/videos/innovation-patient-access/1908-breathe-a-canadian-asthma-app).

breathe: Patient Population

We recruited 344 patients into the RCT between October 31, 2012 - March 31, 2014, of whom 171 were allocated to the *breathe* intervention arm. Consent was withdrawn (n=10) or we were unable to find the patient to consent for data transfer (n=23) in 33 patients, leaving 138 patient that could be used in this analysis. Complete platform utilization data was available in 123/138 (89.1%) participants, and 12 month usability and satisfaction questionnaires were available for 119/138 (86.2%). The majority of the 138 patients were women (100, 72.5%), mean age 45.3±15.8 years, and 134 (97.1%) were Caucasian. Of these participants, 92 (66.7%) had a smartphone and the majority (82.6%) reported being "comfortable" or "very comfortable" using it. Patients recruited had a mean Asthma Control Test score of 18.3 ± 4.9 , suggesting well to somewhat well-controlled baseline asthma [26].

breathe Usability, Patient Satisfaction and Confidence (12 month data)

Usability was evaluated by the System Usability Scale (SUS), a validated composite measure which is scored from 0 to 100, with higher scores representing greater usability (Table 1). The *breathe* system scored at 71.1±19.9 at 12 months indicating good usability, as defined by Bangor et al. [27]. The mean of 7 ease of use questions scaled from 1-very difficult to 5-very easy was 4.1±0.9. A majority found *breathe* components useful and were satisfied with the design. (Table 1)

Satisfaction was evaluated using five-point Likert scale responses, 1-strongly disagree, 3-don't know/neutral, 5-strongly agree. Sixty-four percent of patients agreed or strongly agreed that the *breathe* application was helpful in the management of their asthma. Sixty-five percent of patient were confident that *breathe* was correct when it presented the patient's asthma action plan zone of control. Fifty percent of participants agreed or strongly agreed that they would continue to use the application after the study if it remained available. (Table 1).

Actual breathe Usage

The 123 patients in the intervention arm with utilization data accessed *breathe* 19,678 times (3.08 times pppw - per patient per week), reported symptoms in their diary 16,357 times (2.56 times pppw), reported medication use 1,922 times (combined use of reliever and controller; 0.30 times pppw), and reported peak flow measurements 5864 times (0.92 times pppw). Total counts can include patients accessing the platform multiple times in the same day.

breathe calculated patients' action plan zone of control 17,396 times (2.72 times pppw). Patients were most often in the green zone of control (48% of calculations), followed by yellow zone (24%) and red zone (6%). In 22% of the calculations, breathe did not have enough information to return a zone of control back to the patient based on the programmed algorithm in the *breathe* platform (Figure 3).

breathe sent 50,939 e-mails (7.96 times pppw) to remind participants to take their controller medications or to return to the platform after seven-days of no usage. *breathe* did not log email responses potentially generated by the users.

Tracking patient log-ins to the platform demonstrated a fall in use within the first 4 weeks of initiation and thereafter a standard decay in usage (Figure 4), whereby 60% of the participants used the platform weekly initially and only 30% used the platform in week 45. Figure 4 presents our patient log-in data along with Eysenbach's attrition curve [28].

Further utilization analysis demonstrated patterns of use that related to patient behaviour, *breathe* functionality, or the interaction of both. <u>*Time of Day:*</u> Analyzing logins by time of day revealed two periods of increased utilization (Figure 6). First, there was higher platform use between 5:00 am and

10:00 am, which corresponds to the time of the day when most patients are waking up and preparing for their day. Second, there was a dramatic spike in utilization just after 7:00 pm, the default time of day when the *breathe* system e-mail reminders were automatically sent by the application server. This finding was sustained each month over the 12 months of the study (Figure 7). <u>Symptom Reporting:</u> Evaluation of the Journal functional element within the platform revealed about twice as many reports of good days (a day without symptoms) compared to days with symptoms (Figure 8), which aligns with our expectations for well-controlled asthma. <u>Scheduled Physician Visits:</u> Finally, based on controller medication recording, there was an increase in platform utilization in weeks 26 and 52, corresponding to scheduled follow-up visits. (Figure 5).

The post-hoc analysis of patient factors that may have influenced utilization including age, education level, smartphone use, and asthma control are presented in Table 2. Only age (\geq 50 years) was associated with higher utilization.

Table 1: Usability questionnaire.

SATISFACTION The <i>breathe</i> application that was provided to me by the clinic is helpful in the management of my asthma Disagree or strongly disagree 21/116 (18%) Agree or strongly agree 74/116 (64%)	
The <i>breathe</i> application that was provided to me by the clinic is helpful in the management of my asthma Disagree or strongly disagree 21/116 (18%) Agree or strongly agree 74/116 (64%)	
Disagree or strongly disagree 21/116 (18%) Agree or strongly agree 74/116 (64%)	
Agree or strongly agree 74/116 (64%)	
I would continue to use the Breathe application if it were available to me after the study.	
Disagree or strongly disagree 30/117 (26%)	
Agree or strongly agree 58/117 (50%)	
I was confident that when the Breathe application was correct when it assessed my asthma zone of control. Disagree or strongly disagree 16/115 (14%)	
Agree or strongly agree 75/115 (65%)	
SYSTEM USABILITY SCALE (Score range 0-100)71.1±19.9	
EVALUATION OF SPECIFIC FUNCTIONAL COMPONENTS OF	
(on a scale of 1-very difficult, 3-don't know/neutral, 5-very easy)	
Ease of use: Mean of 7 questions (n=119) 4.1±0.9	
Usefulness: Mean of 12 questions (n=118) 3.6±0.9	
Design of components: Mean of 12 questions reported (n=119)4.2±0.7	

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Table 2: Utilization by Patient Characteristics

Group		Num	ber of weeks with at low week	east one login during 52
Age		n	Mean (SD)	p-value*
	<50	73	18.2 (17.9)	<.001
	≥50	49	30.1 (18.2)	
College Educated				
	No	34	21.6 (20.8)	.420
	Yes	88	23.5 (18.2)	
Use Smartphone				
	No	40	23.8 (19.7)	.656
	Yes	82	22.6 (18.6)	
Baseline ACT Score				
	<20	65	22.7 (18.7)	.969
	≥20	57	23.2 (19.2)	·

* p-value from Wilcoxon Rank-sum test; ACT = Asthma Control Test



Figure 3: Panel A: Total calculations of zone of control calculations per month of the intervention calculated from enrollment Panel B: Percentage of zone of control calculations per month of the intervention.

https://preprints.jmir.org/preprint/10956

Page 18/30

ure 4: Attrition in *breathe* use throughout the 12-months of the study, with Eysenbach's attrition curve plotted as a reference [28].







Figure 5: Self-reported controller medication use showing the effect of clinic visits (surveillance effect) on self-reporting behaviour (clinic visits were scheduled at 6 and 12 months from the beginning of the intervention).



Figure 6: App use tracked by number of logins by time of day exploring the effectiveness of reminders. Note that automatic app reminders are default to send around 7:00pm.



Figure 7: Sustained effect of email reminders on app use over the 12 months of intervention.



Figure 8: Panel A: Number of reported "good days" (no symptoms) and symptom episodes since enrolment. Panel B: Percentage of reported "good days" (no symptoms) and symptom episodes since enrolment.

Discussion

breathe in Context

Despite a decade of mHealth app development, there remains a limited body of evidence demonstrating improved health outcomes with apps [29–31]. Currently, there are three published

randomized controlled trials evaluating patient-facing, multi-functional asthma apps developed to support collaborative self-management. Liu and colleagues [32] showed increased quality of life, increased use of controller medications, improved lung function (8%), and decreased emergency service use. Merchant and colleagues [33] demonstrated the effectiveness of the Propeller Health Asthma Platform at reducing the use of short-acting β -agonist (SABA) by 0.41 activations per day (vs. 0.31 control), increasing the number of SABA-free days by 21% (vs. 17% control). Conversely, Ryan and colleagues [34] found that mobile phone-based monitoring did not improve asthma control or patient self-efficacy compared to a paper based monitoring system. Our experience with an asthma app prototype in a recent pilot study revealed a high level of satisfaction with the app (80% of users viewed the app positively, with the majority wishing to continue using the app after the study), regular participation in self-management, and improvements in asthma-related quality of life [35]. The central question of whether mHealth platforms that support asthma management such as *breathe* are efficacious remains unanswered. We assert that good platform design is a pre-condition to posing and answering this question.

Usability, Satisfaction, Confidence

Patients had a high level of satisfaction with the individual design components of *breathe*. They rated *breathe* usability as good on the validated System Usability Scale and high on standard Likert scales. A central function of the breathe platform was to present patients with a real-time dynamic action plan based on their symptoms and/or peak flow entries. The application effectively returned a dynamic zone of control calculation back to patients. *breathe* patients were confident that the calculated assessment was accurate. By objectively measuring control, *breathe* resolves a long-standing barrier to action plan utilization in the community, the barrier of inaccurate control assessment by patients. Patients that over-estimate control will not activate their action plan as prescribed and thus not experience the substantial associated clinical benefits [5–8].

The *breathe* mHealth platform was an important facilitator of teachable moments and acted as an uni-directional communication bridge between providers and patients in the community through the delivery of 50,939 reminder e-mail messages and communicating asthma control and care recommendations through the platform 19,678 times. An examination of utilization suggests that patients responded to these notifications by accessing the app after the reception of these emails, and patient questionnaires indicate that they had confidence in the care and control recommendations.

App Usage

The goal of user-centred design is to create and sustain a certain level of adherence to the platform, as adherence is a pre-requisite to positive behavioral change and improved health outcomes. Despite good ratings for ease of use and a high degree of satisfaction with the *breathe* system, actual platform use declined substantially over time, which in general aligns with reviews describing attrition rates in eHealth deployments [28,36–38]. In his seminal viewpoint paper "The Law of Attrition" Eysenbach argues the need for a "science of attrition" and recommends that usage metrics be measured, analysed and discussed to identify reasons for attrition [28]. The *breathe* utilization curve differs substantially from Eysenbach specifically related to a dramatic fall in utilization in the first four to six weeks. We evaluated factors associated with increased or decreased platform utilization.

We considered that decreased utilization (attrition) in this study may have been related to population and design characteristics including, technology savviness, patients with relatively good disease control, infrequent physician monitoring, or because patients achieved their expected outcomes (or the correct "digital dose" of the intervention).

Technology savviness: All participants had access to either a smartphone or a computer. Although, 61.8% of our population had a smartphone and reported being comfortable or very comfortable with

its use, one-third did not have a smartphone and therefore accessed the platform by laptop, desktop, or tablet. We considered that the non-smartphone subset may have been less technology savy contributing to the decline in utilization and particularly may have contributed to the sharp decline in the first 4 weeks. However, our post-hoc analysis did not find an association between utilization and having a smartphone.

<u>Age and Education Level</u>: We considered that younger age and higher education level may have impacted utilization. We did not find an association between utilization and education level. In a post-hoc analysis we were able to demonstrate that age ≥ 50 was significantly associated with higher utilization. Whereas general app use is normally greater in a younger population, we speculate that our participants over the age of 50 with a chronic disease may have had a higher level of concern about their chronic disease and potentially find more value in health-related applications than a younger population. We observed that increased utilization was associated with time of day, anticipated physician visits, and e-mail reminders.

<u>Good Disease Control</u>: Patients in this study had relatively well controlled asthma as indicated by high baseline asthma control tests and a high percentage of Good Days when compared to Episode Days. We did not have a specific engagement strategy to motivate patients to return to the platform when they were feeling well. Failure to engage the users in moments of disease stability has been described by other authors as a critical factor affecting attrition, across diseases [39–41]. However, our post-hoc analysis did identify an association between utilization and high vs. low scores on the asthma control test.

Physician Monitoring: In this study, patients were evaluated by a physician only twice after enrolment. Infrequent monitoring may have increased the attrition rate. Increased *breathe* platform utilization was associated with upcoming six and 12-month clinic appointments. An increase in eHealth utilization in response to anticipated clinical review has been described by Mohr et al. as supportive accountability [42] and by others [43,44] as a strong factor influencing sustained adherence. The surveillance effect has a direct influence on how engaged patients are with the platform and how much they adhere to the intervention. Along the same lines, eHealth platforms that provide some level of feedback and peer support appear to demonstrate better adherence rates [45]. The need for regular clinical review to motivate platform adherence aligns with the literature supporting written asthma action plans, where efficacy requires regular clinical review [14]. The finding related to increased medication reporting at six and 12 months also suggests that for most of the year, medication use was under-reported. Self-reported medication use may under-report actual use [46]. New Bluetooth enabled smart inhalers that automatically log medication use [47] will be considered in the future development of *breathe*.

<u>Patients achieved their expected outcomes</u>: Patients were satisfied with breathe and 64% agreed or strongly agreed that "the breathe application is helpful in the management of my asthma. Thus, it is possible that after an interval, having achieved their personal goals, that patients no longer felt a need to use the platform.

<u>*E-mail Reminders*</u>: Increased *breathe* platform utilization was associated in time with e-mail adherence reminders. Others have identified reminders as powerful design features to increase adherence and engagement with eHealth platforms [48], to alert participants of important events [19,49], or to alert them of aspects of the treatment they have missed [45]. Although alarm fatigue has been described in long-term interventions, wherein reminders lose their impact over time [50,51], we demonstrated a sustained effect of reminders over the 12 months.

<u>Usage Analysis Summary</u>: Patterns of use analysis identified physician visits and e-mail reminders as strongly associated with utilization. A post-hoc analysis identified age \geq 50 as significantly associated with higher utilization.

Limitations

The population studied was a convenience sample from primary and specialty clinics with a

dedicated asthma program and at the time on enrolment, patients had relatively good asthma control. As such, patients' evaluation of the app and their utilization patterns may not be representative of the general asthma population. Since this project was completed, native applications have largely supplanted web-browser based apps such as *breathe*. The improved performance of native app platforms may positively impact utilization and reduce attrition.

Conclusions

We followed user centered design methods to develop *breathe*, a multifunctional asthma collaborative self-management platform with content based on international clinical practice guidelines, compliant with national privacy and security specifications, to support patients as active participants in chronic disease management at home, work, and in the community. *breathe* enabled self-management and self-monitoring of asthma patients through assessment of asthma control, real-time access to a dynamic action plan, environmental conditions display, and air quality risk-reduction messaging. Individuals with asthma reported good usability and high satisfaction levels, and had confidence in the platform's assessment of asthma control. We embedded in-platform analytics, evaluated utilization, and examined the utilization patterns in the context of known patient characteristics. We related increased utilization to physician monitoring, e-mail reminders, and age \geq 50 years. Looking to the future, embedded app analytics combined with data-driven design, will enable real-time evaluation of mHealth platforms, enabling innovators to execute design improvements during the deployment of the technology.

Lessons Learned / Future Considerations

As we iterate development of the *breathe* platform based on lessons learned, we will seek to: (1) leverage the surveillance effect of in-platform or in-person patient-physician contact to support utilization; (2) create a specific strategy to engage patients when they are feeling well and/or to reengage as they become unwell; (3) create a strategy to support adherence specifically for asthma patients age <50 years (4) integrate automated logging technology (smart/connected inhalers) to capture actual medication utilization; (5) leverage the sustained impact of patient reminders on utilization; (6) create a more interactive experience to enhance platform use; (7) utilize embedded app analytics that provide continuous evaluation of usage to enable the execution of design improvements during platform deployment; and (8) develop the next version of the breathe platform with a native iOS or Android app.

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Conflicts of Interest

Dr. Morita reports grants from NSERC, CIHR, MITACS, and OCE during the conduct of this study. Dr. Morita is a member of advisory boards at Roche Canada. The work developed in this paper was not funded by any of these companies. Ms. Yeung reports grants from Canada Health Infoway during the conduct of the study. Madonna Ferrone has nothing to disclose. Ann Taite has nothing to disclose. Carole Madeley has nothing to disclose. Ms. Stevens Lavigne reports grants from Canada Health Infoway, from Ontario Ministry of Health and Long-term Care, during the conduct of the study. Dr. To reports grants from Ontario Ministry of Health and Long-term Care, grants from Ontario Ministry of the Environment and Climate Change, grants from CIHR (Canadian Institute for Health Research), grants from Health Canada, grants from CRRN (Canadian Respiratory Research Network), outside the submitted work. Dr. Lougheed received honoraria from the Astra Zeneca Severe Asthma PRECISION Program; and funds paid directly to Queen's University for participation in multi-centre clinical trials from Astra Zeneca, GlaxoSmithKlein, Hoffman LaRoche Ltd., Janssen, and Novartis; grants paid directly to Queen's University from the Ontario Lung Association, the Government of Ontario's Innovation Fund, Allergen NCE, Canadian Institutes of Health Research; and personal fees from Public Service Occupational Health Program Regions and Programs Bureau Health Canada / Government of Canada for preparation of a report on pollution exposure at post and the role of surveillance spirometry, outside the submitted work. Dr. Gupta has nothing to disclose. Mr. Day reports that his employer was paid from grants from Canada Health Infoway and The Lung Association to cost recover his time spent on this project. Dr. Cafazzo reports grants from Canada Health Infoway during the conduct of the study. Dr. Licskai declare that he is a member of advisory boards or equivalent in commercial organizations as AstraZeneca, Novartis, Boehringer Ingelheim, and GlaxoSmithKline; as well as receiving funding from commercial organizations as AstraZeneca, Novartis, Boehringer Ingelheim, Pfizer, and Bayer. The work developed in this projects was not funded by any of these companies.

References

- 1. Public Health Agency of Canada. Report from the Canadian Chronic Disease Surveillance System: Asthma and Chronic Obstructive Pulmonary Disease (COPD) in Canada, 2018 [Internet]. 2018. Available from: http://healthycanadians.gc.ca/publications/diseasesconditions-maladies-affections/mental-illness-2015-maladies-mentales/index-eng.php
- 2. World Health Organization (WHO). Asthma Fact Sheet [Internet]. 2017. Available from: http://www.who.int/mediacentre/factsheets/fs307/en/
- 3. GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990-2016: A systematic analysis for the Global Burden of Disease Study 2016. Lancet 2017;390(10100):1211–1259. PMID:28919117
- Chapman KR, Boulet LP, Rea RM, Franssen E. Suboptimal asthma control: Prevalence, detection and consequences in general practice. Eur Respir J 2008;31(2):320–5. PMID:17959642
- 5. FitzGerald JM, Boulet LP, Mclvor RA, Zimmerman S, Chapman KR. Asthma control in Canada remains suboptimal: The reality of asthma control (TRAC) study. Can Respir J 2006;13(5):253–259. PMID:16896426
- Lai CKW, De Guia TS, Kim YY, Kuo SH, Mukhopadhyay A, Soriano JB, Trung PL, Zhong NS, Zainudin N, Zainudin BMZ. Asthma control in the Asia-Pacific region: The asthma insights and reality in Asia-Pacific study. J Allergy Clin Immunol 2003;111(2):263–268. PMID:12589343
- 7. Rabe KF, Adachi M, Lai CKW, Soriano JB, Vermeire PA, Weiss KB, Weiss ST. Worldwide severity and control of asthma in children and adults: The global asthma insights and reality surveys. J Allergy Clin Immunol 2004;114(1):40–47. PMID:15241342
- 8. Sekerel BE, Gemicioglu B, Soriano JB. Asthma insights and reality in Turkey (AIRET) study. Respir Med 2006;100(10):1850–4. PMID:16564685
- 9. Public Health Agency of Canada. Life and Breath: Respiratory Disease in Canada [Internet]. 2007. Available from: http://www.phac-aspc.gc.ca/publicat/2007/lbrdc-vsmrc/index-eng.php
- 10. Windham BG, Bennett RG, Gottlieb S. Care management interventions for older patients with congestive heart failure. Am J Manag Care 2003;9(6):447–459.
- 11. Lougheed MD, Lemiere C, Ducharme FM, Licskai C, Dell SD, Rowe BH, FitzGerald M, Leigh R, Watson W, Boulet LP. Canadian Thoracic Society 2012 guideline update: Diagnosis and management of asthma in preschoolers, children and adults. Can Respir J 2012;19(2):127–164. PMID:22536582
- 12. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. 2017.
- Lougheed MD, Lemiere C, Dell SD, Ducharme FM, FitzGerald JM, Leigh R, Licskai C, Rowe BH, Bowie D, Becker A, Boulet L-P. Canadian Thoracic Society Asthma Management Continuum – 2010 Consensus Summary for children six years of age and over, and adults. Can Respir J 2010;17(1):15–24.
- 14. Gibson PG, Powell H, Wilson A, Abramson MJ, Haywood P, Bauman A, Hensley MJ, Walters

EH, Roberts JJ. Self-management education and regular practitioner review for adults with asthma. Cochrane Database Syst Rev [Internet] 2002;(3). PMID:12535399

- 15. Caress a-L, Beaver K, Luker K, Campbell M, Woodcock a. Involvement in treatment decisions: what do adults with asthma want and what do they get? Results of a cross sectional survey. Thorax 2005;60(3):199–205. PMID:15741435
- 16. Adams RJ, Smith BJ, Ruffin RE. Patient preferences for autonomy in decision making in asthma management. Thorax 2001;56:126–132. PMID:11209101
- Tsuyuki RT, Sin DD, Sharpe HM, Cowie RL, Nilsson C, Paul Man SF. Management of Asthma Among Community-Based Primary Care Physicians. J Asthma 2005;42(3):163–7. [doi: 10.1081/JAS-200054615]
- Mccurdie T, Taneva S, Casselman M, Yeung M, Mcdaniel C, Ho W, Cafazzo J. mHealth Consumer Apps: The Case for User-Centered Design. Biomed Instrum Technol Mob Heal 2012;46(s2):49–56.
- 19. Goyal S, Morita PP, Lewis GF, Yu C, Seto E, Cafazzo JA. The systematic design of a behavioural mobile health application for the self-management of type 2 diabetes. Can J Diabetes [Internet] Elsevier Inc.; 2016;40(1):95–104. PMID:26455762
- 20. Licskai C, Ferrone M, Taite A, Madeley C, Lavigne AS, To T, Yeung M, Cafazzo JA, Day AG, Lougheed D. The Evaluation of Breathe A Patient Mobile Health (mHealth) App for Adult Asthma. Am J Respir Crit Care Med 2016;193:a1084.
- 21. Morita PP, Cafazzo JA. Challenges and Paradoxes of Human Factors in Health Technology Design. JMIR J Hum Factors 2015;3(1):1–7. [doi: 10.2196/humanfactors.4653]
- Johnson CM, Johnson TR, Zhang J. A user-centered framework for redesigning health care interfaces. J Biomed Inform [Internet] 2005 Feb [cited 2014 Jul 15];38(1):75–87. PMID:15694887
- Lewis JR, Sauro J. The factor structure of the system usability scale. Lect Notes Comput Sci (including Subser Lect Notes Artif Intell Lect Notes Bioinformatics) 2009. p. 94–103. PMID:23941937
- 24. Government of Canada. Air Quality Health Index [Internet]. 2016. Available from: https://www.canada.ca/en/environment-climate-change/services/air-quality-health-index/about.html
- 25. Oinas-Kukkonen H, Harjumaa M. Persuasive systems design: Key issues, process model, and system features. Commun Assoc Inf Syst 2009;24(1):28.
- 26. Nathan RA, Sorkness CA, Kosinski M, Schatz M, Li JT, Marcus P, Murray JJ, Pendergraft TB. Development of the Asthma Control Test: A survey for assessing asthma control. J Allergy Clin Immunol 2004;113(1):59–65. PMID:14713908
- 27. Bangor A, Kortum PT, Miller JT. An empirical evaluation of the system usability scale. Int J Hum Comput Interact 2008;24(6):574–594. PMID:33402155
- 28. Eysenbach G. The law of attrition. J Med Internet Res 2005;7(1):1–9. PMID:15829473
- 29. Wicks P, Chiauzzi E. 'Trust but verify' five approaches to ensure safe medical apps. BMC Med [Internet] BMC Medicine; 2015;13(1):205. PMID:26404791
- 30. Pham Q, Wiljer D, Cafazzo JA. Beyond the Randomized Controlled Trial: A Review of Alternatives in mHealth Clinical Trial Methods. JMIR mHealth uHealth [Internet]

2016;4(3):e107. PMID:27613084

- 31. Huckvale K, Morrison C, Ouyang J, Ghaghda A, Car J. The evolution of mobile apps for asthma: an updated systematic assessment of content and tools. BMC Med [Internet] 2015;13(1):58. PMID:25857569
- 32. Liu WT, Huang CD, Wang CH, Lee KY, Lin SM, Kuo HP. A mobile telephone-based interactive self-care system improves asthma control. Eur Respir J 2011;37(2):310–317. PMID:20562122
- 33. Merchant RK, Inamdar R, Quade RC. Effectiveness of Population Health Management Using the Propeller Health Asthma Platform: A Randomized Clinical Trial. J Allergy Clin Immunol Pract [Internet] Elsevier Inc; 2016;4(3):455–463. PMID:26778246
- 34. Ryan D, Price D, Musgrave SD, Malhotra S, Lee AJ, Ayansina D, Sheikh A, Tarassenko L, Pagliari C, Pinnock H. Clinical and cost effectiveness of mobile phone supported self monitoring of asthma: multicentre randomised controlled trial. Bmj [Internet] 2012;344(mar23 1):e1756-e1756. PMID:22446569
- 35. Licskai CJ, Sands TW, Ferrone M. Development and pilot testing of a mobile health solution for asthma self-management: Asthma action plan smartphone application pilot study. Can Respir J 2013;20(4):301–306. PMID:23936890
- 36. Christensen H, Mackinnon A. The law of attrition revisited. J Med Internet Res 2006;8(3):e20. PMID:15829473
- 37. Christensen H, Griffiths KM, Farrer L. Adherence in internet interventions for anxiety and depression. J Med Internet Res 2009;11(2):1–16. PMID:19403466
- Eysenbach G. The Law of Attrition Revisited Author's Reply. J Med Internet Res [Internet] 2006;8(3):313-e21. [doi: 10.1503/cmaj.050698]
- 39. Kelders SM, Kok RN, Ossebaard HC, Van Gemert-Pijnen JEWC. Persuasive system design does matter: A systematic review of adherence to web-based interventions. J Med Internet Res 2012;14(6):1–24. PMID:23151820
- 40. Brouwer W, Kroeze W, Crutzen R, De Nooijer J, De Vries NK, Brug J, Oenema A. Which intervention characteristics are related to more exposure to internet-delivered healthy lifestyle promotion interventions? A systematic review. J Med Internet Res 2011;13(1):1–19. PMID:21212045
- 41. Schubart JR, Stuckey H., Ganeshamoorthy A, Sciamanna CN. Chronic Health Conditions and Internet Behavioral Interventions User Engagement. Wolters Kluwer Heal 2011;29(2):9–20. [doi: 10.1097/NCN.0b013e3182155274]
- 42. Mohr DC, Cuijpers P, Lehman K. Supportive accountability: A model for providing human support to enhance adherence to eHealth interventions. J Med Internet Res 2011;13(1). PMID:21393123
- 43. Cramer JA, Scheyer RD, Mattson RH. Compliance declines between clinic visits. 2013;
- 44. Osterberg L, Blaschke T, Koop C Everett. Adherence to Medication. N Engl J Med 2005;353:487–497. PMID:2182868
- 45. Logan A g., Irvine MJ, McIsaac WJ, Tisler A, Rossos PG, Easty A, Feig DS, Cafazzo JA. Effect of home blood pressure telemonitoring with self-care support on uncontrolled systolic hypertension in diabetics. Hypertension 2012;60(1):51–7.

- 46. Voils CI, Hoyle RH, Thorpe CT, MacIejewski ML, Yancy WS. Improving the measurement of self-reported medication nonadherence. J Clin Epidemiol [Internet] Elsevier Inc; 2011;64(3):250–254. PMID:21194887
- 47. Burgess SW, Wilson SSI, Cooper DM, Sly PD, Devadason SG. In vitro evaluation of an asthma dosing device: The smart-inhaler. Respir Med 2006;100(5):841–845. PMID:16216485
- 48. Fry JP, Neff RA. Periodic prompts and reminders in health promotion and health behavior interventions: Systematic review. J Med Internet Res 2009;11(2):1–15. PMID:19632970
- 49. Goyal S, Morita PP, Picton P, Seto E, Zbib A, Cafazzo JA. Uptake of a Consumer-Focused mHealth Application for the Assessment and Prevention of Heart Disease: The <30 Days Study. JMIR mHealth uHealth [Internet] 2016;4(1):e32. PMID:27012937
- 50. Cvach M. Monitor alarm fatigue: an integrative review. Biomed Instrum Technol 2012;46(4):268–77.
- 51. Denkinger CM, Grenier J, Stratis AK, Akkihal A, Pant-Pai N, Pai M. Mobile health to improve tuberculosis care and control: A call worth making. Int J Tuberc Lung Dis 2013;17(6):719–727. PMID:23541232